Comparison of Factors Associated With Occludable Angle Between American Caucasians and Ethnic Chinese

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Purpose. To determine if factors associated with gonioscopy-determined occludable angle among American Caucasians are similar to those found in ethnic Chinese.

Methods. This is a prospective cross-sectional study with 120 American Caucasian, 116 American Chinese, and 116 mainland Chinese subjects. All three groups were matched for sex and age (40–80 years). Gonioscopy was performed for each subject (occludable angles = posterior trabecular meshwork not visible for $\geq$2 quadrants). Anterior segment optical coherence tomography and customized software was used to measure anterior segment biometry and iris parameters, including anterior chamber depth/width (ACD, ACW), lens vault (LV), and iris thickness/area/curvature.

Results. In both Chinese and Caucasians, eyes with occludable angles had smaller ACD and ACW, and larger LV and iris curvature than eyes with open angles (all $P < 0.005$). Chinese eyes had smaller ACD and ACW than Caucasian eyes (both $P < 0.01$) in the occludable angle cohort. Iris characteristics did not differ significantly between Chinese and Caucasians in the occludable angle cohort. Based on multivariate logistic regression, gonioscopy-determined occludable angle was significantly associated with LV, iris area, and sex (all $P < 0.03$) in Chinese; and with LV, ACD, iris thickness, age, and sex (all $P < 0.04$) in Caucasians.

Conclusions. Several factors associated with occludable angle differed between Caucasians and Chinese, suggesting potentially different mechanisms in occludable angle development in the two racial groups. This is the first study to demonstrate that lens vault is an important anterior segment optical coherence tomography parameter in the screening for angle closure in Caucasians. In addition, iris thickness was a significant predictor for occludable angles in Caucasians but was not in ethnic Chinese.

Keywords: occludable angle, gonioscopy, ASOCT, angle closure glaucoma, multiethnicity

Worldwide, glaucoma has been identified as a major cause of ocular morbidity and bilateral vision loss, second only to cataract.[1] It is projected that more than 79 million people will have either open-angle glaucoma (OAG) or angle-closure glaucoma (ACG) by 2020, and approximately 25% of all these cases will be the angle-closure form.[1] Although less prevalent than those with OAG, patients with ACG on average suffer considerably greater bilateral vision loss than those with the open-angle form.[2] It is also well known that women are more likely to be affected by glaucomatous disease, especially ACG, for which they comprise nearly 70%.[1] East and Southeast Asian individuals have been consistently found to have much higher prevalence of primary angle-closure glaucoma (PACG) based on population studies.[3] However, the prevalence of angle closure in Caucasians has recently been shown in a meta-analysis to be higher than we previously thought.[4]

Previous studies conducted primarily in Asian subjects have found certain ocular anatomical features, such as shallower anterior chamber, shorter axial length, and smaller corneal diameter to be risk factors for primary angle closure (PAC).[5–9] More recent studies have identified additional anterior chamber anatomical parameters, including anterior segment optical coherence tomography (ASOCT)-measured anterior chamber width (ACW), lens vault (LV), and iris profile parameters, such as iris thickness (IT) and curvature (Icurv), to be useful measurements for angle closure screening.[10–14] Moreover, anterior chamber area (ACA), anterior chamber volume (ACV), and LV were found to be the three most significant determinants of angle width according to a population-based study of Singaporean Chinese.[14]

Our previous studies that compared anterior segment anatomical features across racial groups suggested that Chinese tend to have thicker peripheral irides,[15] smaller ACW and ACD,[16,17] and smaller ACA/ACV[18] than that of age- and sex-matched American Caucasians after controlling for confounders such as refractive status and integral globe size. In this study, we sought to conduct interethnic comparisons of demographic and anatomical factors (including ASOCT-measured anterior chamber biometry and iris characteristics) associated with occludable angles, between American Caucasian and ethnic Chinese. Knowing the factors associated with occludable angle in the two racial groups can provide a better understanding of the potentially different mechanisms of angle closure development in the two ethnic groups. This may in turn guide

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TABLE 1. Demographic and Ocular Characteristics of Subjects in the Open-Angle and Occludable-Angle Groups by Ethnicity

	Open	Occludable	*P* Value
American Caucasian	$n = 96$	$n = 24$	
Age, y	58.7 ± 11.3	65.8 ± 11.4	**0.009**
Sex, f	42.1%	58.3%	0.12*
AL, mm	24.5 ± 1.7	23.5 ± 1.2	**0.003**
SE, diopter	−1.36 ± 5.2	−0.04 ± 1.8	**0.03**
LT, mm	4.39 ± 0.3	4.87 ± 0.4	**<0.0001**
American Chinese	$n = 80$	$n = 36$	
Age, y	56.6 ± 10.4	66.6 ± 12.2	**<0.0001**
Sex, f	44.3%	66.7%	**0.02***
AL, mm	24.8 ± 2.03	23.3 ± 1.1	**<0.0001**
SE, diopter	*-2.64 ± 3.2*	*0.39 ± 1.5*	***<0.0001***
LT, mm	4.39 ± 0.34	4.80 ± 0.6	**0.0003**
Mainland Chinese	$n = 86$	$n = 30$	
Age, y	59.1 ± 11.9	61.63 ± 11.51	0.31
Sex, f	45.9%	70%	**0.02***
AL, mm	23.6 ± 0.9	22.8 ± 0.6	**<0.0001**
SE, diopter	−0.44 ± 2.3	1.04 ± 1.2	**<0.0001**
LT, mm	4.66 ± 0.4	4.88 ± 0.2	**0.0003**

Statistical analyses performed were Student's *t*-tests for continuous data and Fisher's exact (*) test for proportional data. Data are expressed as mean value ± SD. Numbers in bold and italic style denote the comparison is statistically significant ($P < 0.05$).

TABLE 2. Comparison of Anterior Chamber Biometry and Iris Characteristics Between Open-Angle and Occludable-Angle Cohorts Among American Caucasians and Ethnic Chinese

	Open	Occludable	*P* Value
American Caucasian	$n = 96$	$n = 24$	
ACD, mm	3.04 ± 0.33	2.48 ± 0.28	***<0.0001***
ACW, mm	12.31 ± 0.44	12.06 ± 0.34	***0.005***
LV, mm	294.01 ± 249.7	696.60 ± 203.9	***<0.0001***
IT750, mm	0.40 ± 0.07	0.44 ± 0.07	***0.04***
Iarea, mm²	1.53 ± 0.25	1.56 ± 0.27	0.56
Icurv, mm	0.21 ± 0.14	0.32 ± 0.12	***0.0002***
PD, mm	4.35 ± 0.87	4.14 ± 0.98	0.34
Ethnic Chinese	$n = 166$	$n = 66$	
ACD, mm	2.77 ± 0.30	2.31 ± 0.24	***<0.0001***
ACW, mm	11.74 ± 0.42	11.52 ± 0.38	***0.0002***
LV, mm	343.35 ± 254.8	734.51 ± 198.9	***<0.0001***
IT750, mm	0.44 ± 0.06	0.46 ± 0.08	0.07
Iarea, mm²	1.50 ± 0.21	1.58 ± 0.25	***0.03***
Icurv, mm	0.23 ± 0.14	0.35 ± 0.09	***<0.0001***
PD, mm	4.59 ± 0.82	4.27 ± 0.84	***0.01***

Data are expressed as mean value ± SD; *P* values are by pairwise *t*-comparisons. Numbers in bold and italic style denote the comparison is statistically significant. All measurements were obtained by ASOCT. Ethnic Chinese = combined American Chinese and mainland Chinese subjects.

clinicians in the management and screening for PAC and PACG in these different racial groups.

METHODS

Subjects

Institutional review board/ethics committee approval was obtained from the University of California, San Francisco (UCSF) and Zhongshan Ophthalmic Center in Guangzhou. This study adhered to the tenets of the Declaration of Helsinki and the Health Insurance Portability and Accountability Act. Written informed consent was obtained for all individuals who enrolled in this study.

The study sample was composed of three cohorts of American Caucasians, American Chinese, and mainland Chinese residing in Guangzhou, China. The subjects were enrolled over the period from May 2008 through December 2010. Each cohort was designed to have approximately 120 subjects, including 30 people (15 male and 15 female) in each of the fifth to eighth decades of life. All subjects in San Francisco were consecutively recruited from the general ophthalmology clinics at UCSF. Participants at the Guangzhou site were drawn from an ongoing population-based study. At our Guangzhou study site, every 1 of 10 subjects (who met the inclusion/exclusion criteria of the present study) in the ongoing population study were selected to constitute our mainland subgroup in this study, and the recruitment rate was greater than 90%. Inclusion criteria included age between 40 and 80 years, self-reported Caucasian or Chinese ancestry for both parents (the term "Caucasian" for the purpose of this study, included only European-derived white people), and willingness and ability to participate in all study activities. Exclusion criteria included bilateral pseudophakia or aphakia or any prior intraocular surgery or laser treatment with the potential to alter the natural anatomy of the anterior segment, corneal or conjunctival abnormalities that preclude an adequate view of the anterior chamber on the ASOCT images, use of any glaucoma medications, active ocular infection where contact eye examinations might be contraindicated, and high refractive error defined as spherical equivalent (SE) less than −8 or greater than +4 diopter. Each subject underwent gonioscopy, where occludable angles were defined as posterior trabecular meshwork not visible for two or more quadrants on non-indentation gonioscopy.[19,20] Gonioscopy was performed by a single trained glaucoma specialist (SCL) for all subjects recruited from the general ophthalmology clinics at UCSF. Static gonioscopy was performed using a Sussman four-mirror lens, with the eye in the primary position of gaze. Another trained ophthalmologist (DDW) performed gonioscopy for all mainland Chinese subjects recruited.

Image Acquisition

ASOCT imaging (Visante OCT; Carl Zeiss Meditec, Dublin, CA) was performed in a standard dark room (<1 Lux illumination by digital light meter, Easy View model EA30; Extech Instruments, Inc., Waltham, MA). Refractive correction was entered into the program to ensure nonaccommodative status of the tested eyes. The fixation angle was adjusted to align the iris of temporal and nasal quadrants on a horizontal level. The "anterior segment single" mode was used to acquire an image centered over the pupil on the horizontal meridian. Proper eye alignment was indicated by the appearance of an interference beam along the visual axis. Subjects were first allowed 5 minutes for dark adaptation before any image acquisition. To obtain the best-quality image, the examiner adjusted the saturation and noise and optimized the polarization for each scan during the examination. Eighteen scans were acquired by the ASOCT device, the examiner chose the best image using her best judgment at that point, with a focus on achieving an image with neither motion artifacts nor image artifacts due to the eyelids. After completion of each imaging, the single picture determined to be able to provide the best visibility of both scleral spurs (SSs) was selected and saved for analysis. If there was difficulty in terms of identifying the SS, the other

TABLE 3. Comparison of Anterior Chamber Biometry and Iris Characteristics Between American Caucasian and Ethnic Chinese in the Occludable-Angle and Open-Angle Cohorts Separately

	Ethnic Chinese	**American Caucasian**	***P* Value**
Occludable	$n = 66$	$n = 24$	
ACD, mm	2.31 ± 0.24	2.48 ± 0.28	***0.01***
ACW, mm	11.52 ± 0.38	12.06 ± 0.34	***<0.0001***
LV, mm	734.51 ± 198.9	696.60 ± 203.9	0.44
IT750, mm	0.46 ± 0.08	0.44 ± 0.07	0.22
Iarea, mm^2	1.58 ± 0.25	1.56 ± 0.27	0.82
Icurv, mm	0.35 ± 0.09	0.32 ± 0.12	0.34
PD, mm	4.27 ± 0.84	4.14 ± 0.98	0.56
2 quadrants	15.2%	20.8%	0.76
3 quadrants	16.7%	12.5%	
4 quadrants	68.2%	66.7%	
≥ 3 quadrants	84.8%	79.2%	0.53*
Open	$n = 166$	$n = 96$	
ACD, mm	2.77 ± 0.30	3.04 ± 0.33	***<0.0001***
ACW, mm	11.74 ± 0.42	12.31 ± 0.44	***<0.0001***
LV, mm	343.35 ± 254.8	294.01 ± 249.7	0.13
IT750, mm	0.44 ± 0.06	0.40 ± 0.07	***<0.0001***
Iarea, mm^2	1.50 ± 0.21	1.53 ± 0.25	0.36
Icurv, mm	0.23 ± 0.14	0.21 ± 0.14	0.32
PD, mm	4.59 ± 0.82	4.35 ± 0.87	***0.03***
Wide open	92.7%	94.3%	0.63
1 quadrant, narrow	6.7%	5.7%	

Data are expressed as difference in mean value (*P* value). *P* values are by pairwise *t*-comparisons. Numbers in bold and italic style denote the comparison is statistically significant. All measurements were obtained by ASOCT. Wide open, open angle in all 4 quadrants; 1 quadrant, posterior TM not visible in 1 quadrant; 2 quadrants, posterior TM not visible in 2 quadrants; 3 quadrants, posterior TM not visible in 3 quadrants; 4 quadrants, posterior TM not visible in 3 quadrants; ≥3 quadrants, posterior TM not visible in at least 3 quadrants (including 3 and 4).

* *P* value is for comparison between subjects in the occludable angle cohorts with 2 narrow quadrants versus at least 3 narrow quadrants.

TABLE 4. Multivariate Logistic Regressions of Associated Factors for Gonioscopy-Determined Occludable Angle Among American Caucasians and Ethnic Chinese Separately

	American Caucasian		**Ethnic Chinese**	
	β*	***P* Value**	***β****	***P* Value**
Age	−0.17	***0.04***	0.004	0.87
Sex	1.72	***0.04***	0.55	***0.02***
AL	−0.24	0.48	−0.05	0.83
PD	1.48	0.18	−0.40	0.37
ACD	10.6	***0.04***	2.86	0.08
ACW	0.41	0.84	1.42	0.15
LV	−0.02	0.03	−0.0006	***0.003***
IT750	−43.9	***0.009***	−2.80	0.53
Icurv	23.7	0.06	1.84	0.49
Iarea	2.73	0.27	−4.30	***0.02***
R^2	0.76		0.48	

Male was coded as 1 and female as 2 in regression models. Numbers in bold and italic style denote the association is statistically significant ($P < 0.05$).

* Regression coefficient. All measurements except for AL were obtained by ASOCT.

"unused" images that were taken were used to help in identifying the SS.

Image Analysis

Custom software, the Zhongshan angle Assessment Program (ZAAP, Guangzhou, China), was used for all image analysis.[21] All images were dewarped JPEG images exported from the Visante OCT (Carl Zeiss Meditec) for analysis using the ZAAP software. After identifying left and right SSs manually on the images, the algorithm automatically delineates the surfaces of the cornea, irides, and lens. As shown in Figure 1, ACW was measured as the distance between left and right SS (LSS and RSS, respectively). This ACW line was also defined as the interscleral spur (ISS) line. A perpendicular bisector of the ISS line was generated by the program and intersects the corneal endothelium, anterior surface of the lens, and ISS line at points A, B, and C, respectively. The length of BC is measured as LV, which indicates the relative location of the anterior surface of the lens to the ISS line. ACD was measured as the length of AB, indicating the depth of the anterior chamber. Iris thickness (IT; Fig. 2) was defined as the shortest distance between designated locations at the anterior and posterior iris surface. The location was decided by the intersection point of a circle centered at the SS, with a radius of 750 μm (IT750) representing the thickness nearest the iris root. Iris curvature (Icurv) was determined by creating a line from the most peripheral to the pupillary edge of the iris and then measuring the perpendicular distance from this line to the greatest convexity point along the posterior iris surface. Pupillary diameter (PD) was automatically measured as the distance between the pupillary tips of the iris on both sides on the cross-sectional images. An average of the temporal and nasal iris parameters was determined for each eye.

All images were analyzed by a single masked observer (DDW). As indicated above, in the cases when SSs were not adequately identifiable in a given image, alternative images were used to aid SS location. Images of 15 subjects randomized from each cohort were collected for intraobserver measurement repeatability testing 2 weeks after the initial measurements by the same masked observer. The test-retest differences for ACD, ACW, and LV were 0.008 ± 0.01 mm (paired *t*-test, $P = 0.895$), 0.01 ± 0.025 mm (paired *t*-test, $P = 0.723$), and 0.006 ± 0.02 mm (paired *t*-test, $P = 0.841$), respectively. The intraclass correlation coefficients for ACD, ACW, and LV were 96%, 92%, and 94%, respectively. Similarly, the intraclass correlation coefficients for IT750, Icurv, and Iarea were 95%, 89%, and 85%, respectively. The test-retest differences for IT750, Icurv, and Iarea were 0.012 ± 0.054 mm (paired *t*-test, $P = 0.88$), 0.008 ± 0.075 mm (paired *t*-test, $P = 0.33$), and 0.029 ± 0.070 mm^2 (paired *t*-test, $P = 0.63$), respectively. The Tukey mean-difference plot was also performed. The correlation and *P* values were found to be 0.96, $P = 0.3$ for ACD; 0.85, $P = 0.72$ for ACW; 0.97, $P = 0.96$ for LV; 0.88, $P = 0.75$ for IT750; 0.89, $P = 0.56$ for Iarea; and 0.89, $P = 0.25$ for Icurv.

Other Related Examinations

An autorefractor (Automatic Refractor/Keratometer, Model 599; Carl Zeiss Meditec, Dublin, CA) was used to measure noncycloplegic refraction. All raw refractive data were converted to SE (SE = sphere + 0.5 × cylinder) for analysis. A-scan biometry (E-Z Scan A/B 5500+; Sonomed, Inc., Lake Success, NY) was used to measure axial length (AL), anterior chamber depth (ACD), and lens thickness (LT).

Statistical Analysis

Data from the right eye were used for analysis. The left eye's data were used when the right eye did not meet the eligibility

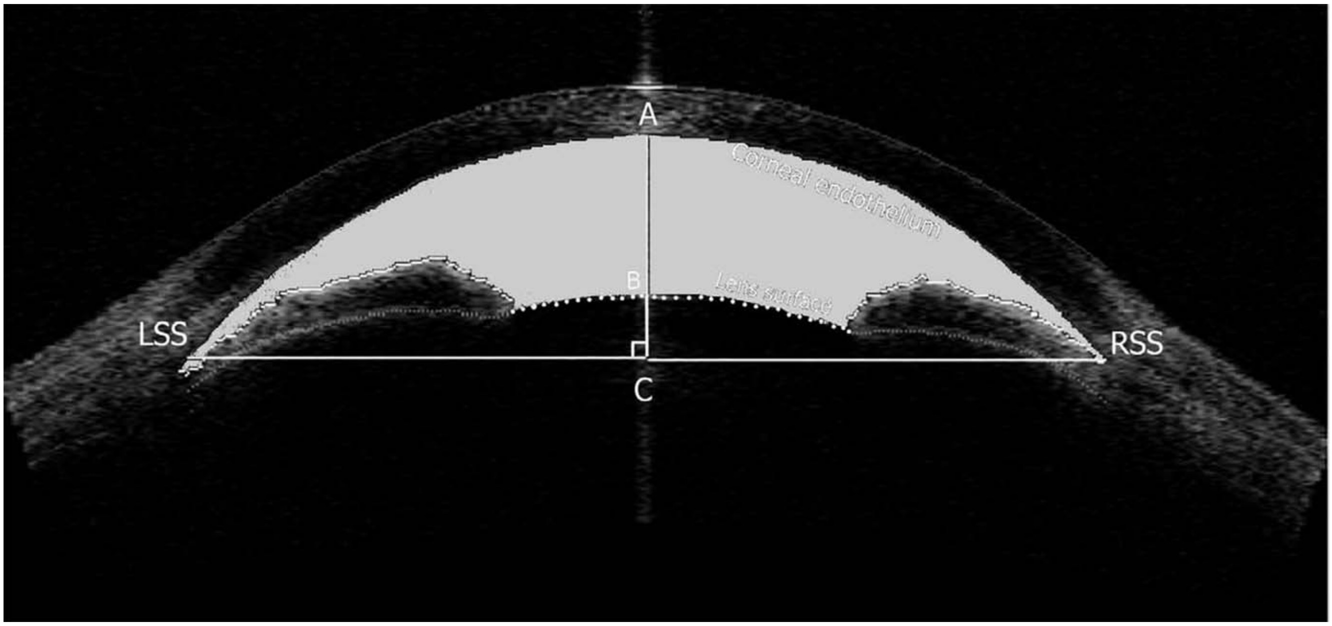

FIGURE 1. Schematic figure illustrating anterior segment biometric parameters measurement. Distance between LSS and RSS was defined as ACW. The perpendicular bisector of the ACW line intersected with corneal endothelium, anterior lens surface, and ACW line at points A, B, and C, respectively. The length of AB represents the ACD, BC represents LV.

criteria. Participants diagnosed with PAC or PACG after the study examinations were excluded, as peripheral anterior synechias (PAS) can lead to incorrect assessments of angle- and iris-related parameters. For comparisons across cohorts, analysis of variance and pair-wise comparison *t*-test were used. Bonferroni adjustment was applied in multiple comparisons. χ^2 test was used for proportion data. Multivariate logistic regression models were built with presence of occludable angle as the dependent variable, and demographic data, ASOCT and A-scan measured parameters as independent variables. With a significance level of 0.05, power of 80%, number of predictor of 10, and a medium effect ($F2 = 0.15$), the sample size for our multivariate regression model was calculated to be 113. A *P* value less than 0.05 was considered statistically significant. Data analysis was performed using JMP 10.0 package (JMP 10.0; SAS, Inc., Cary, NC). With a significance level of 0.05, power of 80%, number of predictors of 10, and a medium effect ($F2 = 0.15$), the sample size for our multivariate regression model was calculated to be 113.

RESULTS

For the American Caucasian, American Chinese, and mainland Chinese cohorts, there were 120, 116, and 116 subjects included for analysis, respectively. Left eye data were used in six (5%), two (1.7%), and five (4.4%) participants from each cohort, respectively. As shown in Table 1, the American Caucasian group had 24 occludable and 96 open-angle subjects with mean ages of 65.8 ± 11.4 and 58.7 ± 11.3 years, respectively. The American Chinese group had 36 occludable and 80 open-angle subjects with mean ages of 66.6 ± 12.2 years and 56.6 ± 10.4, respectively. The mainland Chinese group had 30 occludable and 86 open-angle subjects, with mean ages of 61.6 ± 11.5 and 59.1 ± 11.9 years, respectively. Subjects from all three occludable angle subgroups had older age, higher proportion of female sex, smaller axial length, less myopia, and thicker lens than their open-angle counterparts (Table 1).

When ASOCT-measured anterior chamber biometry was compared between American Chinese and mainland Chinese, none of the parameters were found to be significantly different. Data from these two cohorts was therefore combined to form the ethnic Chinese cohort. When comparing between American Caucasian and ethnic Chinese (Table 2), among all open-angle subjects, no significant differences were found for age ($P = 0.59$), percentage of female participants ($P = 0.63$), SE ($P = 0.83$), or AL ($P = 0.22$), although ethnic Chinese showed significantly thicker lens ($P = 0.002$). When similar comparisons were carried out for occludable-angle cohorts between the two racial groups, no significant differences were detected for any of the parameters compared (all $P > 0.05$). Based on Student's *t*-test comparisons, subjects with occludable angles in the ethnic Chinese cohort showed significantly smaller ACD, ACW, and LV ($P < 0.0001$, $P = 0.0002$, $P < 0.0001$, respectively) than those with open angles. Similar results were found when comparing Caucasians with occludable angle with their open-angle counterparts (ACD, $P < 0.0001$; ACW, $P = 0.005$; LV, $P < 0.0001$). For ASOCT-measured iris characteristics, ethnic Chinese with occludable angles showed significantly larger iris curvature ($P < 0.0001$), and smaller iris area ($P = 0.03$) and pupil diameter ($P = 0.01$) than those with open angles. Peripheral iris thickness was not found to be different between open-angle and occludable-angle Chinese subjects. In the Caucasian cohort, however, subjects with occludable angles showed significantly thicker IT750 ($P = 0.04$) and larger iris curvature ($P = 0.0002$) than those with open angles. No significant difference was detected for iris area and pupil diameters between the open-angle and occludable-angle subgroups.

Comparisons of anterior chamber biometry and iris characteristics between American Caucasian and ethnic Chinese were conducted using Student's *t*-tests in the occludable-angle and open-angle cohorts separately (Table 3). In the occludable-angle cohort, Chinese showed significantly shallower ACD ($P = 0.01$) and smaller ACW ($P < 0.0001$) than Caucasians. In the open-angle cohort, Chinese again showed significantly smaller ACD and ACW (both $P < 0.0001$). Chinese

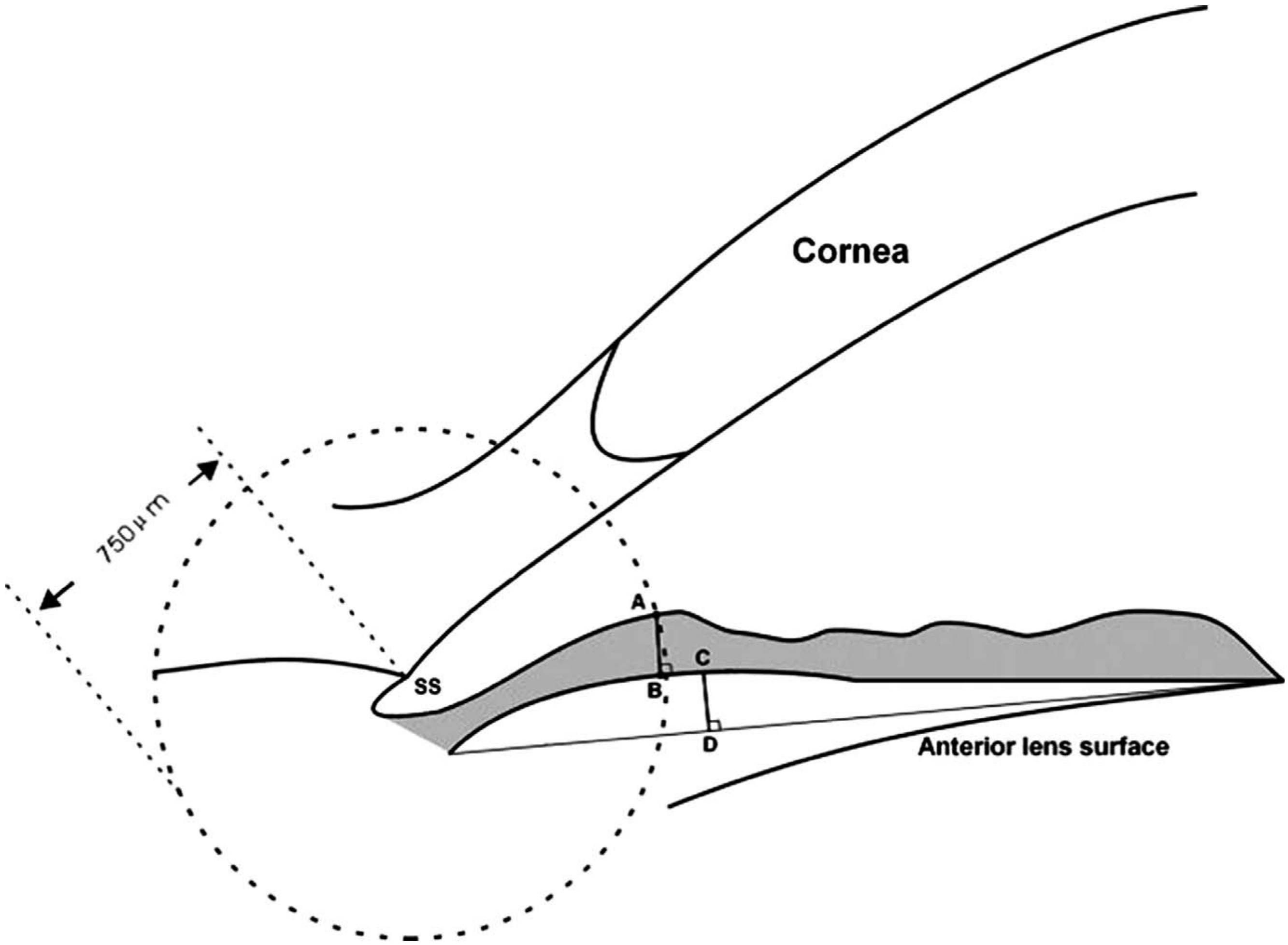

FIGURE 2. Schematic figure illustrating iris parameters measurement. A 750-mm radius circle centering SS crosses the anterior iris surface at point A. The software will identify a point B along the posterior iris surface that locates closest to A. The distance between A and B is iris thickness at 750 mm (IT750). Iris curvature (Icurv) is determined by creating a line from the most peripheral to the pupillary end of the iris, and the perpendicular distance from this line to the most convex point along the posterior iris surface (point C to D) is defined as Icurv. Iris area (Iarea) is the cumulative area of the full length of iris, indicated by the *gray area*.

also had thicker IT750 ($P < 0.0001$) and larger pupil diameter ($P = 0.03$) than Caucasians. Lens vault, iris area, and iris curvatures, however, were not found to be significantly different between Chinese and Caucasians in either the occludable-angle or open-angle group (Table 3).

Multivariate logistic regressions were then performed to detect demographic, A-scan, or ASOCT-measured anterior chamber and iris factors associated with gonioscopy-determined occludable angle in each ethnic group separately (Table 4). SE and LT were not included in the multivariate logistic regression model to avoid colinearity with AL and LV, respectively. In the ethnic Chinese cohort, occludable angle was significantly associated with female sex ($P = 0.02$), larger LV ($P = 0.003$), and greater iris area ($P = 0.02$). In the Caucasian cohort, however, occludable angle was significantly associated with older age ($P = 0.04$), female sex ($P = 0.04$), smaller ACD ($P = 0.04$), thicker IT750 ($P = 0.009$), and larger LV ($P = 0.03$).

DISCUSSION

In this cross-sectional multicenter study, American Caucasians in San Francisco were compared with their age- and sex-matched Chinese counterparts in San Francisco and mainland China with regard to A-scan and ASOCT-derived anterior segment parameters and iris profiles. We found that Chinese had significantly shallower ACD than Caucasians in both open-angle and occludable-angle subgroups. An earlier clinic-based study identified a significant difference in ACD between Hong Kong–based Chinese and American Caucasians only among the narrow-angle subjects.[17] It is possible that differences in the sample size (especially of the open-angle cohort) and imaging protocols might have contributed to the discrepancies. Chinese subjects in both the open- and occludable-angle subgroups were also found to have smaller ACW, which is consistent with what was previously reported where Chinese eyes were compared with Caucasian eyes, or Malaysian and Indian Singaporean eyes.[17,10]

Peripheral iris was found to be significantly thicker in occludable angle versus open angle subjects only among Caucasians, but not in Chinese. Furthermore, in the open-angle groups, Chinese showed thicker peripheral irides (IT750) than Caucasians, whereas this difference did not exist among the occludable angle groups. In a recent multiethnic study, similar results were found where the authors detected no significant differences in IT750 among occludable-angle subjects across different racial groups, whereas Chinese showed significantly thicker IT750 among open-angle subjects.[22] Our finding, however, is inconsistent with a previous report in which

Chinese were found to have thicker irides than Caucasians regardless of whether or not they had narrow angles,[17] although midpoint thickness was used in that study. Compared with the midpoint thickness, the location of 750 μm from the SS used in our study may better reflect drainage angle profile. Our findings on iris thickness suggest that Chinese appear to be potentially handicapped with thicker irides at baseline, although future studies with larger sample sizes, especially for subjects with occludable angles, are desirable. Iris thickness might be mechanistically contributory in both Caucasians and Chinese, although it is thicker in Chinese, which may in part explain the higher risk overall for angle closure in Chinese. Moreover, the development of angle closure is more likely to be a complex trait in which factors besides iris thickness, including dynamic behavior of the iris, iris root insertion, ciliary body size and orientation, and physiological functions of the iris, contribute to the increased risk for angle closure observed in the Chinese population. Studies on iris behavior currently being conducted in our group might be able to provide more information on these mechanisms in the near future.

Although ASOCT measurements have recently become more popular in the detection of angle closure, gonioscopy remains the most easily accessible and commonly practiced method for detecting angle closure in today's clinical practice. Understanding the relationship between certain ASOCT-measured anterior chamber biometry and/or iris characteristics and gonioscopy-determined angle status in each racial group, can provide clinicians with a better sense of the meaning of the ASOCT measurements if they choose to use it as an alternative to gonioscopy in the assessment of angle status. Previously identified risk factors for angle closure development (primarily in Asians) were used as predictors in our multivariate logistic regression analysis for each ethnicity. Predictors for occludable angles differed between American Caucasians and ethnic Chinese, highlighting varying importance of each of the factors in predicting occludable angles in each ethnicity. Lens vault and sex were the only two common factors shared by Chinese and Caucasians in predicting gonioscopy-determined narrow angle. Lens vault represents the part of the lens that bulges above the interscleral spur line, and was shown to be independently associated with narrow angles by Tan et al.[19] It was also reported to be significantly related to ACD,[23] and to have better performance in differentiating angle closure in Chinese subjects than other predictors, such as ACD and AL.[11] Our current study, in addition to confirming the importance of LV in predicting narrow angle in Chinese subjects, reports for the first time that LV was significantly associated with gonioscopy-defined occludable angles in American Caucasians. Future studies done in patients who have PACS/PACG can be used to further elucidate our observation.

Among all iris characteristics, IT750 was associated with occludable angles in American Caucasians only, whereas iris area was found to be associated with occludable angles in ethnic Chinese only. Iris curvature was not an important predictor for occludable angle in either racial group. This asymmetric relationship between iris profile and occludable angle may suggest that a large number of factors affecting iris profile and behavior, and in turn influencing anterior chamber angle, might not have been identified yet. Future studies detecting relationships between dynamic behavior of the iris and risk of developing occludable angles are necessary. From a clinical standpoint, our results suggest that a thicker peripheral iris in a Caucasian eye is associated with increased risk for developing occludable angles, but not necessarily so in a Chinese eye, as open-angle eyes also have thick irides.

Older age was found to be associated with occludable angle only in Caucasians. A previous cross-sectional study done by Sun et al.[24] reported increasing LV and iris thickness/curvature/area with age, which led to a reduction in the dimensions of the anterior chamber and to narrowing of the angle. This may explain why aging is a significant risk factor for PACG. Future longitudinal studies in Chinese and Caucasians are needed to fully elucidate the relationship between gonioscopy-determined angle closure and aging in these two ethnicities.

There are several limitations to our study. First, subjects recruited at San Francisco were clinic-based. Although efforts were made to rule out patients with ocular abnormalities via comprehensive examination and exclusion criteria, selection bias might still be inevitable. Second, only measurements from the horizontal meridian were available due to difficulties in limbal exposure with ASOCT images of vertical quadrants. Because the superior quadrant tends to be the narrowest one among the four quadrants, the addition of data from the vertical meridian may alter the final results. Third, the sample sizes of our occludable-angle groups in both racial groups were relatively small. Future larger studies, including more subjects with occludable angles are needed to further validate our current findings. Last, due to the multicenter nature of our study, it is almost inevitable to have more than one trained ophthalmologists to perform gonioscopy. Although both are well trained and qualified ophthalmologists and the ophthalmologist in Guangzhou also coordinated the study in the United States, differences may still exist.

In summary, we have found that Chinese subjects with occludable angles in our cohort did not have thicker irides than those with open angles, suggesting Chinese may potentially be handicapped with thicker irides at baseline. However, of particular clinical relevance is that iris thickness was an associated factor for having occludable angles in Caucasians. Although iris thickness might be mechanistically contributory to angle closure in both Caucasians and Chinese, the thicker iris found in both open- and occludable-angle Chinese eyes suggests this parameter is not as useful as a distinguishing feature in this ethnicity. Future studies on the dynamic and physiological behavior of the iris and ciliary body are necessary to obtain a complete picture. Moreover, we showed for the first time that predictors for occludable angles differed between Caucasians and ethnic Chinese. Being the only two common factors shared by the two ethnicities, LV and female sex might be important predictors clinically for detecting angle closure in both Chinese and Caucasians.

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