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Ocular Biometric Risk Factors for Progression of Primary Angle Closure Disease: The Zhongshan Angle Closure Prevention Trial

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Abstract

Purpose: To assess baseline ocular biometric risk factors for progression from primary angle closure suspect (PACS) to primary angle closure (PAC) or acute angle closure (AAC).

Design: Prospective observational study.

Participants: 643 mainland Chinese aged 50 to 70 years with untreated PACS.

Methods: Participants received baseline clinical examinations including gonioscopy, anterior segment OCT (AS-OCT) imaging (Visante OCT, Carl Zeiss Meditec, Dublin, CA), and A-scan ultrasound biometry as part of the Zhongshan Angle Closure Prevention (ZAP) Trial. PACS was defined as inability to visualize pigmented trabecular meshwork in two or more quadrants based on static gonioscopy. PAC was defined as development of elevated intraocular pressure (IOP) > 24 mmHg or peripheral anterior synechiae (PAS). Progression was defined as development of PAC or an acute angle closure (AAC) attack. Multivariable logistic regression models were developed to assess biometric risk factors for progression.

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Main Outcome Measures: Progression from PACS to PAC or AAC over 6 years.

Results: 643 untreated eyes (609 non-progressors, 34 progressors) of 643 ZAP participants were included in the primary analysis. In a multivariable model with continuous parameters, narrower horizontal angle opening distance 500 μm from the scleral spur (AOD500; OR=1.10 per 0.01 mm decrease, p=0.03), flatter horizontal iris curvature (IC; OR=1.96 per 0.1 mm decrease, p=0.01), and older age (OR=1.11 per year increase, p=0.01) at baseline were significantly associated with progression (AUC=0.73). Smaller cumulative gonioscopy score was not associated with progression (OR=1.03 per 1 modified Shaffer grade decrease; p=0.85) when replacing horizontal AOD500 in the multivariable model. In a separate multivariable model with categorical parameters, participants in the lowest quartile of horizontal AOD500 (OR=3.10, p=0.002) and IC (OR=2.48, p=0.014) measurements and aged 59 years and older (OR=2.68, p=0.01) at baseline had higher odds of progression (AUC=0.72).

Conclusions: Ocular biometric measurements can help risk stratify patients with early angle closure for more severe disease. AS-OCT measurements of biometric parameters describing the angle and iris are predictive of progression from PACS to PAC or AAC, whereas gonioscopy grades are not.

Précis

Angle width and iris curvature predict progression of primary angle closure suspects to primary angle closure and acute angle closure. Ocular biometric measurements help risk stratify patients with early angle closure for more severe disease.

Introduction

Primary angle closure glaucoma (PACG) is a leading cause of permanent vision loss worldwide, affecting around 20 million people.[1,2] Angle closure, characterized by apposition between the trabecular meshwork and peripheral iris, is the primary anatomical risk factor for PACG. Primary angle closure suspect (PACS), the earliest stage of angle closure, is diagnosed when multiple quadrants of angle closure are present on gonioscopy.[3] PACS progresses to primary angle closure (PAC), which confers a higher risk of PACG, when eyes develop peripheral anterior synechiae (PAS) or elevated intraocular pressure (IOP).[4–6] Laser and surgical treatments help alleviate angle closure, which could delay or prevent the progression of PACS and PAC to PACG.[6,7] Therefore, identifying high-risk angle closure eyes for early intervention is essential to reducing the prevalence of PACG. While the general consensus is that PAC should be treated with laser peripheral iridotomy (LPI) or lens extraction surgery, it is unclear which cases of PACS stand to benefit from treatment.[8,9]

The recent landmark Zhongshan Angle Closure Prevention (ZAP) Trial demonstrated that risk of progression from PACS to PAC or acute angle closure (AAC) is low in mainland Chinese aged 50 to 70 years, even in the absence of treatment with LPI.[6] Based on this finding, we recommended against widespread LPI treatment of PACS eyes. However, without any treatment, more cases of PACS will likely progress to PAC and PACG. This is problematic given that the prevalence of PACG is already expected to rise over the next two decades.[2] In addition, PACG is associated with high rates of unilateral blindness on initial

diagnosis and a three-fold greater risk for severe bilateral visual impairment compared to primary open angle glaucoma (POAG).[10–13] Therefore, there is an urgent need for clinical tools to identify high-risk cases of PACS that could benefit from early intervention.

Ocular biometric parameters measured by anterior segment OCT (AS-OCT) and ultrasound A-scan are established risk factors for angle closure and differ between eyes with open angles, PACS, PAC, and PACG.[14–20] A subset of these biometric parameters are also predictive of incident gonioscopic angle closure and anatomical angle narrowing over a 5-year period.[21–23] While it reasonable to speculate based on these findings that biometric measurements also predict progression from early angle closure (PACS) to more severe disease (PAC and AAC), this has never been demonstrated experimentally. In fact, there is sparse data to guide clinical management of PACS and no quantitative method to identify patients with high-risk PACS. In this study, we use data from the ZAP Trial to assess biometric risk factors for progression from PACS to PAC or AAC and develop statistical models that could help risk stratify patients with early angle closure for more severe disease.

Methods

The ZAP Trial was approved by the Ethical Review Board of Sun Yat Sen University, the Ethical Committee of Zhongshan Ophthalmic Center, and the Institutional Review Boards of Moorfields Eye Hospital and Johns Hopkins University. Ethics committee approval for the current study was also 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

Participants for the current study were identified from the Zhongshan Angle Closure Prevention (ZAP) Trial, a single-center randomized controlled trial based in Guangzhou, China.[24] Eligible participants aged 50 to 70 years with bilateral PACS received complete baseline eye examinations, including gonioscopy, AS-OCT imaging, and ultrasound A-scan biometry, by trained ophthalmologists. PACS was defined as an eye with two or more quadrants of angle closure, defined as inability to visualize pigmented TM based on gonioscopy, in the absence of peripheral anterior synechiae (PAS), IOP greater than 21 mmHg, and evidence of glaucomatous optic neuropathy or anterior segment ischemia from previous acute IOP increase. Participants were re-examined at 2 weeks and 6, 18, 36, 54, and 72 months after baseline examination. Study endpoints included incident PAC, defined as either: 1) IOP measurements above 24 mmHg on two separate occasions; 2) development of at least one clock hour of PAS in any quadrant; or an acute attack of angle closure.

Static gonioscopy was performed under dark ambient lighting standardized at less than 1 lux illumination (EA30 EasyView Light Meter; Extech Instruments, Waltham, MA, USA) with a 1-mm light beam and a Goldmann-type 1-mirror goniolens (Haag-Streit AG, Koniz, Switzerland) prior to pupillary dilation. Gonioscopy was performed by one of two fellowship-trained glaucoma specialists with high intergrader agreement (weighted kappa > 0.80).[24] Care was taken to avoid light falling on the pupil, inadvertent indentation of the

globe, and tilting of the lens greater than 10 degrees. The angle was graded in each quadrant according to the modified Shaffer classification system: grade 0, no structures visible; grade 1, non-pigmented TM visible; grade 2; pigmented TM visible; grade 3, scleral spur visible; grade 4, ciliary body visible. The cumulative gonioscopy score was the sum of gonioscopy grades from all 4 quadrants.

AS-OCT imaging was performed with the Visante AS-OCT system (Carl Zeiss Meditec, Inc., Dublin, CA, USA) under dark ambient lighting standardized at less than 1 lux illumination prior to pupillary dilation. During imaging, eyelids were gently retracted taking care to avoid inadvertent pressure on the globe. At the start of the ZAP Trial, only scans along the horizontal (temporal-nasal) meridian were performed. Partway through the ZAP Trial, scans along the vertical (superior-inferior) meridian were also performed. Ultrasound A-scan biometry (CineScan A/B, Quantel Medical, Bozeman, MT, USA) was performed to measure axial length (AxL) and lens thickness (LT).

Only untreated eyes were included in the analysis in order to assess the natural progression of PACS to PAC or AAC. Eyes that received laser peripheral iridotomy (LPI) were excluded from the study. Eyes that were censored prior to the conclusion of the study due to incomplete follow-up or cataract surgery were excluded from the primary analysis but were included in the sensitivity analysis.

AS-OCT Image Analysis

One AS-OCT image per eye oriented along the horizontal meridian or two images per eye oriented along the horizontal and vertical meridians were analyzed using the custom Zhongshan Angle Assessment Program, which automatically segmented anterior segment structures and produced biometric measurements once the scleral spurs were marked.[25] Image analysis was performed by 5 certified graders who were masked to examination results and intervention assignments. Graders confirmed the segmentation and marked the scleral spurs in each image.[26]

In total, 13 biometric parameters describing the anterior segment were measured in each AS-OCT image.[27] Angle open distance (AOD) was defined as the perpendicular distance from the TM at 500 (AOD500) and 750 (AOD750) μm anterior to the scleral spur to the anterior iris surface, respectively. Trabecular iris space area (TISA) was defined as the areas bounded anteriorly by AOD500 (TISA500) and AOD750 (TISA750), respectively; 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 thickness at 750 (IT750) and 2000 (IT2000) μm from the scleral spur, iris area (IA), iris curvature (IC), lens vault (LV), anterior chamber depth (ACD), anterior chamber width (ACW), anterior chamber area (ACA), and pupillary diameter (PD) were also measured.[27,28]

A set of 20 images from 20 eyes were randomly selected and graded independently by all 5 graders. Inter-grader agreement in the form of intraclass correlation coefficients (ICC) ranged from good to excellent for all AS-OCT parameters: AOD500 (0.83), AOD750 (0.82),

TISA500 (0.90), TISA750 (0.88), IA (0.92), IT750 (0.84), IT2000 (0.74), IC (0.90), ACD (0.99), PD (0.99), ACW (0.95), LV (0.91), ACA (0.99).[29]

Statistical Analysis

Horizontal, vertical, and overall measurements of biometric parameters were calculated by averaging corresponding measurements from horizontal, vertical, or both horizontal and vertical images, respectively. Means and standard deviations were calculated for all continuous variables. Normality of data was assessed using the Shapiro-Wilk test and by plotting histograms of measurement distributions. Means of continuous variables were compared between progressors and non-progressors using the unpaired t-test. Proportions of categorical variables were compared using the Pearson's chi-square test.

Univariable and multivariable logistic regression models were developed to assess the association between baseline horizontal parameter measurements and progression. Vertical and overall parameter measurements were excluded from these models due to weak differences between progressors and non-progressors and number of missing vertical images. Multivariable model A was developed using the best subset selection method to maximize the adjusted R^2. This model was limited to 4 parameters due to the relatively low number of cases of progression (N = 34). In multivariable model B, horizontal AOD500 was replaced with cumulative gonioscopy score as a measure of angle width. Units for biometric parameters were modified for physiologic significance and interpretability of odds ratios. In multivariable model C, continuous measures of horizontal AOD500, horizontal IC, and age were replaced with categorical measures: within or outside the lowest quartile of horizontal AOD500 measurements (AOD500 < 0.042 mm), lowest quartile of horizontal IC measurements (IC < 0.335 mm), and upper half of age (age ≥ 59 years). In multivariable model D, the categorical measure of horizontal AOD500 was replaced with a categorical measure of cumulative gonioscopy score: within or outside the lowest quartile of scores (score < 3). Area under the receiver operating characteristic curve (AUC) metrics were calculated for models A and C to assess predictive performance. A Cox proportional hazard model was developed with the same parameters as multivariable model A but including eyes that were censored prior to the conclusion of the study. This sensitivity analysis was performed to assess for biases associated with excluding these eyes from the primary analysis. All analyses were performed using the R programming interface (version 4.0.3). Statistical analyses were conducted using a significance level of 0.05.

Results

In total, 889 untreated eyes from 889 ZAP Trial participants received baseline clinical examinations. 225 eyes (25.3% of total) were excluded from the primary analysis due to being censored before the last (72-month) visit. 21 eyes (2.4% of total) were excluded due to incomplete horizontal measurements, which included 2 of the 36 untreated eyes that progressed from PACS to PAC or AAC.

643 untreated eyes of 643 participants were included in the current study. All 643 eyes had horizontal images whereas 147 eyes (22.9% of included) were missing vertical images,

which were not collected until partway through the ZAP Trial. All AS-OCT images from these eyes had detectable scleral spurs.

The mean age of participants included in the study was 58.7 ± 5.0 years (range 50–69 years). 116 participants (18.0%) were male and 527 participants (82.0%) were female, which was consistent with the overall distribution of the ZAP Trial (17.0% male, 83.0% female).[6] 34 of the 643 eyes (5.3%) progressed from PACS to PAC or AAC, which was consistent with the overall rate of progression (5.4%) among participants who completed the ZAP Trial. 29 of the 34 (85.3%) progressed due to PAS, and 8 of the 34 (23.5%) progressed due to elevated IOP (N = 4) or AAC (N = 4). The baseline mean modified Shaffer grade was 0.89 ± 0.38.

There were significant differences ($p < 0.05$) between progressors and non-progressors for 5 horizontal, 1 vertical, and 1 overall baseline AS-OCT biometric parameter/s. Progressors had significantly smaller ($p < 0.05$) horizontal measurements of AOD500, AOD750, TISA500, IA, and IC, smaller vertical measurements of TISA500, and smaller overall measurements of TISA500 (Table 1; Supplementary Table 1). Progressors also had higher IOP ($p = 0.03$) and greater LT ($p = 0.03$) at baseline. Difference in age between progressors and non-progressors approached but did not reach statistical significance ($p = 0.051$).

On univariable logistic regression analysis, smaller horizontal measurements of AOD500 (OR = 1.14 per 0.01 mm decrease), AOD750 (OR = 1.07 per 0.01 mm decrease), TISA500 (OR = 1.41 per 0.01 μm^2 decrease), IA (OR = 1.20 per 0.1 mm^2 decrease), and IC (OR = 1.72 per 0.1 mm decrease) and higher baseline IOP (OR = 1.14 per 1 mmHg increase) were significantly associated ($p < 0.05$) with greater odds of progression (Table 2). In multivariable model A (AUC = 0.73), 3 out of 4 selected parameters were significantly associated ($p < 0.03$) with progression (Table 2): older age (OR = 1.11 per year increase), narrower horizontal AOD500 (OR = 1.10 per 0.01 mm decrease), and flatter horizontal IC (OR = 1.96 per 0.1 mm decrease). In multivariable model B, smaller cumulative gonioscopy score (OR = 1.03 per 1 grade decrease; $p = 0.85$) was not associated with progression when replacing horizontal AOD500 (Table 3).

In multivariable model C (AUC = 0.72), the lowest quartile of horizontal AOD500 measurements (OR = 3.10), lowest quartile of horizontal IC measurements (OR = 2.48), and upper half of ages (OR = 2.68) were significantly associated ($p < 0.02$) with increased odds of progression (Table 4). In multivariable model D, the lowest quartile of cumulative gonioscopy scores was not associated with increased odds of progression (OR = 1.51; $p = 0.32$), although the lowest quartile of horizontal IC measurements (OR = 3.08) and upper half of ages (OR = 2.54) remained significantly associated ($p < 0.02$) with progression (Table 5).

Baseline demographics and biometric measurements were similar ($p > 0.15$) between participants included (N = 643) in the primary analysis and participants excluded (N = 225) due to being censored before the last (72-month) visit (Supplementary Table 2). The Cox proportional hazard model, which included all censored eyes, produced results closely resembling multivariable model A (Supplementary Table 3). The same three baseline parameters were significantly associated ($p < 0.03$) with progression, and their hazard ratios

closely approximated corresponding odds ratios from multivariable model A: older age (HR = 1.11 per year increase), narrower horizontal AOD500 (HR = 1.09 per 0.01 mm decrease), and flatter horizontal IC (HR = 1.96 per 0.1 mm decrease).

Discussion

We assessed untreated eyes of ZAP participants and identified horizontal AOD500, horizontal IC, and age as significant risk factors for progression from PACS to PAC or AAC over a 6-year period. Cumulative gonioscopy score was not predictive of progression, providing evidence that OCT imaging of the anterior segment may be a better tool than gonioscopy for determining risk of progression. AS-OCT measurements of biometric parameters can help identify patients with early angle closure who are at higher risk of progression to more severe disease.

A prevailing question in the field of glaucoma is which eyes with early angle closure (PACS) are at higher risk of developing PACG and should be considered for treatment. Our results provide the first evidence that patients with PACS and narrower baseline angle width measured by AS-OCT are at higher risk of progression to PAC or AAC, which in turn increases risk of PACG. In multivariable model A, each 10 μm decrease in horizontal AOD500 increased odds of progression by approximately 10%. In terms of per standard deviation decrease in horizontal AOD500, this translates to an odds ratio of 1.66. This finding provides a quantitative framework for interpreting repeated measures of AOD500, such as longitudinal changes in angle width over time or after treatment with LPI.[30] This finding is also consistent with previous findings by Nongpiur et al. who reported that baseline AS-OCT measurements of angle width (AOD750) are predictive of incident gonioscopic angle closure.[31] Incident PAC and AAC are of greater clinical significance compared to incident PACS, since both are more likely to lead to PACG. Nevertheless, our findings in combination with previous findings together suggest that angle width measurements are predictive of progression across the spectrum of primary angle closure disease (PACD).

Our results suggest that flatter baseline horizontal IC is a risk factor for progression, which is surprising given that greater IC reflects increased pupillary block and is a well-established risk factor for gonioscopic angle closure.[32] One possible explanation for this finding is that eyes with non-pupillary block mechanisms of angle closure, such as plateau iris or thick peripheral iris, are at higher risk for progression. This could in part explain why LPI is not uniformly beneficial in all PACS eyes. An alternative explanation is that eyes with less pupillary block at baseline have more capacity for worsening of pupillary block over time, predisposing them to progression. Given that flatter IC was a significant risk factor for progression, further study of this point is warranted. However, differentiating between these two explanations requires modeling dynamic change-over-time parameters in addition to static parameters. Analysis of dynamic parameters, while important, ultimately fell outside the scope of the current study, which focuses on baseline factors that can help inform clinical decision making at initial diagnosis of PACS.

Older age remained a significant risk factor for progression from PACS to PAC or AAC even after accounting for significant biometric covariates. Age likely serves as a surrogate for a wide range of static biometric parameters that contribute to angle closure, such as ACD, LV, and LT.[14,15,33,34] In addition, age may also be associated with dynamic rates of change over time among biometric parameters.[21] Based on multivariable model A, each year of life increases the odds of progression by approximately 10%. Therefore, the odds of progression is predicted to triple (OR = 2.83) per decade of life, which mirrors the higher prevalence of PACG among elderly mainland and Singaporean Chinese.[35–37] The importance of age as a risk factor for progression highlights a potential limitation of the ZAP Trial cohort; the mean age of participants at enrollment was 59.3 years, and participants over the age of 70 at baseline were excluded to limit participant attrition and need for cataract surgery. Therefore, the low rate of progression observed in the ZAP Trial may be at least partially attributable to the relatively young age of its participants and may not generalize to patients over the age of 70.

Our results indicate that risk of progression is not equal among all PACS eyes, and that some PACS eyes may benefit from prophylactic treatment. Multivariable model C provides a basic quantitative framework to quantify risk conferred by individual parameters and identify patients at higher risk of progression. High-risk features such as horizontal AOD500 < 0.042 mm, horizontal IC < 0.335 mm, and age greater than 58 years confer higher risk of progression than their low-risk counterparts. Our model predicts that patients 59 years of age and older with horizontal AOD500 < 0.042 mm have about 8 times higher risk of progression, and patients with all three high-risk features have about 20 times higher odds. The ZAP Trial reported that the number needed to treat to prevent one case of progression from PACS to PAC was 44 eyes. It is intuitive that only treating a subset of high-risk PACS eyes would be associated with a lower number needed to treat. However, more formal analyses and longitudinal studies are needed to determine the exact benefit of using this approach to risk stratify and manage patients with PACS.

Horizontal measurements of multiple biometric parameters were associated with risk of progression, but only TISA500 was associated in vertical scans. This finding suggests that not all sectoral angle widths contribute equally to risk of progression. We speculate this is related to sectoral differences in angle width; the superior sector of the angle tends to be the narrowest and the temporal and nasal sectors tend to be widest.[38] Baseline angle narrowing in the superior sector is more common, which could explain why biometric parameters describing this sector appear less useful for differentiating between progressors and non-progressors. While there has been a recent trend toward analyzing more AS-OCT images per eye to better represent sectoral variations among biometric parameters, the benefit of this approach appears to be mitigated for predicting progression.[38,39]

Continuous and categorical measures of cumulative gonioscopy score were not significantly associated with progression, which highlights a limitation of gonioscopy in evaluating PACS eyes. Previous studies demonstrated that AS-OCT measurements of angle width and gonioscopy grades are poorly correlated in eyes with PACD.[40,41] Other studies demonstrated that IOP and localized anatomical changes are more strongly correlated with AS-OCT measurements of angle width than gonioscopy grades in subsets of eyes with PACD.[42,43]

Our results suggest that AS-OCT measurements may provide a more clinically useful measure of angle width than gonioscopy grades, at least for predicting progression from PACS to PAC or AAC, and that disagreements between the two could reflect inherent limitations of gonioscopy for evaluating eyes with PACD.

Our study has several limitations. First, it is important to acknowledge that multivariable model A was only moderately predictive (AUC = 0.73) and cannot precisely identify eyes that will progress from PACS to PAC or AAC. We averaged temporal and nasal measurements of biometric parameters to reduce the total number of biometric parameters and avoid potential issues related to intra-eye measurement correlations. We also excluded vertical and overall measurements from our multivariable models due to weak differences between progressors and non-progressors and missing vertical images. It is conceivable that data from individual sectors could provide additional information to predict progression. Therefore, a more robust model utilizing all biometric parameters, perhaps developed using machine-learning methods, may produce better predictive performance. Second, we did not have sufficient numbers of untreated eyes that developed elevated IOP or AAC to perform sub-analyses on these more clinically significant progression subtypes. Third, the number of progressors in our study was small (N = 34), which limited our ability to develop more robust logistic regression models and detect weaker risk factors for progression. Fourth, we worked with a definition of PAC that was narrower than its original epidemiological definition (any PAS or IOP > 21 mmHg).[3] This may limit the generalizability of our findings in clinical or research settings where PACD is more broadly defined. Finally, all subjects in the ZAP Trial were Chinese and between the ages of 50 to 70, which may limit the generalizability of our multivariable models for predicting progression in other populations.

In conclusion, we assessed and modeled biometric risk factors for progression from PACS o PAC in a mainland Chinese population. Our key finding is that AS-OCT measurements of angle width and IC are predictive of progression whereas gonioscopy grades are not. These findings suggest that biometric measurements could help risk stratify patients with early angle closure for disease progression. In addition, eyecare providers may still consider treating some cases of PACS with LPI, especially those with high-risk features (elderly patients with severe angle narrowing or iris flattening). However, further work is needed to assess the clinical benefit of this approach in diverse populations and develop quantitative imaging-based methods to identify treatable PACS and reduce the burden of PACG worldwide.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Table 1:

Differences among baseline demographics and horizontal (h) biometric measurements between progressors and non-progressors.

		Non-Progressors (N = 609)	Progressors (N = 34)	
Parameter	**Units**	**Mean (STD)**	**Mean (STD)**	**P-value** *
Age	Years	58.567 (4.977)	60.294 (5.681)	0.051
Sex	Male/Female	110/499	6/28	1.000
IOP	mmHg	15.170 (2.873)	16.303 (2.974)	**0.028**
Goniscopy score	mShaffer grade	3.584 (1.476)	3.296 (1.336)	0.265
hAOD500	mm	0.088 (0.053)	0.057 (0.050)	**0.001**
hAOD750	mm	0.127 (0.062)	0.102 (0.066)	**0.028**
hTISA500	mm^2	0.055 (0.034)	0.033 (0.021)	**<0.001**
hTISA750	mm^2	0.103 (0.071)	0.092 (0.086)	0.381
hIA	mm^2	1.606 (0.216)	1.526 (0.145)	**0.045**
hIT750	mm	0.495 (0.067)	0.485 (0.071)	0.431
hIT2000	mm	0.616 (0.081)	0.602 (0.088)	0.319
hIC	mm	0.391 (0.088)	0.351 (0.089)	**0.016**
hACD	mm	2.217 (0.198)	2.162 (0.239)	0.144
hPD	mm	4.410 (0.702)	4.477 (0.731)	0.611
hACW	mm	11.520 (0.396)	11.505 (0.399)	0.837
hLV	mm	0.708 (0.241)	0.718 (0.277)	0.829
hACA	mm^2	15.774 (2.008)	15.382 (2.422)	0.303
LT	mm	4.871 (0.297)	4.956 (0.405)	0.113
AXL	mm	22.518 (0.719)	22.381 (0.701)	0.278

Abbreviations: h: Horizontal. IOP: Intraocular Pressure. AOD500/750: Angle Opening Distance 500/750 μm from the scleral spur. TISA500/750: Trabecular-Iris Space Area 500/750 μm from the scleral spur. IA: Iris Area. IT750/2000: Iris Thickness 750/2000 μm from the scleral spur. IC: Iris Curvature. ACD: Anterior Chamber Depth. PD: Pupillary Diameter. ACW: Anterior Chamber Width. LV: Lens Vault. ACA: Anterior Chamber Area. LT: Lens Thickness. AXL: Axial Length.

*P-values calculated using unpaired t-test.

Boldface indicated significant at $P < 0.05$.

Table 2:

Univariable and multivariable logistic regression models of the association between progression and continuous measures of clinical and biometric parameters.

		Univariable		Multivariable Model A	
Parameter	**Interval**	**(95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Sex	Female	1.03 (0.44–2.80)	0.951		
Age	1 year	1.07 (1.00–1.15)	0.053	1.11 (1.03–1.20)	**0.007**
IOP	1 mmHg	1.14 (1.01–1.28)	**0.029**		
Gonioscopy score	1 mShaffer grade	0.88 (0.69–1.11)	0.265		
hAOD500	0.01 mm	0.88 (0.81–0.95)	**0.001**	0.91 (0.84–0.99)	**0.027**
hAOD750	0.01 mm	0.93 (0.88–0.99)	**0.029**		
hTISA500	0.01 mm^2	0.71 (0.54–0.91)	**0.011**		
hTISA750	0.01 mm^2	0.98 (0.89–1.04)	0.574		
hIA	0.1 mm2	0.83 (0.68–0.99)	**0.046**		
hIT750	0.1 mm	0.80 (0.46–1.39)	0.43		
hIT2000	0.1 mm	0.80 (0.52–1.23)	0.318		
hIC	0.1 mm	0.58 (0.36–0.89)	**0.016**	0.51 (0.31–0.84)	**0.010**
hACD	0.1 mm	0.87 (0.72–1.05)	0.145	0.87 (0.71–1.06)	0.162
hPD	mm	1.15 (0.68–1.96)	0.611		
hACW	mm	0.99 (0.90–1.09)	0.837		
hLV	0.1 mm	1.02 (0.88–1.18)	0.829		
hACA	mm^2	0.91 (0.76–1.09)	0.302		
LT	0.1 mm	1.10 (0.98–1.24)	0.11		
AXL	mm	0.76 (0.47–1.24)	0.277		

Abbreviations: h: Horizontal. IOP: Intraocular Pressure. AOD500/750: Angle Opening Distance 500/750 μm from the scleral spur. TISA500/750: Trabecular-Iris Space Area 500/750 μm from the scleral spur. IA: Iris Area. IT750/2000: Iris Thickness 750/2000 μm from the scleral spur. IC: Iris Curvature. ACD: Anterior Chamber Depth. PD: Pupillary Diameter. ACW: Anterior Chamber Width. LV: Lens Vault. ACA: Anterior Chamber Area. LT: Lens Thickness. AXL: Axial Length.

Boldface indicated significant at $P < 0.05$.

Table 3:

Multivariable logistic regression model with horizontal AOD500 replaced by cumulative gonioscopy score.

		Multivariable Model B	
Parameter	**Interval**	**OR (95% CI)**	**P-value**
Age	1 year	1.11 (1.03–1.20)	**0.006**
Gonioscopy score	1 mShaffer grade	0.94 (0.73–1.22)	0.665
hIC	0.1 mm	0.45 (0.27–0.72)	**0.001**
hACD	0.1 mm	0.82 (0.67–1.00)	0.056

Abbreviations. hIC: Horizontal Iris Curvature. hACD: Horizontal Anterior Chamber Depth.

Boldface indicated significant at $P < 0.05$.

Table 4:

Univariable and multivariable logistic regression models of the association between progression and categorical measures of horizontal AOD500 and IC and age.

		Progressors	Univariable		Multivariable Model C	
Parameter	**Interval**	**(N)**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
hAOD500	≥ 0.042 mm	20	-	-	-	-
	< 0.042 mm	14	2.67 (1.30–5.38)	**0.006**	3.10 (1.49–6.37)	**0.002**
hIC	≥ 0.34 mm	19	-	-	-	-
	< 0.34 mm	15	2.24 (1.08–4.52)	**0.026**	2.48 (1.18–5.10)	**0.014**
Age	< 59 years	11	-	-	-	-
	≥ 59 years	23	2.33 (1.14–5.05)	**0.024**	2.68 (1.29–5.90)	**0.01**

Abbreviations: hAOD500: Horizontal Angle Opening Distance 500 μm from the scleral spur. hIC: Horizontal Iris Curvature.

Boldface indicated significant at $P < 0.05$.

Table 5:

Univariable and multivariable logistic regression models of the association between progression and categorical measures of cumulative gonioscopy score, horizontal IC, and age.

		Progressors	Univariable		Multivariable Model D	
Parameter	**Interval**	**(N)**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Gonioscopy score	≥ 3 mShaffer grade	25	-	-	-	-
	< 3 mShaffer grade	9	1.26 (0.55–2.680	0.559	1.51 (0.64–3.29)	0.32
hIC	≥ 0.34 mm	19	-	-	-	-
	< 0.34 mm	15	2.67 (1.30–5.38)	**0.006**	3.08 (1.48–6.34)	**0.002**
Age	< 59 years	11	-	-	-	-
	≥ 59 years	23	2.33 (1.14–5.05)	**0.024**	2.54 (1.23–5.55)	**0.014**

Abbreviations. hIC: Horizontal Iris Curvature.

Boldface indicated significant at $P < 0.05$.