Association Between Baseline Angle Width and Induced Angle Opening Following Prophylactic Laser Peripheral Iridotomy

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PURPOSE. To evaluate the association between baseline angle width and laser peripheral iridotomy (LPI)-induced opening of the anterior chamber angle.

METHODS. Anterior segment optical coherence tomography images captured before and after LPI were analyzed to determine the angle opening distance at 250 μm (AOD250), 500 μm (AOD500), and 750 μm (AOD750) from the scleral spur; trabecular-iris space area at 500 μm (TISA500) and 750 μm (TISA750) from the scleral spur; angle recess area at 750 μm (ARA750) from the scleral spur; and trabecular-iris angle (TIA). Differences in preoperative and postoperative measurements for the anterior chamber angle width parameters were compared by paired Student's *t*-tests. Univariate and linear mixed-effects regression models were used to examine the association between baseline and LPI-induced opening of anterior chamber angle width parameters.

RESULTS. Eighty-four eyes of 52 primary angle closure suspects were included in the analysis. AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA significantly increased following LPI by paired Student's *t*-tests (all $P < 0.0001$). Lower baseline measurements were significantly associated with greater postoperative opening in all anterior chamber angle width parameters in both univariate and linear mixed-effects regression analyses (all $P < 0.05$).

CONCLUSIONS. Our results showed significant opening of the anterior chamber angle width after LPI and demonstrated an inverse association between baseline and LPI-induced opening of the anterior chamber angle width, such that eyes with a more crowded anterior chamber angle undergoing LPI had a greater magnitude of increase in anterior chamber angle width after the procedure.

Keywords: laser peripheral iridotomy, angle opening distance, trabecular-iris space area, angle recess area, trabecular-iris angle

Primary angle closure glaucoma (PACG) is a major cause of bilateral blindness.¹ An accepted practice is to offer laser peripheral iridotomy (LPI) to primary angle closure suspects (PACS) as a preventative intervention to avert progression into primary angle closure (PAC) and PACG.² To effectively prevent PAC and PACG through the use of prophylactic LPI, it is necessary to identify those who would benefit the most from treatment. Anterior segment optical coherence tomography (ASOCT) provides high resolution images that can be analyzed to provide objective and reproducible measurements of anterior chamber parameters.³ Using ASOCT, recent studies have examined the association between LPI-induced widening of the anterior chamber angle and the anterior chamber parameters including iris curvature, iris area, iris thickness, anterior chamber area, anterior chamber depth, anterior chamber volume, and anterior chamber width.^{4,5} However, it is not known whether baseline anterior chamber angle width is associated with widening of anterior chamber angle opening

after LPI. In this study, we used ASOCT to examine the association between baseline angle width and LPI-induced opening of the anterior chamber angle in a cohort of PACS eyes.

METHODS

Approval for this prospective study was obtained from the University of California, San Francisco (UCSF) Committee on Human Research. The study was carried out in accordance with the tenets of the Declaration of Helsinki. Caucasian and Chinese subjects were recruited from the UCSF general ophthalmology and glaucoma clinics between April 2008 and December 2012. All enrolled subjects provided written, informed consent. Inclusion criteria for subject enrollment included: (1) adult patients (age > 18 years) with narrow angles as defined by the Shaffer gonioscopic classification (described below) in at least one eye, (2) self-reported Caucasian or

Chinese ancestry in both parents (the term “Caucasian” for the purposes of this study included only European-derived whites), (3) patients who consented to receiving LPI, and (4) patients who consented to undergo standardized preoperative and postoperative ophthalmic examination and ASOCT imaging. Exclusion criteria for enrollment included the following: (1) eyes with PAC, PACG, or glaucomatous optic neuropathy, (2) eyes with corneal abnormalities such as edema, abrasion or dystrophy, pterygium, and other degenerative changes, (3) eyes with iridociliary cysts, (4) eyes with incomplete LPI perforation, and (5) patients who demonstrated nonadherence to the follow up regimen. The International Society of Geographic and Epidemiologic Ophthalmology scheme provided the basis for the diagnosis of PAC, PACG, and glaucomatous optic neuropathy.⁶ PAC was defined as eyes graded as occludable on gonioscopy with the presence of peripheral anterior synechiae (PAS) or IOP greater than 21 mm Hg. PACG was defined as eyes with PAC and evidence of glaucomatous optic nerve damage. Glaucomatous optic nerve damage was confirmed by a glaucomatous optic nerve appearance (vertical cup:disc ratio > 0.6) and a corresponding reliable visual field defect. A glaucomatous visual field defect was considered to be present when the hemifield test was graded outside normal limits (with a probability of less than 5% based upon comparison with age-matched controls in the pattern deviation plot) and showed a cluster of three or more nonedge contiguous points that did not cross the horizontal meridian. Visual fields were defined as reliable if they fulfilled the following criteria: fixation losses less than 33%, false positives less than 20%, and false negatives less than 20%.

Preoperative and Postoperative Evaluation

All enrolled subjects received a standardized ophthalmic examination that included visual field testing with the Humphrey Field Analyzer (model 750i; Carl Zeiss Meditec, Inc., Dublin, CA), IOP measurement by Goldmann applanation tonometry (model AT900; Haag-Streit AG, Koeniz, Switzerland), slit lamp examination (model BM900; Haag-Streit AG, Koeniz, Switzerland), and gonioscopy with a Zeiss-style 4-mirror lens (model OPDSG; Ocular Instruments, Inc., Bellevue, WA). A single trained ophthalmologist (SCL) performed gonioscopy at ×16 magnification with slit-lamp biomicroscopy in a darkroom setting. The Shaffer gonioscopic classification was used to determine the anterior chamber angle grading in all four quadrants: an angle between the iris and the trabecular meshwork surface of 35° to 45° was classified as grade 4, between 20° and 35° was classified as grade 3, between 10° to 20° was classified as grade 2, and less than 10° was classified as grade 1. Grade 0 was assigned if angle structures were not observed.⁷ For this study, eyes with narrow angles were defined as those with Shaffer grades of 2 or less in three or more quadrants. This definition of narrow angle has previously been used by other studies.^{8–12} To improve accuracy in IOP measurements, the same ophthalmologist (SCL) measured IOP twice for each subject during a designated time period between 1 and 3 PM. From the two IOP measurements, an average was derived for statistical analysis. If the two IOP values differed by more than 2 mm Hg, then a third measurement was performed and the median value was used.

Laser Peripheral Iridotomy

All LPIs were performed by the same ophthalmologist (SCL). After pharmacologic pupil constriction with topical 2% pilocarpine, topical proparacaine hydrochloride ophthalmic solution 0.5% (Alcaine; Alcon Pharmaceuticals, Fort Worth, TX) was applied to the surgical eye for anesthesia. An ocular

Abraham lens filled with Hypromellose 2.5% ophthalmic lubricant solution (Goniovise; HUB pharmaceuticals, Rancho Cucamonga, CA) was placed on the cornea and a neodymium:yttrium aluminum garnet (Nd:YAG) laser was used to create a peripheral iridotomy approximately 1 mm from the limbus in the superotemporal region between the 10 and 11 and 1 and 2 o'clock positions on the right and left irides, respectively. Triple bursts of 7 mJ per laser shot were used initially to achieve patency, and then single bursts of 6 mJ per laser shots were used to enlarge the iridotomy. An average of 25 shots was used. At the end of every procedure, the performing physician confirmed the achievement of full-thickness perforation. The size of the iridotomy was approximately 1.5 mm in diameter. Immediately following the procedure, topical 0.1% apraclonidine (Iopidine; Alcon Pharmaceuticals, Fort Worth, TX) and 1% prednisolone acetate (Pred Forte; Allergan Pharmaceuticals, Irvine, CA) were applied. IOP was measured approximately 1 hour after the procedure. Patients with significantly elevated IOP received appropriate topical ocular hypotensives for IOP control prior to leaving the clinic. All patients were instructed to use 1% prednisolone acetate four times a day for 3 days. Post LPI assessment was performed 2 to 3 weeks after the procedure. The post LPI ASOCT image was obtained at this visit, gonioscopic examination was performed, and all iridotomies were examined for patency and confirmed to be of adequate size. LPI was repeated if patency could not be confirmed.

Anterior Segment Optical Coherence Tomography

All qualified study subjects received imaging in the dark with ASOCT (Visante OCT; Carl Zeiss Meditec, Inc., Dublin, CA), a noncontact OCT system using 1310-nm wavelength light to capture high resolution, cross-sectional images of the anterior segment of the eye. Each ASOCT scan captured both the temporal and nasal quadrants (nasal-temporal 0°–180°) in a single image while the patient looked straight ahead. An experienced operator, masked to the standardized ophthalmic examination findings, performed all the ASOCT scans. Three to five images were acquired for each eye and the image with the best quality was selected for analysis using the Zhongshan Angle Assessment Program (ZAAP; Zhongshan Ophthalmic Centre, Guangzhou, China). Image quality was evaluated on the basis of a steady central fixation as judged by a clear corneal reflection, good visibility of the scleral spurs, the presence of continuity in anterior segment structures, and the absence of motion artifacts. Both eyes from the same subject were included for analysis in the ZAAP software program if the ASOCT images passed our quality threshold.

The ZAAP software program contained algorithms that automatically defined the borders and curvatures of anterior segment structures after the scleral spurs were localized manually on the ASOCT images. Measurements for both the nasal and temporal angles were simultaneously produced. Since the peripheral iridotomies were created closer to the temporal angles, only the nasal angles were analyzed in this study. The following parameters were derived from the ZAAP software program: pupil diameter (PD), central corneal thickness (CCT), anterior corneal curvature (ACC), posterior corneal curvature (PCC), iris curvature (ICURV), iris area (IAREA), iris thickness at 750 μm from the scleral spur (IT750), iris thickness at 2000 μm from the scleral spur (IT2000), lens vault (LV), anterior chamber area (ACA), anterior chamber volume (ACV), trabecular-iris space area at 500 μm from the scleral spur (TISA500), trabecular-iris space area at 750 μm from the scleral spur (TISA750), angle opening distance at 250 μm from the scleral spur (AOD250), angle opening distance at 500 μm from the scleral spur

FIGURE 1. An illustration of TISA500 and TISA750. TISA500 was defined as the trapezoidal area with the following boundaries: anteriorly, a perpendicular line between the inner corneoscleral wall and the iris surface at 500 μ m anterior to the scleral spur; posteriorly, a line perpendicular to the inner corneoscleral wall extending from the scleral spur to the iris surface; superiorly, the inner corneoscleral wall; and inferiorly, the iris surface. The same method was used for TISA750.

(AOD500), angle opening distance at 750 μ m from the scleral spur (AOD750), and angle recess area at 750 μ m from the scleral spur (ARA750). The ZAAP software program does not evaluate the parameter trabecular-iris angle (TIA). Instead, TIA measurements were calculated by using the angle function in the built-in version 3.0 software of the Visante OCT, which defined the iris root as the vertex of the angle with the two sides of the angle formed by extending lines from the vertex to points of standardized length on the posterior surface of the cornea and the anterior surface of the iris.

The ASOCT parameters listed above were defined previously in other studies. PD was calculated by measuring the distance between the pupil edges on the cross-sectional images.¹³ CCT was measured from the anterior to the posterior surface of the cornea at the center of the ASOCT image.¹⁴ ACC was defined as the radius of curvature of the anterior surface of the cornea.¹⁴ PCC was defined as the radius of curvature of the posterior surface of the cornea.¹⁴ To calculate ICURV, a line was drawn from the most peripheral to the most central point of the iris pigmented epithelium, and a perpendicular line was extended from this line to the iris pigmented epithelium at the point of greatest convexity.¹³ IAREA was defined as the cumulative cross-sectional area of the full length (from spur to pupil) of the iris.¹³ For parameters associated with iris thickness, a circle centered at the scleral spur was drawn with a radius of 750 μ m, and the point of intersection between the circle and the anterior surface of the iris was identified. The shortest distance from this point to the posterior surface of the iris was calculated as IT750. The same method was used for IT2000.¹⁵ LV was defined as the perpendicular distance between the anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs.¹⁶ ACA was defined as the cross-sectional area of the anterior chamber bounded by the corneal endothelium anteriorly, and the anterior surface of iris and the anterior surface of lens (within the pupil)

FIGURE 2. An illustration of AOD250, AOD500, AOD750, and ARA750. AOD250 was defined as the length of the line extending from the anterior iris to the corneal endothelium, perpendicular to the line drawn along the trabecular meshwork at 250 μ m anterior to the scleral spur. The same method was used for AOD500 and AOD750. ARA750 was defined as the area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium that is drawn to the iris surface from a point 750 μ m anterior to the scleral spur (*shaded area*).

posteriorly.¹⁷ ACV was calculated by rotating the ACA 360° around a vertical axis through the midpoint of the ACA.¹⁷ TISA500 was defined as the trapezoidal area with the following boundaries: anteriorly, a perpendicular line between the inner corneoscleral wall and the iris surface at 500 μ m anterior to the scleral spur; posteriorly, a line perpendicular to the inner corneoscleral wall extending from the scleral spur to the iris surface; superiorly, the inner corneoscleral wall; and inferiorly, the iris surface. The same method was used for TISA750.¹⁸ An illustration of TISA500 and TISA750 is provided in Figure 1. AOD250 was defined as the length of the line extending from the anterior iris to the corneal endothelium, perpendicular to the line drawn along the trabecular meshwork at 250 μ m anterior to the scleral spur.^{19,20} The same method was used for AOD500 and AOD750. ARA750 was defined as the area bordered by the anterior iris surface, corneal endothelium, and a line perpendicular to the corneal endothelium that is drawn to the iris surface from a point 750 μ m anterior to the scleral spur.^{20,21} An illustration of AOD250, AOD500, AOD750, and ARA750 is provided in Figure 2 and an illustration of TIA is provided in Figure 3.

Statistical Analysis

All statistical analyses were conducted with R-statistics (Ver. 2.15.1 software for Macintosh; R Foundation for Statistical Computing, Vienna, Austria) and *P* values less than 0.05 were considered to indicate statistical significance. Mean and SD were calculated for all variables using data from both eyes. Differences in preoperative and postoperative measurements of AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA were compared by paired Student's *t*-tests. Univariate and linear mixed-effects regression models, the latter adjusting for age, sex, preoperative IOP, preoperative PD, preoperative CCT, preoperative ACC, preoperative PCC, preoperative ICURV, preoperative IAREA, preoperative IT750, preoperative IT2000, preoperative LV, preoperative ACA, preoperative ACV, and the use of both eyes in the same subject, were used to

FIGURE 3. An illustration of TIA. TIA was measured in degrees by using the angle function in the built-in version 3.0 software of the Visante OCT, which defined the iris root as the vertex of the angle with the two sides of the angle formed by extending lines from the vertex to points of standardized length on the posterior surface of the cornea and the anterior surface of the iris.

evaluate the association between baseline and LPI induced changes in AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA. Change was calculated as (postoperative mean – preoperative mean). Because manual scleral spur localization is subjective in nature, to ensure consistency, a single trained ophthalmologist (TK), masked to the patient's clinical examination results, manually located the scleral spurs on all ASOCT images. To evaluate intraobserver variance, 20 eyes were randomly selected and the anterior segment biometric parameters were remeasured by the same observer at a separate session. The intraobserver reproducibility was assessed with the intraclass correlation coefficient (ICC).

RESULTS

A total of 74 consecutively enrolled Caucasian and Chinese patients received LPI and agreed to participate in the study during the specified time period. Among them, 22 subjects were excluded from the study due to one or more of the following reasons: (1) the subject could not or did not complete the ASOCT examination, (2) poor ASOCT imaging quality (evaluated on the basis of corneal reflection, visibility of the scleral spurs, continuity of anterior segment structures, and motion artifacts), and (3) incomplete data in at least one of the analysis variables. Following exclusion, 52 patients were available among whom 84 eyes were included in the analysis. There were no significant differences in age ($P = 0.733$, unpaired Student's t -test), sex ($P = 0.317$, Fisher's Exact test), race ($P = 0.808$, Fisher's Exact test), and residual narrow angle ($P = 0.778$, Fisher's Exact test) between the included and excluded subjects. Table 1 provides the demographics and baseline clinical characteristics of the included study subjects.

Table 2 lists the preoperative and postoperative measurements of AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA as well as the differences between the two sets of measurements by paired Student's t -tests. All anterior chamber angle width parameters significantly increased

TABLE 1. Demographics and Baseline Clinical Characteristics of the Study Population

No. Patients/Eyes	52/84
Sex, Male:Female	26:26
Ethnicity, Caucasian:Chinese	28:24
Age, y	65.3 ± 11.5*
Preoperative Shaffer Gonioscopy	
Grade of all 4 quadrants†	1.3 ± 0.5*
Preoperative IOP, mm Hg	17.0 ± 4.0*
Preoperative PD, mm	4.03 ± 0.82*
Preoperative CCT, μm	547.5 ± 31.2*
Preoperative ACC, mm	7.31 ± 0.54*
Preoperative PCC, mm	6.54 ± 0.49*
Preoperative ICURV, mm	0.343 ± 0.110*
Preoperative IAREA, mm ²	1.58 ± 0.28*
Preoperative iris thickness 750, mm	0.477 ± 0.102*
Preoperative iris thickness 2000, mm	0.466 ± 0.091*
Preoperative LV, μm	767.3 ± 241.7*
Preoperative ARA, mm ²	17.4 ± 2.6*
Preoperative ACV, mm ³	113.1 ± 22.8*

* Data are expressed as mean value ± SD.

† Evaluation of the anterior chamber angle was based on the Shaffer gonioscopic grading classification: an angle between the iris and the trabecular meshwork surface of 35° to 45° was classified as grade 4, between 20° and 35° was classified as grade 3, between 10° to 20° was classified as grade 2, and less than 10° was classified as grade 1. Grade 0 was assigned if angle structures were not observed.

following LPI (all $P < 0.0001$). AOD250 significantly increased from a pre-LPI average of 0.084 ± 0.072 mm to a post LPI average of 0.130 ± 0.073 mm, a 54.3% increment. AOD500 significantly increased from a pre-LPI average of 0.125 ± 0.077 mm to a post LPI average of 0.205 ± 0.089 mm, a 63.6% increment. AOD750 significantly increased from a pre-LPI average of 0.204 ± 0.091 mm to a post LPI average of 0.314 ± 0.116 mm, a 53.8% increment. TISA500 significantly increased from a pre-LPI average of 0.055 ± 0.032 mm² to a post LPI average of 0.083 ± 0.033 mm², a 49.9% increment. TISA750 significantly increased from a pre-LPI average of 0.104 ± 0.046 mm² to a post LPI average of 0.154 ± 0.052 mm², a 48.2% increment. ARA750 significantly increased from a pre-LPI average of 0.127 ± 0.076 mm² to a post LPI average of 0.186 ± 0.087 mm², a 46.8% increment. TIA significantly increased from a pre-LPI average of $16.0^\circ \pm 6.56^\circ$ to a post LPI average of $24.3^\circ \pm 6.31^\circ$, a 51.8% increment.

Table 3 summarizes the results of univariate and linear mixed-effects regression analyses of the association between baseline and LPI-induced changes in AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA. The linear mixed-effects regression models adjusted for age, sex, preoperative IOP, preoperative PD, preoperative CCT, preoperative ACC, preoperative PCC, preoperative ICURV, preoperative IAREA, preoperative IT750, preoperative IT2000, preoperative LV, preoperative ACA, preoperative ACV, and the use of both eyes in the same subject. In both univariate and linear mixed-effects regression models, lower baseline measurements were significantly associated with greater postoperative increases in all anterior chamber angle width measurements (all $P < 0.05$). Overall, these results showed opening of the anterior chamber angle after LPI and demonstrated an inverse association between baseline and LPI-induced increase in the anterior chamber angle width.

Table 4 displays the intraobserver reproducibility of anterior segment biometric parameters measurements in a randomly selected subset of 20 eyes. All parameters demonstrated fair to excellent reproducibility with ICC.

TABLE 2. Comparisons Between Preoperative and Postoperative Anterior Chamber Angle Width Parameters in Primary Angle Closure Suspects

Parameter	Preoperative Measurements*	Postoperative Measurements*	Outcome Difference (%)	P Value†
AOD250, mm	0.084 ± 0.072	0.130 ± 0.073	0.046 (54.3% increase)	<0.0001
AOD500, mm	0.125 ± 0.077	0.205 ± 0.089	0.080 (63.6% increase)	<0.0001
AOD750, mm	0.204 ± 0.091	0.314 ± 0.116	0.110 (53.8% increase)	<0.0001
TISA500, mm ²	0.055 ± 0.032	0.083 ± 0.033	0.028 (49.9% increase)	<0.0001
TISA750, mm ²	0.104 ± 0.046	0.154 ± 0.052	0.050 (48.2% increase)	<0.0001
ARA750, mm ²	0.127 ± 0.076	0.186 ± 0.087	0.059 (46.8% increase)	<0.0001
TIA, degrees	16.0 ± 6.56	24.3 ± 6.31	8.3 (51.8% increase)	<0.0001

* Data are expressed as mean value ± SD.

† P values by paired Student's *t*-tests.

DISCUSSION

This study evaluated the association between baseline and post LPI changes in four anterior chamber angle width parameters measured at different distances from the scleral spur in PACS eyes. Our results showed widening of the anterior chamber angle after LPI as evidenced by significant increases in AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA. These findings are consistent with previous imaging studies using ASOCT to examine anterior chamber angle width before and after LPI.^{4,5} The novelty of our study lies in the demonstration of an inverse relationship between baseline and LPI-induced widening of the anterior chamber angle, specifically showing that more angle crowding at baseline is correlated with a greater magnitude of increase in the width of the anterior chamber angle after LPI. Baseline measurements of AOD250, AOD500, AOD750, TISA500, TISA750, ARA750, and TIA represent novel predictors of the amount of anterior chamber angle widening after LPI.

Because controversy exists in the literature regarding the parameter that most closely reflects angle status, the present study defined anterior chamber angle width using four different parameters (AOD, TISA, ARA, and TIA). Although all four parameters represent aspects of the anterior chamber angle width, AOD measured length in millimeters, TISA and ARA measured area in millimeters squared, while TIA measured the angle in degrees. Amerasinghe et al. recommended the use of AOD as an ASOCT surrogate for gonioscopy after demonstrating that AOD is more highly correlated with the clinical gonioscopic assessment of angle width than TISA.²² Narayanaswamy et al. also supported the utility of AOD as a useful angle measurement for identifying individuals with gonioscopic narrow angles in gradable ASOCT images. The

same group did caution that AOD is influenced by iris contour and when used in isolation could result in a false interpretation of the angle status.²⁰ Because AOD is a point distance and treats the iris surface as a straight line, its accuracy might be decreased in the presence of irregularities in the iris curvature and thickness.²³ TISA, however, does not harbor this potential source of error because it is a measurement of area and, therefore, less likely to be influenced by localized variations in the iris contour, as these tend to average out over a measurement of area. Iris thickness has been shown to influence variance in AOD, but not in TISA.²⁴ Radhakrishnan et al. used TISA as a surrogate for measurements of angle width and reported an excellent correlation between TISA and gonioscopy.²⁵ Since TISA only measured the filtering area in front of the scleral spur, whereas ARA also measured the nonfiltering region behind the scleral spur, it has been suggested that ARA may be less sensitive in identifying narrow angles in eyes with a relatively deep angle recess.²⁵ Although other studies have examined the correlation between anterior chamber angle width parameters and gonioscopy, gonioscopic assessment is subjective and can be difficult to perform in a reproducible fashion, which may limit its potential as a reference standard. Since different factors account for variability among AOD, TISA, ARA, and TIA, each parameter likely has its own advantage and disadvantages, and should be used in conjunction to give a more complete picture of the angle status.

Our results demonstrated widening of the anterior chamber angle after LPI, and suggest that a narrower anterior chamber angle width at baseline is associated with a greater angle opening after LPI. An explanation for this finding can be found by examining one of the main anatomic features of the eye that leads to narrowing of the anterior chamber angle. A primary

TABLE 3. Associations Between Preoperative and Post Laser Peripheral Iridotomy Changes in Anterior Chamber Angle Width Parameters in Primary Angle Closure Suspects

Outcome	Predictor	P Values of Univariate Regression Model	Regression Coefficients	P Values of Linear Mixed-Effects Regression Model*	Regression Coefficients
Δ AOD250	Preoperative AOD250	<0.0001	−0.4411	0.0002	−0.4513
Δ AOD500	Preoperative AOD500	0.0022	−0.3369	0.0161	−0.3202
Δ AOD750	Preoperative AOD750	0.0032	−0.3685	0.0003	−0.5739
Δ TISA500	Preoperative TISA500	0.0006	−0.3100	0.0054	−0.2864
Δ TISA750	Preoperative TISA750	0.0020	−0.3274	0.0062	−0.3279
Δ ARA750	Preoperative ARA750	0.0008	−0.3304	0.0446	−0.2262
Δ TIA	Preoperative TIA	0.0001	−0.4191	0.0002	−0.3874

* Adjusted for age, sex, preoperative IOP, preoperative PD, preoperative CCT, preoperative ACC, preoperative PCC, preoperative ICURV, preoperative IAREA, preoperative IT750, preoperative IT2000, preoperative LV, preoperative ACA, preoperative ACV, and the use of both eyes in the same subject.

TABLE 4. Reproducibility of Anterior Segment Biometric Parameter Measurements in a Random Subset of 20 Eyes

Parameters	ICC	Mean	Difference	95% CI
PD, mm	1.000	4.345	0.001	1.000, 1.000
CCT, μ m	0.996	540.690	0.100	0.990, 0.998
ACC, mm	0.982	7.489	0.001	0.958, 0.992
PCC, mm	0.971	6.698	0.010	0.931, 0.988
ICURV	0.934	0.259	0.001	0.843, 0.973
IAREA	0.988	1.500	0.014	0.969, 0.995
IT750	0.762	0.438	0.008	0.498, 0.898
IT2000	0.934	0.454	0.005	0.844, 0.973
LV	0.963	804.460	13.600	0.915, 0.984
ACA	1.000	17.760	0.001	1.000, 1.000
ACV	1.000	118.600	0.044	1.000, 1.000
AOD250, mm	0.859	0.099	0.016	0.683, 0.941
AOD500, mm	0.905	0.177	0.002	0.779, 0.961
AOD750, mm	0.933	0.266	0.023	0.841, 0.973
TISA500, mm ²	0.936	0.065	0.006	0.851, 0.974
TISA750, mm ²	0.958	0.129	0.009	0.898, 0.958
ARA750, mm ²	0.914	0.138	0.010	0.799, 0.965

CI, confidence interval.

mechanism behind a narrow anterior chamber angle is pupillary block.²⁶ In pupillary block, aqueous outflow resistance at the level of the pupil results in a build-up of pressure in the posterior chamber that causes anterior iris bowing and subsequent narrowing of the angle. The presence of iris convexity signifies pupillary block and the severity of iris bowing serves as an indicator of the degree of relative pupillary block, a key determinant of angle width. The creation of a hole in the peripheral iris through LPI allows the aqueous humor to bypass pupillary block and enter the anterior chamber, thereby equalizing the pressure gradient between the two chambers, and allowing the iris to flatten and fall back from the angle. After LPI, the amount of increase in anterior chamber angle width depends on the amount of reduction in the forward bowing of the iris. In eyes where the only mechanism behind angle closure is pupillary block, LPI should flatten the iris by eliminating the pressure gradient between the two chambers. Assuming LPI completely flattens the iris, the amount of posterior iris movement following LPI should be associated with the degree of pupillary block before LPI. A narrower angle before LPI, due to a higher degree of pupillary block, should demonstrate a proportionally wider opening of the anterior chamber angle after LPI as a result of a greater amount of posterior iris displacement. Support for this concept can be found in the Liwan Eye Study, where it was documented that the narrowest angle on ultrasound biomicroscopy (UBM) evaluation at baseline had the greatest proportional amount of increase in angle opening after LPI.²⁷

The finding that a narrower anterior chamber angle width at baseline is associated with a greater angle opening after LPI, suggests that pupillary block may be the dominant factor behind angle narrowing in our PACS study population. Several studies have demonstrated other mechanisms behind angle closure for cases of persistent angle closure following LPI. The reported rates of persistent angle closure after LPI in populations that also included PAC and PACG were 11% in New Zealand,²⁸ 13% in China,²⁹ 20% to 58% in Singapore,^{30–32} 38% in Japan,³³ 55% in Switzerland,³⁴ and 56% in Hong Kong.³⁵ Using UBM, the Hong Kong based study found shorter distances between the trabecular meshwork and the ciliary process in acute PAC eyes, suggesting that an anteriorly positioned ciliary body was associated with angle crowding and persistent angle closure after LPI.³⁵ Plateau iris syndrome,

as this condition is known, is characterized by persistent angle narrowing despite a patent LPI, and is due to an anteriorly positioned ciliary process that prevents the iris root from falling away from the trabecular meshwork following iridotomy.³⁶ A large lens relative to the size of the eye can also exacerbate the effects of plateau iris syndrome.²⁶ With a large lens, the distance between the lens equator and the ciliary body is shortened, and the lens may push the peripheral iris and pull the anterior ciliary body towards the trabecular meshwork. It is reasonable to expect that eyes with narrow angles due to plateau iris syndrome and large lens might reap less benefit from LPI compared with eyes with narrow angles due to pupillary block alone.

The present study demonstrated that a more crowded angle is associated with a greater magnitude of post LPI increase in anterior chamber angle width in PACS eyes. Our study population of PACS limits extrapolation of the findings to individuals with PAC and PACG. There are indications that the reverse association may occur in those with the more severe forms of the disease. PAS in individuals with anatomically narrow angles is a pathognomonic sign for PAC and PACG. Su et al. demonstrated a correlation between anterior chamber angle width and the degree of PAS, with the narrowest angles demonstrating the highest clock hours of PAS.³⁷ In a 3 year follow up period, one out of three eyes of patients with PAS who received LPI experienced PAS extension.³⁸ LPI can effectively treat eyes with angle closure when the only underlying mechanism is pupillary block, but tends to be less effective in eyes with PAS. Because prolonged episodes of appositional angle closure in pupillary block lead to PAS formation,³⁹ it is reasonable to assume that LPI is more beneficial in treating patients at an earlier stages of the disease before the onset of PAS leading to poor treatment response.

This study has several potential limitations. First, the ZAAP software program depended upon manual identification of the scleral spur as a measurement reference point for image processing. Although manual scleral spur localization is subjective in nature, our study design attempted to control for this by utilizing a single ophthalmologist to read all the ASOCT images and then selecting a random subset of 20 ASOCT images for reproducibility testing by the same ophthalmologist at a separate session. The random subset of 20 ASOCT images selected for reproducibility testing yielded fair to excellent intraobserver correlations. Second, the present study recruited subjects from a university-based general ophthalmology and glaucoma clinic, so our study population may have suffered from selection bias despite consecutive subject enrollment. Hence, the results of this study may not apply to the general population. Third, the study only recruited subjects who are PACS, so our findings may not be fully extrapolated to those with PAC and PACG. Fourth, it is also possible that the inclusion of both eyes from a single patient may have influenced the results, although we performed mixed-effects regression analysis to account for the use of both eyes. Fifth, measurements for both the nasal and temporal angles were simultaneously produced. However, the peripheral iridotomies were created closer to the temporal angles, so only the nasal angles were analyzed in this study under the assumption that they may be less affected by proximity to the peripheral iridotomies in comparison with the temporal angles. But it is possible that utilizing only nasal angles may not reveal the overall effect of LPI in the general angle status. The final limitation is the lack of gonioscopic correlation and UBM data to compare with the ASOCT parameters. UBM data would also have allowed us to determine the association of plateau iris configuration with our outcomes. To help assess whether the excluded group had an excess of plateau iris configuration and, thus, may have biased our results, we used residual

narrow angle as a surrogate marker for plateau iris and did not find a difference with our included study group.

In summary, this is the first study to show an inverse relationship between baseline and LPI-induced widening of the anterior chamber angle width. Because only a minority of individuals identified as PACS progresses to PAC and PACG, prophylactic LPI in PACS remains to some extent controversial despite its effectiveness in PAC prevention as it may result in a large number of unnecessary LPIs. An objective preoperative evaluation that includes measurements of baseline AOD, TISA, ARA, and TIA, along with other clinical parameters identified as determinants of angle width, may provide a quantitative adjunct to clinical judgment for identifying individuals who would benefit the most from prophylactic treatment. Further studies on a larger population are warranted to confirm our findings.

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