Glaucomatous Progression after Laser Peripheral Iridotomy in Eyes with Different Angle-closure Mechanisms: a Longitudinal Study

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Purpose: To assess and compare longterm changes of anterior chamber angle, intraocular pressure (IOP) and visual field (VF) after laser peripheral iridotomy (LPI) in eyes with different angle closure mechanisms based on anterior segment-optical coherence tomography (AS-OCT) image.

Methods: In this retrospective longitudinal study, 111 patients with primary angle closure (PAC) who underwent LPI and at least five serial follow-up VF tests over at least 2 years were classified into three groups based on their initial AS-OCT images: 52 (47%) with pupillary block (PB), 29 (26%) with plateau iris configuration (PIC), and 30 (27%) with thick peripheral iris roll (TPIR).

Results: Within 1 month after LPI, IOP decreased and angle widened significantly only in the PB group. Among 111 eyes, 5 (10%) of 52 eyes with PB, 7 (24%) of 29 with PIC, and 6 (20%) of 30 with TPIR showed VF progression during follow up period. Over a mean follow-up of 5.3 years, the risk of VF progression was higher in the PIC (adjusted hazard ratio [HR] = 6.352; \( p = 0.008 \)) and TPIR (adjusted HR = 4.351; \( p = 0.058 \)) groups than in the PB group.

Conclusions: Following LPI, eyes with non-PB-associated PAC, especially those with PIC, showed limited reductions in IOP and angle widening and greater risk of VF progression than eyes with PB-associated PAC. Non-PB eyes at baseline may experience a poorer disease course after LPI than PB eyes.

Key words: Anterior segment optical coherence tomography; Laser peripheral iridotomy; Plateau iris configuration; Primary angle closure glaucoma; Visual field

Introduction

Primary angle-closure glaucoma (PACG) is a common cause of irreversible blindness worldwide. Compared with primary open angle glaucoma, PACG is associated with an approximately 3-fold higher risk of severe visual impairment.\(^1\) The primary pathogenic mechanism of PACG is angle closure, in which the peripheral iris is in contact with the trabecular meshwork, resulting in secondary elevation of intraocular pressure (IOP).

In eyes with chronic asymptomatic PACG, the peripheral iris slowly or intermittently covers the trabecular meshwork, resulting in the gradual elevation of IOP over a long period of time.\(^1\) Therefore, the natural course of asymptomatic PACG is clinically silent, in contrast to acute angle-closure attack. Similar to other forms of glaucoma, however, asymptomatic PACG can lead to glaucomatous optic nerve damage and visual field (VF) defects. The International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classifies primary angle-closure sus-
pect (PACS) and primary angle-closure (PAC) eyes as those with a narrow or occludable angle predisposing to PACG without damage to the optic disc or VF. Population-based studies have shown that the 5 years incidence of conversion of PACS to PAC (elevated IOP) was 22%, and the 5 years incidence of conversion of PAC to PACG was 28.5% for initial PAC.

Various mechanisms may be responsible for angle closure in eyes with PACG. To date, three to four categories have been described: 1) pupillary block (PB), 2) plateau iris configuration (PIC), 3) thick peripheral iris roll (TPIR), and/or 4) exaggerated lens vault (ELV). Long-term changes in the anterior segment (AS) of eyes with asymptomatic PACG (including PACS and PAC) differ according to their mechanisms of angle closure. Furthermore, laser peripheral iridotomy (LPI) affected angle widening only in eyes with PB. Another study using cluster analysis showed that the ability of LPI to reduce IOP was limited to eyes with PB-like features, not those with PIC-like features. To our knowledge, however, VF progression in eyes with PACG classified by angle-closure mechanisms has not been determined.

To extend these findings, we hypothesized that the course of VF progression would differ in eyes having different angle-closure mechanisms. In the present study, VF progression was analyzed in subjects with PACG, including PACS and PAC, who underwent prophylactic LPI and were followed up for at least 2 years (mean, 5.3 years) with at least five serial VF tests. In addition, changes in IOP and angle parameters during the follow-up period were assessed by Goldmann applanation tonometry (GAT) and AS-optical coherence tomography (AS-OCT) imaging.

Methods

Participants

This retrospective, longitudinal observational study was approved by the Institutional Review Board of Asan Medical Center (IRB approval number: 2017-1311; Seoul, Korea), and adhered to the tenets of the Declaration of Helsinki. Informed consent was waived due to its retrospective design. The records of patients who initially visited the glaucoma clinic of Asan Medical Center from January 2010 to December 2016 were reviewed for eligibility. All participants were diagnosed with PACG (including PACS and PAC) by a single glaucoma specialist (K.R.S), having extensive experience with gonioscopic examinations, according to ISGEO criteria. Because the goal of this study was to assess the progression or development of VF defects, participants diagnosed with PACS and PAC were combined and categorized as PACG suspect.

Subjects with PACG or PACG suspect were included if they 1) were followed up for at least 2 years after LPI, 2) had undergone at least five serial VF tests (Humphrey field analyzer; Swedish Interactive Threshold Algorithm [SITA] 24-2, Carl Zeiss Meditec Inc., Dublin, CA, USA) at different visits, and 3) had undergone prophylactic LPI at the first or second visit. Details of the LPI protocol have been described. All participants underwent AS-OCT (Visante OCT, ver 3.0, Carl Zeiss Meditec Inc., Dublin, CA, USA) imaging before (baseline) and 1 month after LPI, and annually thereafter. The patency of the LPI site was assessed at every visit by slit lamp examination performed by a glaucoma specialist (K.R.S).

Subjects were excluded if they 1) had used or were using topical or systemic medications that may have affected the angle or pupillary reflex, 2) had a history of previous intraocular surgery (e.g., cataract/glaucoma surgery, laser trabeculoplasty, laser iridoplasty) before study initiation, and 3) had poor-quality AS-OCT images. If participants had undergone cataract surgery or another type of intraocular surgery, including glaucoma surgery, after a minimum follow-up of 2 years, their medical records and VF test results up to the time of those surgeries were used for analysis. Because peripheral anterior synechiae (PAS) could alter the effects of LPI and the natural course of disease, any eye with extensive PAS (more than one quadrant) at baseline was excluded. Because acute angle-closure attack could alter angle structure during the short term period and influence the natural course of disease in eyes with angle closure, participants who experienced an acute angle-closure attack during the follow-up period were also excluded.
this study, an acute angle-closure attack was defined as ocular or periocular pain, nausea or vomiting, or intermittent blurred vision with haloes; an IOP >30 mmHg; and at least three of the following four criteria: conjunctival injection, corneal epithelial edema, a mid-dilated unreactive pupil, and a shallow anterior chamber. If both eyes of a subject were eligible, only one randomly selected eye was included.

Classification of angle-closure mechanism

Participants were qualitatively classified according to their baseline (pre-LPI) AS-OCT images, taken using enhanced AS single mode (scan length, 16 mm; 256 A-scans) at the horizontal meridian. Internal fixation was used in all subjects, and all scans were taken by a single well-trained operator who was masked to other clinical findings, minimizing operator-associated variability. Three images of each eye were acquired, with the highest-quality image, defined as the image showing good visibility of the scleral spur, selected for analysis. The criteria for classification of angle-closure mechanisms have been thoroughly described. In brief, eyes with PB showed a convex forward iris profile, with a typical bombe appearance, a very small zone of iris-lens contact in the center, and a shallow peripheral anterior chamber. Eyes with PIC showed the peripheral iris arising from its root in apposition or in close proximity to the angle wall and then turning sharply away from the angle toward the visual axis, the presence of a central flat iris plane, a central anterior chamber that was relatively deep, and a shallow peripheral anterior chamber. Eyes with TPIR showed a thick iris, appearing as prominent peripheral circumferential folds occupying a large proportion of the angle, a relatively deep central anterior chamber, and a shallow peripheral anterior chamber. Eyes with ELV were characterized by a lens that pushed the iris forward, resulting in a small anterior chamber volume and markedly reduced space between the iris and corneal angle surface, along with an iris that covered the anterior surface of the lens, giving rise to a “volcano-like” configuration. All eyes were classified by two independent glaucoma specialists (J.K and K.R.S) in a masked fashion. Any disagreement between these specialists was settled by consensus.

AS-OCT parameters, defined as described, were measured quantitatively using intrinsic built-in software (Visante version 3.0). After two scleral spur (SS) locations in the horizontal sectional images were marked, the software automatically calculated the anterior chamber depth (ACD, mm), lens vault (LV, mm), angle opening distance at 500 microns anterior to the SS (AOD500, mm), and trabecular-iris space area at 500 microns anterior to the SS (TISA500, mm²). AOD500 and TISA500 were calculated at both nasal and temporal angles, and their means were analyzed.

Determination of VF progression

All subjects underwent VF (SITA 24-2) tests at each visit, with only reliable VF test results, defined as having false positive rates <15%, false negative rates <15%, and fixation loss rates <20%, were included. VF progression in PACG suspect was defined as a new-onset glaucomatous VF defect (pattern standard deviation [PSD] <5%, glaucoma hemifield test outside normal limits). Based on the criteria of the early manifest glaucoma trial (EMGT), VF progression in eyes with PACG was defined as three or more of the same test locations showing statistically significant progression from baseline in three consecutive VF tests.

Changes in IOP and angle parameters after LPI

To assess the direct, short-term effects of LPI on IOP, IOP was measured by GAT before and 1 month after LPI. Following LPI, all patients were administered topical flurometholone four times per day for 1 week and re-visited the clinic 1 week and 1 month after LPI. The numbers of topical antiglaucoma medications were altered after LPI at the discretion of each ophthalmologist. Because IOP is influenced by the use of antiglaucoma medications, the numbers of antiglaucoma medications used before and 1 month after LPI were determined. Mean and peak IOPs during the 1 month follow-up period after LPI were calculated. All participants underwent AS-OCT imaging 1 month after LPI, using the protocol described above. Angle parameters (AOD500, TISA500) were calculated by intrinsic software. Long-term changes in angle parameters were as-
sessed by comparing AS-OCT images taken 1 month after LPI and at the last visit of each participant.

**Statistical analysis**

Continuous variables were expressed as the mean ± standard deviation (SD), and categorical variables as frequencies (%). Agreement between the two examiners on initial classification of angle-closure mechanisms was assessed by Kappa statistics. Demographic and ocular characteristics were compared among the subject groups by analysis of variance (ANOVA) and post-hoc Tukey tests. Categorical variables were compared using chi-square tests. Factors associated with VF progression were identified by Cox regression analysis. Using the PB group as the reference, the HR and 95% confidence interval of each of the other groups for VF progression were assessed by the final multivariate Cox regression model, after adjusting for other possible factors identified on univariate models. The effects of LPI on IOP and angle parameters were compared among groups using ANOVA. Individual changes in IOP and angle parameters (before vs. 1 month after LPI and 1 month after LPI vs. last visit) were assessed using paired t-tests. A two-sided p-value less than 0.05 was defined as statistically significant. All statistical analyses were performed using SPSS software version 18.0 for Windows (IBM Corp., Armonk, NY, USA).

**Results**

After excluding participants with poor-quality AS-OCT images (i.e., an undetectable or ambiguous SS), 115 participants met our inclusion and exclusion criteria and were evaluated. Participants classified as having ELV tended to undergo cataract surgery at a relatively early point, with most followed up for less than 2 years after LPI. Furthermore, because the lens component was determined to be the primary cause of angle closure in some ELV patients, they underwent cataract surgery rather than LPI as initial treatment. Therefore, only four participants were classified

| Table 1. Demographics, ocular characteristics, and baseline anterior segment-optical coherence tomography parameters of three groups |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age (years) | 64.8 ± 7.9 | 65.0 ± 7.2 | 60.1 ± 7.9 | 0.017<sup>*</sup> | PB = PIC > TPIR |
| Sex (female) | 45 (87) | 20 (69) | 25 (83) | 0.143 | |
| PACG suspect/PACG | 42/10 | 22/7 | 26/4 | 0.569 | |
| SE (diopters) | 0.94 ± 0.8 | 0.85 ± 1.0 | 0.61 ± 1.1 | 0.339 | |
| CCT (micron) | 537 ± 33 | 527 ± 31 | 541 ± 30 | 0.252 | |
| AL (mm) | 22.3 ± 0.6 | 23.0 ± 0.7 | 22.6 ± 0.7 | 0.009<sup>†</sup> | PB < PIC |
| Initial MD (dB) | -1.6 ± 2.0 | -1.3 ± 3.6 | -0.8 ± 2.1 | 0.368 | |
| Initial PSD (dB) | 2.5 ± 1.8 | 2.8 ± 2.7 | 2.2 ± 2.1 | 0.554 | |
| Initial VFI (%) | 97 ± 4.5 | 96 ± 8.7 | 98 ± 4.5 | 0.465 | |
| Follow up period (months) | 67 ± 34 | 63 ± 30 | 58 ± 30 | 0.474 | |
| Baseline AS-OCT | | | | |
| ACD (mm) | 2.01 ± 0.20 | 2.20 ± 0.24 | 2.06 ± 0.23 | 0.011<sup>†</sup> | PB < PIC |
| LV (mm) | 1.12 ± 0.25 | 0.92 ± 0.38 | 0.93 ± 0.29 | 0.034<sup>‡</sup> | PB > PIC |
| AOD500 (mm) | 0.119 ± 0.068 | 0.191 ± 0.130 | 0.142 ± 0.121 | 0.056 | PB < PIC |
| TISA500 (mm²) | 0.051 ± 0.029 | 0.080 ± 0.044 | 0.054 ± 0.045 | 0.026<sup>‡</sup> | PB < PIC |

Values are presented as mean ± standard deviation or number (%).
PB = pupillary block; PIC = plateau iris configuration; TPIR = thick peripheral iris roll; PACG = primary angle closure glaucoma; SE = spherical equivalent; CCT = central corneal thickness; AL = axial length; MD = mean deviation; PSD = pattern standard deviation; VFI = visual field index; AS-OCT = anterior segment-optical coherence tomography; ACD = anterior chamber depth; LV = lens vault; AOD500 = angle opening distance at 500 micron anterior to the scleral spur; TISA500 = trabecular-iris space area at 500 micron anterior to the scleral spur.
<sup>†</sup>Figures with statistical significance.

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as ELV. Due to the small sample size of the ELV group, only three groups (PB, PIC, and TPIR) were included in our analysis, as in a previous study. No eye experienced LPI site occlusion during follow-up visits.

Of the 111 included subjects, 52 (47%) were classified as PB, 29 (26%) as PIC, and 30 (27%) as TPIR. The two examiners agreed in classifying 100 eyes and disagreed for 11, yielding a Kappa coefficient of 0.846, similar to previous findings. Of the 11 eyes with disagreement, eight were initially classified as PIC by one examiner and as TPIR by the other, and three were initially classified as PB by one examiner and as TPIR by the other. The mean follow-up period was 63 months (median: 55 months, range: 24-157 months).

Table 1 shows the demographic and ocular characteristics of the three groups. Subjects in the TPIR group were younger than those in the PB and PIC groups. Axial length (AL) was significantly shorter in the PB than in the PIC group (22.3 vs. 23.0 mm; \( p = 0.009 \)). Gender distribution, proportion of eyes with PACG, spherical equivalent, central corneal thickness, initial VF MD, PSD, visual field index, and follow-up period were similar among the three groups (\( p > 0.140 \) each). Baseline AS-OCT parameters showed distinct differences, especially between the PB and PIC groups, with the PB group having significantly shallower ACD, higher LV, and narrower angle parameters (AOD500, TISA500) than the PIC group.

Table 2 shows the proportion of participants in the three groups with VF progression, according to their initial status (PACG suspect vs. PACG). VF progression occurred in 12 (57%) of the 21 eyes initially diagnosed with PACG compared with 6 (7%) of 90 initially diagnosed with PACG suspect. When assorted by group, 5 (10%) of 52 eyes with PB, 7 (24%) of 29 with PIC, and 6 (20%) of 30 with TPIR showed VF progression.

### Table 2. Proportion of participants with VF progression during follow up period in three groups, according to initial diagnosis (PACG suspect or PACG)

|                  | PB   | PIC  | TPIR |
|------------------|------|------|------|
| Initial PACG suspect (new onset of VF defect) | 2/42 (5) | 2/22 (9) | 2/26 (7) |
| Initial PACG (worsening of VF defect) | 3/10 (30) | 5/7 (71) | 4/4 (100) |
| Total            | 5/52 (10) | 7/29 (24) | 6/30 (20) |

Values are presented as number (%).

VF = visual field; PACG = primary angle closure glaucoma; PB = pupillary block; PIC = plateau iris configuration; TPIR = thick peripheral iris roll.

### Table 3. Multivariable Cox regression analysis for assessing the risk of visual field progression according to the groups divided by angle closure mechanism (PB regarded as reference), while adjusting for other possible variables

| Variable                              | Adjusted HR | 95% CI   | \( p \)-value |
|---------------------------------------|-------------|----------|---------------|
| Groups (reference: PB)                |             |          |               |
| PIC                                   | 6.352       | 1.63-24.72 | 0.008*        |
| TPIR                                  | 4.351       | 0.95-19.85 | 0.058         |
| Other covariates\(^1\)                |             |          |               |
| Age (years)                           | 1.090       | 1.00-1.18 | 0.039\(^\dagger\) |
| Initial PACG (reference: PACG suspect)| 14.514      | 3.68-57.18 | <0.001\(^\dagger\) |
| IOP (untreated, mmHg)                 | 1.157       | 1.01-1.32 | 0.030\(^\dagger\) |
| Initial MD (dB)                       | 1.167       | 0.83-1.65 | 0.381         |
| Initial PSD (dB)                      | 1.083       | 0.77-1.53 | 0.652         |

PB = pupillary block; HR = hazard ratio; CI = confidence interval; PIC = plateau iris configuration; TPIR = thick peripheral iris roll; PACG = primary angle closure glaucoma; IOP = intraocular pressure; MD = mean deviation; PSD = pattern standard deviation.

*Statistical significance; \(^\dagger\)Variables with \( p < 0.10 \) in univariate Cox analysis were included.
Table 3 summarizes the result of Cox regression analysis. To assess the risk factors for VF progression, all putative variables (age, gender, initial PACG, mean untreated IOP, mean follow-up IOP, peak follow-up IOP, CCT, AL, initial VF MD, initial PSD, baseline AS-OCT parameters) were initially screened by univariate Cox regression analysis. Using a cut-off p-value of 0.10, age, initial PACG (vs. PACG suspect), untreated IOP, initial VF MD, and initial PSD were found to be statistically significant. The final multivariate Cox regression analysis found that, after adjusting for other variables, the risk of VF progression was significantly higher for PIC than for PB (adjusted HR = 6.352; p = 0.008), and was also higher for TPIR than for PB, with borderline significance (adjusted HR = 4.351; p = 0.058). In addition,

Table 4. Changes of IOP and number of antiglaucoma medications after LPI in three groups

|                      | PB (n = 52) | PIC (n = 29) | TPIR (n = 30) | p-value | Post hoc |
|----------------------|------------|-------------|--------------|---------|----------|
| IOP (mmHg)           |            |             |              |         |          |
| Before LPI           | 15.8 ± 4.1 | 15.5 ± 3.3  | 14.8 ± 3.4   | 0.530   |          |
| One month after LPI  | 13.1 ± 2.9 | 14.7 ± 3.2  | 14.4 ± 2.4   | 0.042*  | PB < PIC |
| p-value*             | <0.001     | 0.090       | 0.335        |         |          |
| Number of antiglaucoma medications |          |             |              |         |          |
| Before LPI           | 0.3 ± 0.8  | 0.6 ± 1.1   | 0.5 ± 1.0    | 0.251   |          |
| One month after LPI  | 0.4 ± 0.8  | 1.1 ± 1.3   | 0.6 ± 1.0    | 0.011†  | PB < PIC |
| p-value†             | 0.146      | 0.019†      | 0.702        |         |          |
| Follow up period     |            |             |              |         |          |
| Peak IOP (mmHg)      | 16.1 ± 3.3 | 16.3 ± 2.7  | 16.9 ± 5.8   | 0.667   |          |
| Mean IOP (mmHg)      | 14.0 ± 2.4 | 14.2 ± 2.6  | 14.3 ± 2.9   | 0.804   |          |
| Mean number of medications | 0.7 ± 1.0 | 1.2 ± 1.1  | 0.6 ± 1.1    | 0.061   |          |

Values are presented as mean ± standard deviation.
IOP = intraocular pressure; LPI = laser peripheral iridotomy; PB = pupillary block; PIC = plateau iris configuration; TPIR = thick peripheral iris roll.
*Figures with statistical significance; †Paired t-test (comparison between ‘before LPI’ and ‘one month after LPI’).

Table 5. Short-term changes of angle parameters one month after LPI in three groups

|                      | PB (n = 52) | PIC (n = 29) | TPIR (n = 30) | p-value | Post hoc |
|----------------------|------------|-------------|--------------|---------|----------|
| AOD500 (mm)          |            |             |              |         |          |
| Before LPI           | 0.119 ± 0.068 | 0.191 ± 0.130 | 0.142 ± 0.121 | 0.056   | PB < PIC |
| One month after LPI  | 0.168 ± 0.076 | 0.184 ± 0.088 | 0.159 ± 0.071 | 0.560   |          |
| Change*              | 0.049 ± 0.067 | -0.007 ± 0.146 | 0.017 ± 0.120 | 0.197   |          |
| p-value†             | <0.001†     | 0.824       | 0.517        |         |          |
| TISA500 (mm²)        |            |             |              |         |          |
| Before LPI           | 0.051 ± 0.029 | 0.080 ± 0.044 | 0.054 ± 0.045 | 0.026†  | PB < PIC |
| One month after LPI  | 0.064 ± 0.030 | 0.068 ± 0.032 | 0.059 ± 0.026 | 0.609   |          |
| Change*              | 0.013 ± 0.024 | -0.012 ± 0.048 | 0.005 ± 0.047 | 0.085   |          |
| p-value†             | 0.006†      | 0.261       | 0.613        |         |          |

Values are presented as mean ± standard deviation.
LPI = laser peripheral iridotomy; PB = pupillary block; PIC = plateau iris configuration; TPIR = thick peripheral iris roll; AOD500 = angle opening distance at 500 micron anterior to the scleral spur; TISA500 = trabecular-iris space area at 500 micron anterior to the scleral spur.
*Difference between ‘one month after LPI’ and ‘before LPI’ (positive means increase, whereas negative means decrease); †Paired t-test (comparison between ‘before LPI’ and ‘one month after LPI’); ‡Figures with statistical significance.
older age, initial PACG, and higher untreated IOP were significantly associated with VF progression (all \( p < 0.05 \)).

Table 4 shows the changes of IOP and number of antiglaucoma medications after LPI for the three groups. Before LPI, IOP and number of antiglaucoma medications did not differ significantly in the three groups. One month after LPI, only the PB group showed a significant change (decrease) in IOP, from 15.8 mmHg to 13.1 mmHg (\( p < 0.001 \)), whereas the PIC and TPIR groups did not. The mean number of antiglaucoma medications was significantly higher after than before LPI in the PIC group (1.1 vs. 0.6; \( p = 0.019 \)). However, peak \( (p = 0.667) \) and mean \( (p = 0.804) \) IOP during the follow-up period after LPI were similar in the three groups. The mean number of antiglaucoma medications during follow-up was higher in the PIC group (1.2) than in the PB (0.7) and TPIR (0.6) groups.

Table 5 shows the short-term changes in angle parameters in the three groups. Before LPI, the angles were narrower in the PB than in the PIC group. Compared with angle parameters before LPI, AOD500 \( (p < 0.001) \) and TISA500 \( (p = 0.006) \) 1 month after LPI were significantly widened only in the PB group. Angle parameters in the TPIR were slightly higher 1 month after than before LPI, although the differences were not statistically significant. In the PIC group, however, angle parameters showed a slight, but not significant, decrease 1 month after compared with before LPI.

Table 6 shows the long-term changes in angle parameters after LPI for the three groups. None of these groups showed significant changes in angle parameters from 1 month after LPI to their last visit. AOD500 and TISA500 decreased slightly in the TPIR group, but increased slightly in the other two groups. At last follow-up visit, TISA500 was significantly smaller in the TPIR than in the other two groups \( (p = 0.032) \).

**Representative cases**

Fig. 1 and 2 show representative eyes with PB and PIC, respectively, with all AS-OCT images obtained before LPI. The angle was wider in the eye with PIC (Fig. 2) than in the eye with PB (Fig. 1). Serial VF tests showed the development and progression of glaucomatous VF defects in the PIC eye (Fig. 2), whereas VF results remained normal in the PB eye (Fig. 1) during the course of follow-up.

**Discussion**

This study found that PB was the most common mechanism of PAC, being present in 47% of the eyes examined.
During a mean follow-up of 5.3 years, 18 (16%) eyes showed VF progression, according to EMGT criteria. A previous study assessing 5 years progression to PACG in a population-based cohort of PAC reported that 28.5% (8/28) of eyes showed new-onset glaucomatous VF defect; however, no features were found to predict progression. The pres-

Figure 1. Two representative cases which classified as pupillary block based on their initial anterior segment-optical coherence tomography (AS-OCT) images. AS-OCT images showed closed angle with marked iris convexity. Serial visual field tests remained stable during follow up period.

Figure 2. Two representative eyes classified as having plateau iris configuration based on their initial anterior segment-optical coherence tomography (AS-OCT) images. AS-OCT images showed the peripheral iris arising from its root in apposition or in close proximity to the angle wall and then turning sharply away from the angle toward the visual axis, as well as a centrally plateau-like flat iris plane. Serial visual field tests showed significant widening of initial scotomas.
ent study found that, compared with eyes in the PB group, eyes in the PIC group tended to require more antiglaucoma medications and showed limited IOP lowering and angle widening in response to LPI, resulting in a greater degree of VF progression.

Many studies have reported the effect of LPI on AS morphological changes in eyes with angle closure.\textsuperscript{13,18,19,23-25} Fewer studies, however, have compared AS changes in groups assorted by angle-closure mechanisms. We previously reported wider angles after LPI in eyes with PB, but not PIC.\textsuperscript{8} In addition, eyes classified as having PIC-like features based on cluster analysis showed less angle widening 2 weeks after LPI than eyes classified as having PB-like features. Moreover, angle widening 2-3 weeks after LPI was lower in eyes with thicker than thinner peripheral irises at baseline.\textsuperscript{26} Similarly, PACS eyes with thicker peripheral irises at baseline showed less angle widening both 2 weeks and 3 years after LPI than eyes with thinner peripheral irises.\textsuperscript{14} These findings suggest that the effects of LPI on angle widening are affected by baseline iris configuration or thickness. Similarly, the present study found that AOD500 and TISA500 measured 1 month after LPI were significantly wider only in the PB group. By contrast, these angles were slightly narrower in the PIC group 1 month after LPI and showed gradual long-term narrowing after LPI in the TPIR group.

Our group previously assessed the effect of LPI on IOP based on mechanism of angle closure, finding that LPI had a greater effect on IOP lowering in the PB group than in other groups, including eyes with PIC and TPIR.\textsuperscript{8,10} The present study assessed the effects of LPI on IOP and number of antiglaucoma medications. We found that IOP was significantly reduced after LPI only in the PB group, whereas the number of antiglaucoma medications was significantly increased after LPI only in the PIC group. During the follow-up period after LPI, patients with PIC used a higher mean number of antiglaucoma medications (1.2) than those with PB (0.7) or TPIR (0.6), indicating that LPI had little effect on IOP lowering in PIC and that these eyes required more intense antiglaucoma treatment than eyes with PB or TPIR.

In our cohort, 6.6% (6/90) of participants who were initially diagnosed with PACG suspect, having no glaucomatous optic disc change or VF defects, progressed to PACG over a mean follow-up period of 5.3 years. By comparison, a population-based study reported that 28.5% of eyes with PAC (excluding those with PACS) progressed to PACG during the 5 years follow-up period.\textsuperscript{4} Most (19/28, 68%) of the eyes in that study, however, did not undergo LPI during follow-up.\textsuperscript{4} By contrast, all eyes in our cohort underwent LPI and were examined regularly by a glaucoma specialist. Furthermore, the present study included eyes with PACS and PAC, and combined them into a group with PACG suspect. All of these factors may have contributed to the relatively lower rate of VF progression in our cohort than in the previous study.

Our multivariate Cox regression analysis revealed that PIC was associated with a greater risk of VF progression than PB, even after adjusting for other covariates including age, IOP, or initial PACG (relative to PACG suspect). Studies using various imaging modalities have found PIC in about one-third of eyes with PACS or PAC after LPI.\textsuperscript{27,28} However, the clinical significance of PIC after LPI remains unclear. Our longitudinal study results may provide valuable information on the clinical importance of PIC after LPI.

LPI is usually performed as a prophylactic treatment in eyes with asymptomatic angle closure. However, its efficacy in preventing progression to PACG in all eyes remains unknown.\textsuperscript{1} The primary effect of LPI has been regarded as angle widening through the reduction of iris curvature.\textsuperscript{8,25} However, this effect would not last long in all eyes, with angle width reported to decrease starting 18 months after LPI.\textsuperscript{18} The clinical effect of LPI on disease progression, including VF progression, remains undetermined. LPI has been reported to induce severe AS inflammation and iris pigment dispersion in some eyes, especially those with a thicker iris, causing a significant spike in IOP.\textsuperscript{1,29} More specific guidelines are required for the use of LPI in the treatment of eyes with asymptomatic angle closure.\textsuperscript{1} Findings from the present study, such as the lack of effect of LPI on angle and IOP over the short- and long-term in non-PB eyes (PIC, TPIR), may provide a framework for specifying indi-
This study had several limitations. Similar to previous studies,\textsuperscript{5-8} we classified the mechanisms of angle closure based on AS-OCT images alone, not with ultrasound biomicroscopy (UBM). Although AS-OCT may provide limited visualization of structures behind the iris, UBM also has some disadvantages, including the need for direct contact with the eyeball, making patients uncomfortable, and its relatively longer examination time. Furthermore, UBM is performed when patients are in supine position, a less physiologic posture than that of AS-OCT, in which patients are sitting. Indirect signs of AS-OCT images, including a central flat iris plane and the contour of the peripheral iris root, would be accurate enough to diagnose PIC.\textsuperscript{\textdegree} Another limitation may be the subjective nature of our classification method, in which eyes were classified using AS-OCT images taken before LPI without any quantitative analysis. This intuitive, qualitative method may be a better reflection of the real clinical situation and has been validated by many previous studies.\textsuperscript{5-8} However, more standardized and universally accepted classification criteria would be required for further studies. Another limitation was that the participants in this study were not population-based cohorts, with all participants regularly examined and administered antiglaucoma medications if needed. Thus, the natural course of patients classified as having PB, PIC, and TPIR may be different from that in our cohort. Clinically, however, there are ethical difficulties designing a study assessing the pure natural course of a disease without treating patients.

To summarize, the current study found that non-PB eyes, especially those with PIC, were at greater risk of future VF progression and using more antiglaucoma medications, than PB eyes after LPI. IOP lowering and angle widening after LPI were more limited in non-PB than in PB eyes. Non-PB eyes may show a poorer prognosis after LPI than PB eyes. A more standardized method of classifying mechanisms of angle closure is required.

Conflicts of Interest
The authors declare no conflicts of interest relevant to this article.

References
1. Sun X, Dai Y, Chen Y, et al. Primary angle closure glaucoma: what we know and what we don’t know. Prog Retin Eye Res 2017;57:26-45.
2. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol 2002;86:238-42.
3. Thomas R, George R, Parikh R, et al. Five year risk of progression of primary angle closure suspects to primary angle closure: a population based study. Br J Ophthalmol 2003;87:450-4.
4. Thomas R, Parikh R, Muliyil J, Kumar RS. Five-year risk of progression of primary angle closure to primary angle closure glaucoma: a population-based study. Acta Ophthalmol Scand 2003;81:480-5.
5. Moghimi S, Zandvakil N, Vahedian Z, et al. Acute angle closure: qualitative and quantitative evaluation of the anterior segment using anterior segment optical coherence tomography. Clin Exp Ophthalmol 2014;42:615-22.
6. Shabana N, Aquino MC, See J, et al. Quantitative evaluation of anterior chamber parameters using anterior segment optical coherence tomography in primary angle closure mechanisms. Clin Exp Ophthalmol 2012;40:792-801.
7. Zhang Y, Li SZ, Li L, et al. Quantitative analysis of iris changes following mydriasis in subjects with different mechanisms of angle closure. Invest Ophthalmol Vis Sci 2015;56:563-70.
8. Kwon J, Sung KR, Han S. Long-term changes in anterior segment characteristics of eyes with different primary angle-closure mechanisms. Am J Ophthalmol 2018;191:54-63.
9. Chansangpetch S, Rojanapongpun P, Lin SC. Anterior segment imaging for angle closure. Am J Ophthalmol 2018;188:xvi-xxix.
10. Kwon J, Sung KR, Han S, et al. Subclassification of primary angle closure using anterior segment optical coherence tomography and ultrasound biomicroscopic parameters. Ophthalmology 2017;124:1039-47.
11. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191-4.
12. Han S, Sung KR, Lee KS, Hong JW. Outcomes of laser peripheral iridotomy in angle closure subgroups according to anterior segment optical coherence tomography parameters. Invest Ophthalmol Vis Sci 2014;55:6795-801.
13. Lee KS, Sung KR, Shon K, et al. Longitudinal changes in anterior segment parameters after laser peripheral iridotomy assessed by anterior segment optical coherence
tomography. Invest Ophthalmol Vis Sci 2013;54:3166-70.
14. Sung KR, Lee KS, Hong JW. Baseline anterior segment parameters associated with the long-term outcome of laser peripheral iridotomy. Curr Eye Res 2015;40:1128-33.
15. Wang N, Wu H, Fan Z. Primary angle closure glaucoma in Chinese and Western populations. Chin Med J (Engl) 2002;115:1706-15.
16. He M, Foster PJ, Johnson GJ, Khaw PT. Angle-closure glaucoma in East Asian and European people. Different diseases? Eye (Lond) 2006;20:3-12.
17. Lee KS, Sung KR, Kang SY, et al. Residual anterior chamber angle closure in narrow-angle eyes following laser peripheral iridotomy: anterior segment optical coherence tomography quantitative study. Jpn J Ophthalmol 2011;55:213-9.
18. Jiang Y, Chang DS, Zhu H, et al. Longitudinal changes of angle configuration in primary angle-closure suspects: the Zhongshan Angle-Closure Prevention Trial. Ophthalmology 2014;121:1699-705.
19. Ang BC, Nongpiur ME, Aung T, et al. Changes in Japanese eyes after laser peripheral iridotomy: an anterior segment optical coherence tomography study. Clin Exp Ophthalmal 2016;44:159-65.
20. Heijl A, Leske MC, Bengtsson B, et al. Measuring visual field progression in the Early Manifest Glaucoma Trial. Acta Ophthalmol Scand 2003;81:286-93.
21. Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol 2003;121:48-56.
22. Öhnell H, Heijl A, Brenner L, et al. Structural and functional progression in the early manifest glaucoma trial. Ophthalmology 2016;123:1173-80.
23. Zheng C, Guzman CP, Cheung CY, et al. Analysis of anterior segment dynamics using anterior segment optical coherence tomography before and after laser peripheral iridotomy. JAMA Ophthalmol 2013;131:44-9.
24. Zebardast N, Kavitha S, Krishnamurthy P, et al. Changes in anterior segment morphology and predictors of angle widening after laser iridotomy in South Indian eyes. Ophthalmology 2016;123:2519-26.
25. How AC, Baskaran M, Kumar RS, et al. Changes in anterior segment morphology after laser peripheral iridotomy: an anterior segment optical coherence tomography study. Ophthalmology 2012;119:1383-7.
26. Lee RY, Kasuga T, Cui QN, et al. Association between baseline iris thickness and prophylactic laser peripheral iridotomy outcomes in primary angle-closure suspects. Ophthalmology 2014;121:1194-202.
27. Kumar RS, Baskaran M, Chew PT, et al. Prevalence of plateau iris in primary angle closure suspects an ultrasound biomicroscopy study. Ophthalmology 2008;115:430-4.
28. Kumar RS, Tantisevi V, Wong MH, et al. Plateau iris in Asian subjects with primary angle closure glaucoma. Arch Ophthalmol 2009;127:1269-72.
29. Wang W, Zhou M, Huang W, et al. Does acute primary angle-closure cause an increased choroidal thickness? Invest Ophthalmol Vis Sci 2013;54:3538-45.
30. Parc C, Laloum J, Bergès O. Comparison of optical coherence tomography and ultrasound biomicroscopy for detection of plateau iris. J Fr Ophthalmol 2010;33:266.e1-3.