Plateau Iris and Severity of Primary Angle Closure Glaucoma



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• PURPOSE: To compare the distribution of plateau iris in eyes across varying severity of primary angle closure glaucoma (PACG) using standardized ultrasound biomicroscopy (UBM) criteria.

• DESIGN: Cross-sectional study.

• METHODS: UBM was performed on 210 patients with PACG who had previously undergone laser peripheral iridotomy. Plateau iris was defined as the presence of all the following UBM criteria in ≥ 2 quadrants of the angle: anteriorly directed ciliary body, absent ciliary sulcus, iris angulation, flat iris plane, and iridotrabecular contact. Disease severity was based on the visual field mean deviation (MD) and classified as early-to-moderate (MD ≥ -12 dB), advanced (-12.01 dB to -20 dB), and severe (MD < -20 dB).

• RESULTS: Of 210 subjects recruited, 23 were excluded because of poor quality UBM images. The remaining 187 patients were categorized as having early-to-moderate (n = 103), advanced (n = 38), and severe PACG (n = 46). Of these subjects, 48.1% were male, and 90.9% were of Chinese ethnicity. The overall proportion of plateau iris was 36.9%, with 32.0% (33/103) in early-to-moderate, 34.2% (13/38) in advanced, and 50% (23/46) in severe PACG (P = .03), comparing severe PACG with early-to-moderate groups). Among the severe PACG group, those with plateau iris configuration had significantly smaller anterior chamber area (P = .03) and volume (P = .01) compared with those without plateau iris.

• CONCLUSION: The higher proportion of plateau iris configuration in eyes with severe PACG compared with early-to-moderate PACG suggest that this may be a contributory factor for disease severity. (Am J Ophthalmol 2020;220:1–8. © 2020 Elsevier Inc. All rights reserved.)

Accepted for publication Jul 21, 2020.

Inquiries to Tin Aung, Singapore Eye Research Institute, The Academia, 20 College Road, Discovery Tower Level 6, Singapore 169856; e-mail: aung.tin@singhealth.com.sg **P**RIMARY ANGLE CLOSURE GLAUCOMA (PACG), A MAjor form of glaucoma in Asia estimated to affect >20 million people,¹ has higher rates of blindness at presentation compared with primary open-angle glaucoma.^{2,3} The reason(s) why some PACG eyes develop advanced disease is not known. Importantly, we currently have no data to inform clinical practice about which individuals in the early stages of disease are at greater risk for development of advanced PACG and blindness.

Laser peripheral iridotomy (LPI) is commonly performed as the initial treatment option in the management of PACG because it relieves pupil block, flattens the iris, and widen the angles. However, several studies have reported that despite a patent LPI, many eyes have residual angle closure,^{4–6} highlighting the importance of non– pupil block mechanisms in PACG.

Advances in anterior segment imaging have augmented our understanding of the role of non-pupil block mechanisms such as plateau iris in the pathogenesis of PACG.⁷⁻ ⁹ Plateau iris results from large or anteriorly positioned ciliary processes, which push up the peripheral iris and cause apposition to the trabecular meshwork despite LPI. It has been shown to be an important cause of persistent angle closure after LPI as well as after lens extraction. Using standardized ultrasound biomicroscopy (UBM)defined criteria,¹⁰ the proportion of plateau iris was found to be 18.2%-36.9% in eves with PACG after LPI.^{11–15} Whether this proportion varies with worsening PACG disease severity is unknown. We hypothesized that the proportion of plateau iris will be greater in post-LPI eyes with severe PACG compared with mild cases because this may be a contributory factor for disease severity.

The purpose of this study was to compare the distribution of plateau iris in eyes across varying PACG disease severity using standardized UBM criteria. Disease severity was based on the visual field mean deviation (MD) and classified as early-to-moderate PACG, advanced PACG, and severe PACG.¹⁶

METHODS

APPROVAL FOR THE STUDY WAS GRANTED BY THE INSTITUtional review board of the SingHealth Centralized Institutional Review Board. The study was conducted in accordance with the tenets of the Declaration of Helsinki, and written informed consent was obtained from all subjects before study enrollment.

From the Singapore Eye Research Institute (M.E.N., S.V., T.A.T., T.T.W., T.A.), the Singapore National Eye Centre (M.E.N., T.T.W., S.A.P., T.A.), Duke-National University of Singapore Medical School (M.E.N., T.T.W., S.A.P., T.A.), and the Department of Ophthalmology (T.A.), Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

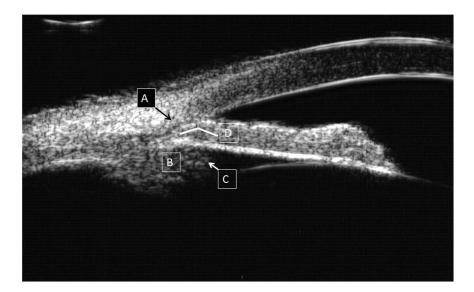


FIGURE 1. Ultrasound biomicroscopy image of a quadrant of an eye with primary angle closure glaucoma with plateau iris showing irido-angle contact (A), anteriorly directed ciliary process (B), absent ciliary sulcus (C), and iris angulation and flat iris plane (D).

This was a prospective phenotyping study of PACG details of which have been described previously.¹⁵ Briefly, subjects diagnosed with PACG were recruited from glaucoma clinics of the Singapore National Eve Centre. All subjects had undergone LPI before recruitment into the study, but we excluded those who had undergone any other surgical procedure including argon laser peripheral iridoplasty. All subjects underwent a standardized ophthalmic examination that included testing of visual acuity, slitlamp examination, measurement of intraocular pressure (IOP) with Goldmann applanation tonometry, stereoscopic evaluation of the optic disc, visual field testing (Humphrey Visual Field Analyzer II; Carl Zeiss Meditec, Dublin, California, USA, using the Swedish interactive threshold algorithm with a 24-2 standard test pattern), and imaging with UBM and anterior segment optical coherence tomography (ASOCT). Static gonioscopy was performed using a Goldmann 2-mirror lens by an experienced examiner under dark conditions at high magnification (\times 16). Indentation gonioscopy with a Sussman 4mirror lens was used to discern the presence or absence of peripheral anterior synechiae (PAS). A-scan ultrasonography (model US-800; Nidek Co, Ltd, Tokyo, Japan) was used to measure axial length (AL) and lens thickness (LT).

PACG was defined as the presence of glaucomatous optic neuropathy (defined as loss of neuroretinal rim with a vertical cup-to-disc ratio (VCDR) of >0.7 or notching with nerve fiber layer defect attributable to glaucoma) with compatible visual field loss, in association with a closed angle (presence of $\geq 180^{\circ}$ angle in which the posterior trabecular meshwork was not visible on nonindentation gonioscopy). We used the glaucoma staging system by Mills and associates¹⁶ to categorize the severity of glaucoma based on visual field MD as early-to-moderate (MD \geq -12 dB), advanced (-12.01 dB to -20 dB), and severe (MD < -20 dB).¹⁷ Presenting IOP was defined as the first IOP reading measured by Goldmann applanation tonometry before the initiation of IOP-lowering treatment (medical or laser). Age at diagnosis was the age at which the subject was diagnosed with PACG. These data were extracted from the case records.

Details of the UBM technique and grading of images have been described previously.¹⁵ In brief, UBM was performed with the patient in a supine position in darkroom conditions using a 50-MHz transducer (Paradigm Medical Instruments, Salt Lake City, Utah, USA, or Suowei Electronic Technology, Tianjin, China). Radial scans were performed in the inferior, temporal, superior, and nasal quadrants of the angle. One scan in each quadrant per eye was recorded for analysis. Plateau iris was defined as the presence of all the following UBM criteria¹⁰ in ≥ 2 quadrants of the angle: 1) the ciliary process was anteriorly directed, supporting the peripheral iris so that it was parallel to the trabecular meshwork; 2) the iris root had a steep rise from its point of insertion, followed by a downward angulation from the corneoscleral wall; 3) presence of a central flat iris plane; 4) an absent ciliary sulcus; and 5) iridotrabecular contact (above the level of the scleral spur) in the same quadrant (Figure 1).

Details of the ASOCT imaging have been described previously.¹⁸ In brief, ASOCT (Visante; Carl Zeiss Meditec) imaging was performed for all participants under standardized dark conditions (0 lux) by a single operator. The scans were centred on the pupil and a single cross-sectional horizontal image (nasal-temporal angles at 0-180°) was obtained and evaluated for each subject. The only observer input was to determine the position of the scleral spurs. The images were processed using customized software, the Zhongshan

TABLE 1. Differences in the Proportion of Plateau Iris Across Primary Angle Closure Glaucoma Disease Severity

	Early-to-Moderate vs Advanced PACG	Advanced vs Severe PACG	Early-to-Moderate vs Severe PACC
Difference in proportion	2.2%	15.8%	18%
95% confidence interval	-13.9% to 20.1%	-5.3% to 34.8%	1.2%-34.1%
P value	.80	.14	.03

	Early-to-Moderate, n = 103	Advanced PACG, n = 38	Severe PACG $n = 46$
Plateau iris by number of quadrants, <i>n</i> (%)			
0-1	70 (68.0)	25 (65.8)	23 (50.0)
2	17 (16.5)	5 (13.2)	11 (23.9)
3	10 (9.7)	6 (15.8)	9 (19.6)
4	6 (5.8)	2 (5.2)	3 (6.5)
Quadrant-wise distribution of plateau iris, n	<i>n</i> = 61	<i>n</i> = 28	<i>n</i> = 35
(%)			
Superior	35 (57.4)	19 (67.9)	22 (62.9)
Nasal	18 (29.5)	9 (32.1)	15 (42.9)
Inferior	34 (55.7)	14 (50.0)	17 (48.6)
Temporal	29 (47.5)	9 (32.1)	19 (54.3)

TABLE 2. Distribution of Plateau Iris by Quadrants Across Primary Angle Closure Glaucoma Disease Severity

Angle Assessment Program (ZAAP, Guangzhou, China),¹⁹ by a single experienced observer (M.E.N.) who was masked to the clinical data. The algorithm then automatically calculated the anterior segment parameters. The following anterior chamber parameters were assessed: angle opening distance 750 µm from the scleral spur (AOD750), anterior chamber depth, width, area, and volume, iris thickness 750 µm from the scleral spur (IT750), and lens vault (LV).

One eye of each subject was analyzed. The study eye was randomly selected for bilateral cases, whereas the affected eye was used in unilateral cases. Statistical analyses were performed using MedCalc for Windows (version 15.0; MedCalc Software, Ostend, Belgium). Comparison of the proportion of plateau iris between the 2 groups was assessed by χ^2 test, and the difference between the 2 proportions and a 95% confidence interval (CI) for this difference was also computed. Differences in mean values of parametric data between these 2 groups were examined using the independent samples Student *t* test.

RESULTS

UBM IMAGES OF 210 SUBJECTS WITH PACG WERE OBTAINED. Of these, 23 were excluded because of poor quality images,

and the remaining 187 were categorized as early-tomoderate PACG (n = 103), advanced (n = 38), and severe PACG (n = 46). Of these subjects, 48.1% were male, and 90.9% were of Chinese ethnicity. The mean visual field MD and VCDR were -12.7 ± 8.9 dB and 0.77 ± 0.14 , respectively.

The overall proportion of plateau iris was 36.9%. The proportion of plateau iris by severity was 32.0% (33/103) in the early-to-moderate, 34.2% (13/38) in the advanced, and 50% (23/46) in the severe PACG groups, respectively. Comparison of the differences in the proportion between the 3 groups is shown in Table 1. We found a significantly greater proportion of plateau iris in the severe PACG group compared with the early-to-moderate group (P = .03; 95% CI of the difference 1.2%-34%). No significant differences were found between early-to-moderate and advanced PACG (P = .80) and between advanced and severe PACG (P = .14). Table 2 shows the distribution of plateau iris by quadrants. On quadrant-wise analysis, the highest proportion of plateau iris was found in the superior quadrant across the 3 severity groups.

We found a significant difference in the proportion of plateau iris between the early-to-moderate and severe PACG groups, and therefore we then performed a subanalysis comparing the demographic and anterior segment

TABLE 3. Comparison of Ocular Parameters in Severe a	nd Early-to-Moderate Prima	ary Angle Closure Glaucoma ($n = 149$)

	Severe PACG, n = 46	Early-to-Moderate PACG, n = 103	<i>P</i> Value
Age at diagnosis (y)	62.5 ± 9.6	66.3 ± 9.0	.04
Presenting IOP (mm Hg)	29.4 ± 12.0	20.9 ± 8.8	.001
Visual field mean deviation (dB)	-26.56 ± 3.50	-6.00 ± 2.79	<.001
Vertical cup-to-disc ratio	0.87 ± 0.07	0.73 ± 0.15	<.001
Axial length (mm)	23.15 ± 1.16	23.11 ± 1.06	.86
Lens thickness (mm)	4.27 ± 0.99	4.24 ± 0.94	.87
Angle opening distance 750 (mm)	0.24 ± 0.11	0.24 ± 0.10	.96
Anterior chamber depth (mm)	2.14 ± 0.31	$\textbf{2.19} \pm \textbf{0.30}$.37
Anterior chamber width (mm)	11.45 ± 0.43	11.44 ± 0.42	.97
Anterior chamber area (mm ²)	15.75 ± 2.74	16.27 ± 2.70	.28
Anterior chamber volume (mm ³)	103.0 ± 21.6	106.1 ± 21.4	.41
Iris thickness 750 (mm)	0.48 ± 0.07	0.46 ± 0.08	.36
Lens vault (µm)	849.1 ± 252.5	840.6 ± 279.0	.86
Gonio Shaffer grading	1.73 ± 0.84	$\textbf{2.18} \pm \textbf{0.69}$.001
Total extent of PAS	$\textbf{2.54} \pm \textbf{3.23}$	1.05 ± 1.92	.001
Quadrant-wise distribution of presence of PAS,			
n (%)			
Superior	22 (47.8)	22 (21.4)	.001
Nasal	12 (26.1)	15 (14.6)	.09
Inferior	14 (30.4)	17 (16.5)	.05
Temporal	12 (26.1)	13 (12.6)	.04

IOP = intraocular pressure; PACG = primary angle closure glaucoma; PAS = peripheral anterior synechiae. Values are mean \pm SD unless otherwise noted.

parameters between the 2 groups (Table 3). Subjects with severe disease were diagnosed at a significantly younger age (62.5 \pm 9.6 years) compared with those with early-to-moderate PACG (66.3 \pm 9.0 years, P = .04), they had a significantly higher presenting IOP (29.4 \pm 12.0 vs 20.9 \pm 8.8 mm Hg, P = .001), and greater extent of PAS (2.54 \pm 3.23 vs 1.05 \pm 1.92, P = .001). The highest proportion of PAS was in the superior quadrant in both groups, with significant differences observed in the superior (P = .001) and temporal (P = .04) distribution of PAS between the groups. Comparison between the 2 groups revealed no significant differences in any of the ASOCT-based anterior segment parameters (Table 3).

Among the severe PACG group, those with plateau iris syndrome were found to have significantly smaller AOD750 (P = .001), anterior chamber area (P = .03) anterior chamber volume (P = .01), greater extent of PAS (P = .004) compared with those without plateau iris (Table 4). A significantly greater distribution of PAS in the superior (P = .003) and temporal (P = .01) quadrants of eyes with plateau iris was also observed. Amongst the early-to-moderate group (Table 5), the IT750 was significantly thicker in those with plateau iris compared with those with no plateau iris (0.50 ± 0.09 mm vs 0.45 ± 0.08 mm; P = .02). No significant differences were observed in the extent or distribution of PAS.

DISCUSSION

IN THIS STUDY, WE INVESTIGATED THE DISTRIBUTION OF plateau iris amongst eyes with varying PACG disease severity. A higher proportion of plateau iris was observed in severe PACG compared with early-to-moderate PACG, and these subjects were also characterized by a younger age of onset of PACG, higher presenting IOP, and greater extent of PAS.

Several studies have reported varying degrees of persistent angle closure after LPI in patients with PACG, with plateau iris the most common etiology.^{14,20–23} Using standardized UBM criteria, the proportion of plateau iris in PACG eyes after LPI was reported to be around 30%.^{12–14} With persistent angle closure caused by plateau iris, there is a tendency toward development of PAS and subsequent elevated IOP, which in the long term can lead to progression of glaucoma.

Our quadrant-wise analysis showed that the greatest proportion of plateau iris was in the superior quadrant. Likewise, PAS was also most commonly observed in the superior quadrant, and with a greater proportion in eyes with plateau iris. It is not known whether the closed angles in eyes with plateau iris predisposes them to a greater risk of development of PAS; such as association is difficult to establish in the current study. It is also important to

TABLE 4. Comparison of Biometric Parameters in Severe Primary Angle Closure Glaucoma Group With and Without Plateau Iris (<i>n</i> =
46)

	Plateau Iris, n = 23	No Plateau Iris, n = 23	P Value
Age at diagnosis (y)	63.2 ± 10.2	61.8 ± 9.1	.67
Presenting IOP (mm Hg)	30.5 ± 13.0	28.1 ± 11.0	.59
Visual field mean deviation (dB)	-27.46 ± 3.23	-25.52 ± 3.61	.08
Vertical cup-to-disc ratio	0.87 ± 0.06	0.88 ± 0.08	.62
Axial length (mm)	22.91 ± 0.91	23.38 ± 1.34	.17
Lens thickness (mm)	4.45 ± 0.92	4.09 ± 1.04	.22
Angle opening distance 750 (mm)	0.19 ± 0.09	0.29 ± 0.11	.001
Anterior chamber depth (mm)	2.07 ± 0.31	2.22 ± 0.30	.09
Anterior chamber width (mm)	11.43 ± 0.44	11.46 ± 0.42	.80
Anterior chamber area (mm ²)	14.91 ± 2.50	16.57 ± 2.76	.03
Anterior chamber volume (mm ³)	95.5 ± 18.6	110.4 ± 22.2	.01
Iris thickness 750 (mm)	0.45 ± 0.05	0.44 ± 0.07	.89
Lens vault (µm)	881.6 ± 275.1	816.6 ± 229.2	.38
Gonio Shaffer grading	1.40 ± 0.71	2.07 ± 0.85	.006
Total extent of PAS	3.87 ± 3.32	1.22 ± 2.58	.004
Quadrant-wise distribution of presence of			
PAS, <i>n</i> (%)			
Superior	16 (69.6%)	6 (26.1%)	.003
Nasal	8 (34.8%)	4 (17.4%)	.18
Inferior	11 (47.8%)	3 (13.0%)	.01
Temporal	8 (34.8%)	4 (17.4%)	.18

 $IOP = intraocular pressure; PACG = primary angle closure glaucoma; PAS = peripheral anterior synechiae Values are mean <math>\pm$ SD unless otherwise noted.

acknowledge the potential confounding effect of LPI in the development of PAS, since the common site for LPI is the superior part of the iris.

Interestingly, our study also revealed significant differences in the mean age of diagnosis of PACG in subjects with severe compared with early-to-moderate PACG. This suggests that the subjects in the severe group either developed severe disease at an earlier age or underwent rapid disease progression. When compared with the earlyto-moderate group, the patients with severe PACG also had a greater IOP at presentation. Of note, none of our subjects had previously had an acute attack of angle closure. It is plausible that the asymptomatic and often insidious nature of PACG may have deterred these individuals from seeking treatment at an earlier disease stage. While it is imperative to recognize the factors that may confer predispositions toward development of severe disease, the substantial clinical heterogeneity of PACG^{18,24} renders it likely that susceptibility to severe disease is mediated by distinct mechanisms that may be specific to individual patients. Apart from plateau iris, other factors including biometric features and genetic factors may contribute to the predisposition toward severe PACG or blindness.

The plateau iris eyes in the severe PACG group in our study were found to have smaller anterior chamber dimen-

sions compared with those without plateau iris. Our findings somewhat concur with the those of Kwon and associates²⁵ when they retrospectively evaluated the long-term changes in the anterior segment of 133 angleclosure eyes categorized according to disease mechanisms, namely pupillary block, plateau iris configuration, thick peripheral iris roll, and exaggerated LV based on baseline ASOCT before LPI. They found that in all 4 groups, the anterior chamber depth decreased and LV increased over time; however, the rate of decrease in anterior chamber depth and increase in LV was greatest in the plateau iris group. Also, angle widening was reported in the pupillary block and thick peripheral iris roll groups, but not the in the plateau iris group.²⁵

Despite the various available treatment options for plateau iris,^{26–29} the optimal choice of management is still undetermined because there have been no randomized controlled trials that have evaluated the efficacy of these treatment modalities. Lens extraction not only results in deepening of the anterior chamber and widening of the angles in eyes with PACG, but UBMbased studies have also shown that it reduces the anterior positioning of the ciliary processes.^{23,28,30} However, in 1 study which solely comprised of eyes with plateau iris configuration, Tran and associates²⁹ found that the

	Plateau Iris, n = 33	No Plateau Iris, n = 70	P Value
Age at diagnosis (y)	64.8 ± 9.6	67.2 ± 8.6	.26
Presenting IOP (mm Hg)	22.4 ± 12.0	20.1 ± 6.2	.30
Visual field mean deviation (dB)	-6.68 ± 2.67	-5.66 ± 2.80	.08
Vertical cup-to-disc ratio	0.77 ± 0.11	0.71 ± 0.16	0.05
Axial length (mm)	23.04 ± 1.11	23.15 ± 1.04	.63
Lens thickness (mm)	4.22 ± 0.99	4.26 ± 0.92	.84
Angle opening distance 750 (mm)	0.20 ± 0.11	0.26 ± 0.08	.007
Anterior chamber depth (mm)	2.20 ± 0.28	$\textbf{2.19} \pm \textbf{0.32}$.88
Anterior chamber width (mm)	11.44 ± 0.46	11.45 ± 0.41	.91
Anterior chamber area (mm ²)	16.24 ± 2.76	16.29 ± 2.69	.93
Anterior chamber volume (mm ³)	103.3 ± 23.1	107.2 ± 20.5	.55
Iris thickness 750 (mm)	0.50 ± 0.09	0.45 ± 0.08	.009
Lens vault (μm)	806.5 ± 217.8	856.6 ± 300.9	.39
Gonio Shaffer grading	1.96 ± 0.75	2.28 ± 0.64	.02
Total extent of PAS	1.48 ± 2.51	0.84 ± 1.55	.18
Quadrant-wise distribution of presence of			
PAS, <i>n</i> (%)			
Superior	9 (27.3)	13 (18.6)	.32
Nasal	8 (24.2)	7 (10.0)	.06
Inferior	5 (15.2)	12 (17.1)	.80
Temporal	5 (15.2)	8 (11.4)	.60

TABLE 5. Comparison of Biometric Parameters in Early-to-Moderate Primary Angle Closure Glaucoma Group With and WithoutPlateau Iris (n = 103)

IOP = intraocular pressure; PACG = primary angle closure glaucoma; PAS = peripheral anterior synechiae Values are mean \pm SD unless otherwise noted.

iridociliary apposition persisted after lens extraction. This suggests that lens extraction may not always favorably alter the angle anatomy in eyes with plateau iris.²⁹ Lens extraction and endocyclophotocoagulation has been considered as an alternative treatment option for PACG eyes with plateau iris.^{31,32} The endocyclophotocoagulation treatment was targeted specifically at what is believed to be the anatomic abnormality, the large ciliary processes which push up the peripheral iris and maintain its apposition to the trabecular meshwork. In both these studies, the authors found that the combined procedure resulted in opening of the anterior chamber angle and flattening of the ciliary processes in the treated areas. While Hollander and associates³¹ reported a significant reduction in the IOP and number of medications, Francis and associates³² found that the IOP did not change significantly at 6 months, but the average number of glaucoma medications per patient decreased.

Our study had several limitations. Our study sample was relatively small, and in particular, the sample size of the advanced PACG group (n = 38) may not have been sufficient to reveal significant differences in the proportion of plateau iris when compared with the severe PACG group. Our study was cross-sectional; therefore, we could only

assess associations and not causality. The clinic-based study comprised subjects that were followed-up in glaucoma clinics, and therefore it may not be possible to extrapolate these findings to all patients with PACG. The duration between LPI and study recruitment varied among subjects; this may have also impacted disease outcome because of differences in the disease management. However, these data were not available. We excluded subjects with previous surgery such as trabeculectomy or lens extraction in order to minimize this variation in management and to exclude changes in anterior segment anatomy caused by surgery. However, this may have inadvertently included mainly cases of PACG that were responsive to medical therapy. Lastly, our study population was predominantly Chinese, and it is not known if the results would be the same in other ethnic groups.

In summary, our findings of a greater proportion of plateau iris in severe PACG compared with early-tomoderate cases emphasizes the need to consider the presence of plateau iris as a possible factor for disease severity or worsening. Future research involving longitudinal study designs is warranted to better elucidate the optimum management strategy for patients with persistent angle closure after LPI that are caused by plateau iris.

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ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST. Funding/Support: Supported in part by grants from the National Medical Research Council, Singapore (NMRC/STAR/0023/2014 and MOH-000273). Financial Disclosures: Dr Nongpiur received an educational grant from Allergan. Dr Aung received grant support and honoraria and is a consultant for Alcon, Novartis, Santen, and Allergan. Dr Perera has received honoraria from Allergan, Santen, Alcon, Novartis, Leica, Ivantis, Glaukos, and Mundipharma and is a consultant for Allergan, Santen, Alcon, and Novartis. Dr Wong has received grant support and honoraria and is a consultant for Santen. Drs Verma and Tun indicate no financial conflict of interest. All authors attest that they meet the current ICMJE criteria for authorship.

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