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# Subclassification of Primary Angle Closure Using Anterior Segment Optical Coherence Tomography and Ultrasound Biomicroscopic Parameters

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***Purpose:*** To classify eyes with primary angle closure (PAC) in terms of the features visualized using anterior segment optical coherence tomography (AS-OCT) and ultrasound biomicroscopy (UBM).

***Design:*** Retrospective, observational study.

***Participants:*** A total of 73 eyes of 73 patients with PAC.

***Methods:*** Participants' eyes that had undergone laser peripheral iridotomy (LPI) were imaged using AS-OCT and UBM under the same lighting conditions. Anterior chamber depth, anterior chamber width, iris cross-sectional area, peripheral iris thickness, iris curvature, lens vault (LV), and angle opening distance 500 μm from the scleral spur (SS) were determined using the AS-OCT image; trabecular-ciliary process angle (TCA), trabecular-ciliary process distance (TCPD), and ciliary body (CB) thickness 1 mm posterior to the SS were estimated on the UBM image using ImageJ software (Wayne Rasband, National Institutes of Health, Rockville, MD). Iris insertion, iris angulation, iris convexity, presence of ciliary sulcus, irido-angle contact, and CB orientation assessed on the UBM image were included. Partitioning around the medoids algorithm was used for cluster analysis based on the parameters obtained using AS-OCT and UBM. Axial length and pupil diameter were incorporated into statistical models.

***Main Outcome Measures:*** Clinical and anatomic characteristics were compared between the clusters, as classified using the partitioning around medoids algorithm method.

***Results:*** Cluster analysis revealed that 2-group clustering produced the best results. The 2 clusters, which were defined in terms of parameters obtained using AS-OCT and UBM, showed differences in iris curvature (0.16±0.08 vs. 0.11±0.04 mm), TCA (91.0°±13.4° vs. 63.7°±6.2°), TCPD (0.99±0.22 vs. 0.78±0.16 mm), CB orientation (neutral/anterior, 35/13 vs. 0/25), and iris insertion (basal/middle/apical, 37/9/2 vs. 12/11/2). Pre-LPI intraocular pressure (IOP) (18.8±5.4 vs. 16.2±4.5 mmHg; $P = 0.037$) and percentage of IOP reduction after LPI (22.3%±17.9% vs. 8.3%±19.5%; $P < 0.003$) showed a significant difference between the 2 clusters.

***Conclusions:*** The most distinct difference between the 2 subgroups in the cluster analysis was TCA, suggesting that the position of the CB is important in subclassifying PAC. By using UBM, clinicians may obtain more clues about the mechanisms of PAC; in turn, they may learn to predict the IOP-lowering effects of LPI. *Ophthalmology 2017;■:1–9 © 2017 by the American Academy of Ophthalmology*

Primary angle-closure glaucoma (PACG) is one of the leading causes of blindness.[1–3] Primary angle closure (PAC) is principally caused by pupillary block (PB), which is defined as resistance to aqueous flow from the posterior chamber to the anterior chamber. For this reason, laser peripheral iridotomy (LPI), which eliminates PB, is the standard treatment for PAC. However, a considerable proportion of eyes with PAC develop peripheral anterior synechiae, and many show persistent angle closure or an increase in intraocular pressure (IOP) after LPI. Indeed, some studies have reported that LPI might not be effective in treating all narrow angles.[4–8] Therefore, several investigators have suggested that other pathogenic mechanisms contribute to PAC, such as forward movement of the lens or a plateau iris configuration.[9–12] Thus, some researchers have attempted to subclassify eyes with PAC to characterize these different disease entities using specific anatomic characteristics; to do so, they have used anterior segment optical coherence tomography (AS-OCT) images, which offer qualitative and quantitative features of the anterior chamber angle and anterior segment (AS).[13–16]

In a previous study in which we assessed eyes with PAC using AS-OCT images, we identified 2 distinct clusters that showed completely different features in terms of anterior chamber angle and AS.[13] In a follow-up study, we demonstrated that the outcomes of LPI differed between the 2 clusters, indicating that the mechanisms of PAC development also differ.[14] However, it was hard to determine the PAC mechanisms using only AS-OCT-derived parameters, because one possible cause of PAC is plateau iris, which



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can be diagnosed only if the structures behind the iris are assessed. Specifically, to elucidate the mechanism of PAC, the relationship between the iris and the ciliary body (CB) should be assessed, as should the size of the CB and the presence of a ciliary sulcus or other features not visualized using AS-OCT.

With the use of ultrasound biomicroscopy (UBM), which uses ultrasound to image the deeper structures of the eye, it may be possible to image structures behind the iris.[15,17] Thus, to test the hypothesis that PAC can be more accurately subclassified using both devices and that such subgrouping may elucidate the pathogenic mechanism of PAC, we performed both AS-OCT and UBM in the present study.

## Methods

### Subjects

We reviewed the medical records of consecutive patients with PAC or PACG who had visited the glaucoma clinic of Asan Medical Center, Seoul, South Korea, and met the inclusion criteria. Previously, we reported that PAC and PACG did not differ in terms of clustering or AS parameter characteristics.[13] In the present study, we pooled eyes with PAC or PACG and defined them as "angle-closure" eyes. The study was approved by the Institutional Review Board of Asan Medical Center and followed the tenets of the Declaration of Helsinki.

All participants underwent a complete ophthalmic examination, including a review of their medical history, measurement of best-corrected visual acuity (to confirm that visual acuity was adequate for automated perimetry), slit-lamp biomicroscopy, Goldmann applanation tonometry, gonioscopy, funduscopic examination using a 90- or 78-diopter lens, stereoscopic optic disc photography, retinal nerve fiber layer photography, measurement of central corneal thickness (DGH-550 instrument; DGH Technology Inc., Exton, PA), a visual field (VF) test (Humphrey field analyzer; Swedish Interactive Threshold Algorithm 24-2; Carl Zeiss Meditec, Dublin, CA), axial length measurement (IOLMaster; Carl Zeiss Meditec Inc.), UBM (HiScan; Optikon, Rome, Italy), and AS-OCT (Visante OCT, ver. 2.0; Carl Zeiss Meditec).

Primary angle closure or PACG was determined on the basis of gonioscopic examination. Specifically, PAC was diagnosed when an eye had an occludable angle (pigmented posterior trabecular meshwork was not visible on nonindentation gonioscopy for at least 180° in the primary position) and exhibited features indicative of trabecular obstruction by the peripheral iris—elevated IOP, peripheral anterior synechiae, iris whorling (distortion of the radially oriented iris fibers), "glaukomflecken" lens opacity, or excessive pigment deposition on the trabecular surface—without a glaucomatous optic disc or any VF change.[12,16,18] Eyes with PAC showing glaucomatous optic disc changes (neuroretinal rim thinning, disc excavation, or optic disc hemorrhage due to glaucoma) or a glaucomatous VF change (pattern standard deviation <5%, and values outside normal limits in the glaucoma hemifield test) were considered to have PACG.[18] Only reliable VF test results (false positives: <15%; false negatives: <15%; fixation loss: <20%) were included in the analysis. We excluded patients who (1) had used or were using topical or systemic medications that may have affected the angle or the pupillary reflex; (2) had a history of intraocular surgery, including cataract surgery, laser trabeculoplasty, and laser iridoplasty; and (3) were unable to fixate before the AS-OCT examination. Patients who answered any of the following criteria also were excluded: those with a history of (1) acute PAC (defined on the basis of ocular or periocular pain), (2) nausea or vomiting, or (3) intermittent blurred vision with haloes were also excluded; those with a presenting IOP more than 30 mmHg; and those who had experienced at least 3 of the following: conjunctival injections, corneal epithelial edema, mid-dilated unreactive pupil, or shallow anterior chamber.[19] All eyes were newly diagnosed cases, and AS-OCT and UBM were performed 2 weeks after LPI. The pre-LPI IOP was measured before both LPI and IOP-lowering medication in all participants. The IOP measured at 1 month after LPI was used for analysis. If both eyes qualified in terms of the inclusion criteria, the right eye was selected for analysis.

### Gonioscopy

Before AS-OCT and UBM, all patients underwent a slit-lamp examination and gonioscopy, which were conducted by an independent observer (K.R.S.) who has extensive experience performing such examinations. All eyes were examined using a Sussman 4-mirror gonioscope (Ocular Instruments, Bellevue, WA) in a darkened room (0.5 cd/m$^2$). Both static and dynamic gonioscopy were performed using the Sussman lens, with the eye in the primary gaze position. Indentation gonioscopy was performed to determine whether the angle closure was due to apposition or to peripheral anterior synechiae. To avoid miosis, the examiner took care to ensure that light did not fall on the pupil during the examinations.

### Anterior Segment Optical Coherence Tomography and Ultrasound Biomicroscopy Imaging

In all participants, AS-OCT was performed in terms of the nasal and temporal angle (0°−180°); the optical coherence tomography scanner was operated in the enhanced AS single mode (scan length: 16 mm; 256 A-scans). Ultrasound biomicroscopy was conducted under topical anesthesia using 0.5% proparacaine (Alcaine; Alcon, Fort Worth, TX). An eyecup was inserted that depended on the ocular aperture size, and it was filled with sterile normal saline. The subject was then asked to fixate on a ceiling target; the fellow eye was used to maintain accommodation and fixation. The UBM device was equipped with a 35-MHz transducer, which had a wide-view probe that enabled up to 70 μm of axial and lateral resolution in the AS, with a penetration of 7 to 8 mm.[20] Cross-sectional images were obtained from the nasal and temporal angles (0°−180°). All images were acquired under the same lighting conditions (3.25 cd/m$^2$) by a single, well-trained operator.

### Image Analysis

The AS parameters of the AS-OCT images were evaluated by a single examiner (J.K.) who was blinded to the other test results and clinical information of the participants. Anterior chamber depth, angle-opening distance 500 μm anterior to the scleral spur (SS), lens vault (LV), and anterior chamber width were measured by the in-built software of the AS-OCT scanner. Iris cross-sectional area, iris thickness 750 μm from the SS ($IT_{750}$), iris curvature, and anterior chamber area were determined using the AS-OCT images. Likewise, UBM-derived parameters, such as trabecular-ciliary process angle (TCA), trabecular-ciliary process distance (TCPD), and CB thickness 1 mm posterior to the SS were determined using the UBM images by another well-trained examiner (J.W.S.), who had been masked to all other tests, including the AS-OCT. We also assessed CB orientation (neutral/anterior), iris insertion (basal/middle/apical), iris angulation (none/mild/pronounced), iris