Dynamic Changes in Anterior Segment (AS) Parameters in Eyes with Primary Angle Closure (PAC) and PAC Glaucoma and Open-Angle Eyes Assessed Using AS Optical Coherence Tomography

Youngrok Lee, Kyung Rim Sung, Jung Hwa Na, and Jae Hong Sun

PURPOSE. To evaluate serial changes in anterior segment (AS) parameters in terms of variation in pupil diameter (PD) using AS optical coherence tomography (OCT) in eyes with primary angle closure or primary angle closure glaucoma (PCG), age-matched open-angle (AO) eyes, and young open-angle (YO) eyes.

METHODS. Forty-four PCG (mean ± SD: 62.2 ± 7.5 years), 36 AO (62.0 ± 12.3 years), and 58 YO eyes (29.1 ± 7.0 years) were imaged under four standardized lighting conditions (3.25, 100.8, 426, and 1420 cd/m²). PD, anterior chamber depth (ACD), iris cross-sectional area (IA), iris thicknesses at 750 and 1500 μm from the scleral spur (IT750, IT1500), iris curvature (IC), lens vault (LV), and anterior chamber area (ACA), were calculated. The slope of the change in each AS parameter in terms of variation in PD was determined by a linear mixed-effect model.

RESULTS. The mean ACD was significantly shallower (P < 0.001), the IC higher (P < 0.001), the IT750 greater (P = 0.026), the ACA smaller (P < 0.001), the LV greater (P < 0.001), and the IA wider (P = 0.019) in PCG eyes compared with AO eyes. However, the mean slope of no parameter differed significantly between PCG and AO eyes. The mean slopes of IC, IT1500, and IA differed between AO and YO eyes.

CONCLUSIONS. Older eyes showed significantly different dynamic AS parameter responses in terms of change in PD compared with younger eyes. Thus, the authors suggest that changes in the dynamic features of AS parameters with age may contribute to angle closure development, in addition to any predisposing anatomic condition. (Invest Ophthalmol Vis Sci. 2012;53:693–697) DOI:10.1167/iovs.11-8389

Primary angle closure glaucoma (PACG) is one of the leading causes of blindness, especially in Asian eyes.1-3 Previous reports have described the anatomic characteristics of eyes with PACG, including short axial length (AXL), the existence of narrow angles, the presence of a shallow anterior chamber, and a thick lens.4-7

In the past, diagnosis of angle closure depended entirely on clinical examination. In other words, subjective gonioscopy observation was used. Recent advances in imaging devices enable various anterior segment (AS) parameters to be measured. AS optical coherence tomography (AS OCT) provides an image of the entire AS in a single frame and AS parameters may be quantitatively measured using a noncontact method with the patient in a sitting position.8,9 Using AS OCT, Wang et al.10,11 reported that iris curvature (IC), area (IA), and iris thickness (IT) were independently associated with the existence of a narrow angle.

Dynamic changes in intraocular structures caused by variation in illumination or pharmacologic dilation have been suggested to be risk factors for glaucoma development.12-15 This idea is persuasive because not every patient with an anatomically narrow angle develops primary angle closure (PAC).16,17 Narrow angles associated with nonphysiologic dynamic changes in AS structure may be associated with development of PAC.12-15

Quigley et al.12 reported that iris volume loss when the pupil diameter was 3 to 7 mm, and smaller changes in iris cross-sectional area on pupil dilation, were potential risk factors for angle closure. Apte and Denis13 supported that observation by estimating iris volume using AS OCT; the cited authors found that an increment in iris volume after pupil dilation in narrow-angle eyes predisposed patients to acute angle closure.

In the present study, we evaluated serial changes in AS parameters on exposure to different standardized lighting conditions, thus affecting pupil dilation, and compared the data from PAC/PACG (PCG) eyes with those of age-matched open-angle (AO) eyes. Additionally, we imaged young open-angle (YO) eyes using the same protocol and compared the data with those from AO eyes to investigate the effects of aging on dynamic changes in AS parameters.

METHODS

Subjects

PCG subjects who agreed to participate in the study and met the inclusion criteria were consecutively recruited at the glaucoma clinic of the Asan Medical Center, Seoul, Korea. All subjects underwent a complete ophthalmic examination, including a review of medical history; measurement of best-corrected visual acuity (BCVA) (to confirm that VA was adequate for performance of automated perimetry); slit-lamp biomicroscopy; Goldmann applanation tonometry (GAT); gonioscopy; dilated fundoscopic examination using a 90° or 78°diopter (D) lens; stereoscopic optic disc photography; retinal nerve fiber layer photography; central corneal thickness measurement (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); AXL measurement (IOL Master; Carl
Zeiss Meditec); and AS OCT (Visante OCT, version 2.0; Carl Zeiss Meditec).

The study was approved by the Institutional Review Board of the Asan Medical Center, and we followed the tenets of the Declaration of Helsinki. PG was diagnosed by gonioscopic examination. PAC was considered present when an eye had an occludable angle and exhibited features indicating that trabecular obstruction by the peripheral iris had occurred. Such features included elevated intraocular pressure (IOP), the presence of peripheral anterior synchiae (PAS), iris whoring (distortion of radially orientated iris fibers), “glaucomflecken” lens opacity, or excessive pigment deposition on the trabecular surface but without development of a glaucomatous optic disc or any visual field (VF) change.18 PAC eyes showing glaucomatous optic disc changes (neuroretinal rim thinning, disc excavation, and/or optic disc hemorrhage attributable to glaucoma) or a glaucomatous VF change (pattern SD <5 and values outside normal limits in the glaucoma hemifield test) were considered to have PACG.19 Subjects with AO eyes were recruited from patients visiting our general ophthalmology clinic for treatment of dry eye or mild conjunctivitis, those who attended for routine eye examinations, and volunteer hospital staff. YO eyes (age <40 years) were recruited in the same manner. Both AO and YO eyes were normal on gonioscopic examination and showed no evidence of a glaucomatous optic disc or a VF change and IOP elevation. We excluded subjects with a history or current use of topical or systemic medication that could affect the angle or the pupillary reflex, those with a history of previous intraocular surgery including cataract surgery, or laser trabeculoplasty, or laser iridoplasty, and laser iridotomy, and those unable to fixate before conduct of the AS OCT examination. A previous history of acute PAC defined as the presence of the following symptoms: ocular or periocular pain, nausea, or vomiting, and a history of intermittent blurring of vision with haloes; a history of previous intraocular surgery including cataract surgery, or laser trabeculoplasty, or laser iridoplasty, and laser iridotomy, and those unable to fixate before conduct of the AS OCT examination. A previous history of acute PAC defined as the presence of the following symptoms: ocular or periocular pain, nausea, or vomiting, and a history of intermittent blurring of vision with haloes; a presenting IOP of >30 mm Hg and the presence of at least three of the following signs: conjunctival injection, corneal epithelial edema, mid-dilated unreactive pupil, and shallow anterior chamber were excluded.19 Eyes diagnosed with secondary angle closure (such as neovascular or uveitic glaucoma) were also excluded. All eyes were newly diagnosed cases and AS OCT imaging was performed before starting any glaucoma medication.

If both eyes qualified in terms of inclusion criteria, one eye was randomly selected for analysis.

Gonioscopy

Before AS OCT imaging, all subjects underwent a slit-lamp examination and gonioscopy conducted by an independent observer (KRS) with extensive experience in the performance of such tests. All subjects were examined using a Sussman lens in a darkened room (0.5 cd/m²). A 1-mm light beam was reduced to a narrow slit. The vertical beam was horizontally offset when superior and inferior angles were calculated, and the horizontal beam was vertically offset when nasal and temporal angles were measured. Both static and dynamic gonioscopy were performed using a Sussman lens, with the eye in the primary gaze position. Indentation gonioscopy was performed to determine whether angle closure was attributable to apposition or to PAS. Care was taken to ensure that light did not fall on the pupil.

AS OCT Imaging

All participants were imaged in terms of the nasal and temporal angle (0–180°) using AS OCT (Visante OCT, version 2.0; Carl Zeiss Meditec) operating in the enhanced AS single mode (scan length 16 mm; 256 A-scans), over four sessions using four different standardized lighting conditions (3.25, 100.8, 426, and 1420 cd/m²), grading from dark to light, by a single well-trained operator (JHN). The room in which AS OCT imaging was performed had four-graded lighting controlled by four-leveled switches. Lighting condition was changed by turning the switch at each session. Thus, the same four-leveled lighting conditions were provided to all participants. Participants were asked to sit back after imaging and wait for 30 seconds, during which the lighting conditions were changed. After 30 seconds of adaptation to the new lighting conditions, imaging was resumed. Thus, four images, obtained under four different lighting conditions, were obtained from each participant.

AS parameters of each of the four images were evaluated by an independent examiner (YL) who was masked to other test results and clinical information on participants. Pupil diameter (PD), anterior chamber depth (ACD), IA, IT at 750 and 1500 μm from the scleral spur (IT750, IT1500), IC, lens vault (LV), and anterior chamber area (ACA) were determined using ImageJ software (version 1.44; developed by Wayne Rasband, National Institutes of Health, Bethesda, MD; available at http://rsb.info.nih.gov/ij/index.html; Fig. 1). ACD was defined as the distance from the corneal endothelium to the anterior surface of the lens capsule. The scleral spur was defined as the point at which a change in curvature of the inner surface of the angle wall became apparent, and often presented as an inward protrusion of the sclera.20 After determination of scleral spur location, IT750 and IT1500 were defined as iris thicknesses measured at 750 and 1500 μm from the spur.11 IA was defined as the cross-sectional area of both the nasal and temporal sides. IC was defined as the maximum perpendicular distance between the iris pigment epithelium and the line connecting the most peripheral to the most central point of the epithelium.11 LV was defined as the perpendicular distance between the anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs.21 Three eyes were excluded due to inadequate

Figure 1. Anterior segment parameters measured by AS OCT and calculated using ImageJ software. ACA, anterior chamber area; ACD, anterior chamber depth; AS OCT, anterior segment optical coherence tomography; IC, iris curvature; IT750/1500, iris thickness 750/1500 μm from the scleral spur; LV, lens vault; SS, scleral spur.
TABLE 1. Anterior Segment (AS) Parameters of the Primary Angle Closure/Primary Angle Closure Glaucoma Group, and the Age-Matched Open-Angle Group, as Determined by AS OCT When Pupils Were Either Constricted or Dilated

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Constricted</th>
<th>Dilated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value AO PCG</td>
<td>P Value</td>
<td>Value AO PCG</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>3.020 ± 0.400</td>
<td>2.100 ± 0.280</td>
</tr>
<tr>
<td>Pupil diameter, mm</td>
<td>2.550 ± 0.550</td>
<td>2.630 ± 0.480</td>
</tr>
<tr>
<td>IC, mm</td>
<td>0.076 ± 0.084</td>
<td>0.201 ± 0.111</td>
</tr>
<tr>
<td>IT750, mm</td>
<td>0.424 ± 0.091</td>
<td>0.472 ± 0.081</td>
</tr>
<tr>
<td>IT1500, mm</td>
<td>0.459 ± 0.076</td>
<td>0.490 ± 0.072</td>
</tr>
<tr>
<td>LV, mm</td>
<td>0.384 ± 0.310</td>
<td>0.780 ± 0.402</td>
</tr>
<tr>
<td>AC area, mm²</td>
<td>17.820 ± 3.550</td>
<td>11.040 ± 2.190</td>
</tr>
<tr>
<td>Iris area mm²</td>
<td>3.620 ± 0.380</td>
<td>3.840 ± 0.390</td>
</tr>
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</table>

AC, anterior chamber; ACD, anterior chamber depth; AO, age-matched open-angle group; AS OCT, anterior segment optical coherence tomography; IC, iris curvature; IT750/1500, iris thickness 750/1500 μm from the sclera spur; LV, lens vault; PCG, primary angle closure or primary angle closure glaucoma group.

Mean AXL was also significantly different between AO and YO eyes (24.0 ± 1.7 mm, 25.1 ± 2.1 mm, respectively, P = 0.027).

All analyzed parameters, with the exception of PD, differed significantly between PCG and AO eyes, when pupils were either constricted or dilated (Table 1). When pupils were constricted, the mean ACD was 3.02 ± 0.40 mm in AO eyes and 2.10 ± 0.28 mm in PCG eyes (P < 0.001). The mean IC was significantly higher (P < 0.001), the IT750 greater (P = 0.026), the ACA smaller (P < 0.001), the LV greater (P < 0.001), and the IA wider (P = 0.019) in PCG eyes compared with AO eyes. The findings were similar after pupil dilation.

When we compared AO and YO eyes, ACD and IT did not significantly differ when pupils were either constricted or dilated (Table 2). However, when pupils were constricted, the PD was significantly smaller (P < 0.001), the IC higher (P < 0.001), the IA wider (P = 0.003), the LV greater (P < 0.001), and the ACA smaller (P = 0.009) in AO compared with YO eyes. The findings were similar when pupils were dilated.

On comparison of the slopes of various AS parameters with variation in PD, the mean slopes of all parameters did not significantly differ between PCG and AO eyes (Table 3), indicating that the extent of change in AS parameters on variation in PD did not differ between PCG and YO eyes. However, the mean slopes of IC, IT1500, and IA, on variation in PD, differed significantly between AO and YO eyes (Table 4), which suggested aging substantially affected the dynamic changes of iris-related parameters.

ACD and LV showed strong correlation. IT750, IT1500, and IC showed moderate correlation. IT1500, IT750, and ACA showed weak correlation. Pupil diameter showed no correlation with other parameters.

TABLE 2. Anterior Segment Parameters of Older and Young Open-Angle Subjects as Determined by AS OCT When Pupils Were Either Constricted or Dilated

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Constricted</th>
<th>Dilated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value Older Young</td>
<td>P Value</td>
<td>Value Older Young</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>3.020 ± 0.400</td>
<td>3.120 ± 0.250</td>
</tr>
<tr>
<td>Pupil diameter, mm</td>
<td>2.550 ± 0.550</td>
<td>3.140 ± 0.750</td>
</tr>
<tr>
<td>IC, mm</td>
<td>0.076 ± 0.084</td>
<td>0.005 ± 0.020</td>
</tr>
<tr>
<td>IT750, mm</td>
<td>0.424 ± 0.091</td>
<td>0.415 ± 0.058</td>
</tr>
<tr>
<td>IT1500, mm</td>
<td>0.459 ± 0.076</td>
<td>0.459 ± 0.087</td>
</tr>
<tr>
<td>LV, mm</td>
<td>0.384 ± 0.310</td>
<td>0.124 ± 0.179</td>
</tr>
<tr>
<td>AC area mm²</td>
<td>17.820 ± 3.550</td>
<td>19.530 ± 2.650</td>
</tr>
<tr>
<td>Iris area mm²</td>
<td>3.620 ± 0.380</td>
<td>3.340 ± 0.460</td>
</tr>
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</table>

Abbreviations as in Table 1.
IC, IT750, and ACA) as well as age showed significant changes as to the change of PD in univariate linear regression analysis and thus all those parameters were included in multivariate linear regression analysis. The dynamic changes of AS parameters were independently associated with change of age and PD (Table 5).

**DISCUSSION**

As expected, PCG eyes differed significantly in terms of AS parameters compared with age-matched open-angle eyes. The ACD was shallower, iris bowing (estimated by IC) was more pronounced, the iris was thicker, the LV greater, and the IA wider. All these features contributed to rendering the ACA shallower, iris bowing (estimated by IC) was more pronounced, and the iris thicker in PCG eyes than that in open-angle eyes. This was the case when pupils were either constricted or dilated. The observations that iris bowing was more prominent and the iris thicker in PCG eyes than that in open-angle eyes are in line with previous studies.10,11,22 Cheung et al.22 showed that iris bowing is an important biomechanic parameter determining angle width, independent of ACD. Wang et al.13 found that higher IC, IA, and IT values were significantly associated with a narrow angle after adjustment for the covariates age, sex, ACD, axial length, and pupil size.

However, when we compared the dynamic changes in various AS parameters on changes in PD under different lighting conditions, no parameter was significantly different in terms of mean slope when PCG and AO eyes were compared. In other words, the extent of any change in an AS parameter with respect to variation in PD did not significantly differ between the two groups.

When mean slope values of young and older open-angle eyes were compared, however, statistically significant differences were apparent when PD varied; this was especially true when iris-related parameters were examined. These differences in the dynamic response of AS parameters on aging may be principally caused by a sluggish pupillary response to changes in lighting conditions. When pupils were either dilated or constricted, both PCG eyes and open-angle eyes of similar age had a significantly smaller pupil size than did young eyes. When we assessed the relationship between PD change and various AS parameter changes, age was independently associated with those changes. Therefore, aging seems to substantially influence dynamic changes in AS parameters.

When we compared the characteristics of AS parameters between young and older open-angle eyes, most parameters were significantly different when pupils were either dilated or constricted. Again, this was especially true of iris-related parameters, although both groups had open angles and similar ACD values. Anterior chamber angle parameters, especially ACD, have been reported to decrease with age.8,23–25 Also, ACD reduction and subsequent narrowing of the anterior chamber angle on aging have been suggested as the possible explanation as to why aging is an important risk factor for PAC. In our present study, older and young open-angle eyes showed no significant difference in ACD, but both IC and IA did differ significantly. Incremental changes in IC and IA may contribute to a decrease in the ACA of older eyes. Therefore, when our observations and prior reports are considered together, changes in IC and IT, as well as a decrease in ACD, on aging, may possibly explain why aging is a risk factor for development of PAC. In addition, variation in the dynamic behavior of AS parameters in terms of pupillary differences between young and older eyes may be one reason why aging is a risk factor for development of PAC.

Either an increase in, or a reduced level of decrease in, iris cross-sectional area or iris volume on pupil dilation, has been suggested to contribute to the pathogenesis of PAC.12–15 However, in our present analysis, the PCG and the AO groups did not differ significantly in terms of the mean slope of IA change when pupil diameter varied. A possible explanation is that our PCG eyes included some eyes at advanced stages of PACG, and that such eyes were affected by iris atrophy. Any increment in iris area or thickness may not be apparent in eyes in which the iris is atrophic; inclusion of measurements on such eyes may thus affect the mean values of slopes. Plateau iris configuration that has anteriorly positioned ciliary body may affect the measurement of AS parameters such as IC or IT. AS OCT has limited tissue penetration and scan depth and thus the ciliary body could not be well visualized; thus, this could also be a limita-
tion of the present study. Some of PCG eyes had PAS in anterior chamber angle, which may also affect peripheral iris-related parameters, so this could also be a drawback of the present study. Additionally, seamless video imaging can represent a real-time status of iris, pupil, and lens position. However, we used the 4-time-point acquisition as a surrogate measure for evaluation of serial images; therefore, this point could be a limitation.

In summary, our results indicated that PCG eyes differed in terms of AS parameters from age-matched open-angle eyes, when pupils were either dilated or constricted, but the AS parameters responded similarly to changes in lighting conditions, as assessed using AS OCT. Therefore, we believe that anatomic changes in AS parameters are indeed important in the pathogenesis of PAC. However, when it is considered that the AS parameters of older eyes showed substantially different dynamic responses to pupil change, compared with that of young eyes, changes in the dynamic behavior of AS parameters on aging may contribute to PAC, in combination with any predisposing anatomic condition, and this may explain why aging is a crucial risk factor in terms of PAC development.

References