Comparison of Anterior Segment Parameters Between the Acute Primary Angle Closure Eye and the Fellow Eye

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PURPOSE. To investigate features of the anterior segment (AS) of the affected eye compared to the fellow eye within the same patient in acute primary angle closure (APAC).

METHODS. Thirty-six patients with unilateral APAC were imaged with AS optical coherence tomography (OCT) before medical or laser treatment for the acute attack. Anterior chamber depth (ACD), iris curvature (IC), iris thickness at 750 μm from the scleral spur (IT750), lens vault (LV), anterior chamber area (ACA), and iris area were estimated by using ImageJ software (version 1.46). Conditional logistic regression analysis was performed to find the associated factors with the prediction of APAC.

RESULTS. When compared to fellow eyes, affected eyes showed significantly shallower ACD (1.90 ± 0.24 and 1.55 ± 0.30 mm, respectively; P < 0.001), smaller ACA (12.96 ± 2.38 and 10.41 ± 2.34 mm², respectively; P < 0.001), and greater LV (1.06 ± 0.31 and 1.26 ± 0.36 mm, respectively; P = 0.017). Less IC (odds ratio [OR]*100: 0.935 [95% confidence interval: 0.894, 0.979], P = 0.004) and IT750 (OR*100: 0.904 [0.829, 0.987], P = 0.024), greater central corneal thickness (OR*100: 2.100 [1.245, 3.542], P = 0.005), greater LV (OR: 66.7 [2.529, 1761.3], P = 0.012), less ACA (OR: 0.386 [0.193, 0.774], P = 0.007), and less ACD (OR*100: 0.912 [0.855, 0.972], P = 0.005) were significantly associated with prediction of APAC.

CONCLUSIONS. Greater LV was the most prominent feature of affected eyes compared to fellow eyes in APAC patients when assessed by AS OCT. This may play a role in the development of acute attack in primary angle closure.

Keywords: primary angle closure, acute attack, anterior segment OCT, lens vault

Primary angle closure glaucoma (PACG) is one of the leading causes of blindness worldwide.1–3 Early detection of anterior chamber angle closure and timely prophylactic management are of paramount importance in the clinical care of PACG.

Primary angle closure glaucoma can be categorized into several subtypes according to the time course of presenting symptoms. Acute primary angle closure (APAC) is characterized by sudden elevation in intraocular pressure (IOP) with findings such as corneal edema and shallow anterior chamber and symptoms such as blurred vision and severe ocular pain or headache, nausea, and vomiting. Persistent IOP elevation causes irreversible loss of vision; therefore, this finding is considered an ocular emergency. However, chronic angle closure is oftentimes asymptomatic. The subacute type of PACG usually presents in cycles of recurrent episodes and spontaneous recovery of mild symptoms.

Primary angle closure glaucoma can progress from one type to another; for example, subacute PACG can suddenly develop into acute PACG. The causative factor for acute manifestation is of specific interest. When compared with other subtypes, APAC eyes have shown increased choroidal thickness, unchanged iris volume according to physiologic mydriasis, and increment of lens vault in previous studies.4–10 Because APAC is an ocular emergency that can lead to blindness, identifying causative factors to predict the occurrence of acute disease is of importance for the clinical care of PACG.

Thus, the aim of this study was to investigate the anterior segment structural features of affected eyes compared to those of fellow eyes within the same patients with APAC before medical or laser treatment for the acute attack. To evaluate anterior segment structural features, we used anterior segment optical coherence tomography (AS OCT), which images anterior segment structures in vivo status with a noncontact method and provides reproducible and quantitative output.11–13

METHODS

Subjects

Patients with APAC who were examined at the glaucoma clinic of the Asan Medical Center (seen by KRS) from March 2008 to January 2013 and who met the inclusion criteria were consecutively enrolled in this study. 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, fundoscopic examination using a 90- or 78-diopter lens, stereoscopic optic disc photography, retinal nerve fiber
were considered to have PACG.15 Only reliable VF test results and/or optic disc hemorrhage attributable to glaucoma) or a optic disc changes (neuroretinal rim thinning, disc excavation, false-positive errors calculated by using ImageJ software. SS, scleral spur.

layer photography, central corneal thickness (CCT) measurement (DGH-550 instrument; DGH Technology, Inc., Exton, PA, USA), a visual field (VF) test (Humphrey field analyzer, Swedish Interactive Threshold Algorithm 24-2; Carl Zeiss Meditec, Dublin, CA, USA), and AS OCT (Visante OCT, version 2.0; Carl Zeiss Meditec). Informed consent was obtained from all participants. The study was approved by the Institutional Review Board of the Asan Medical Center, and the tenets of the Declaration of Helsinki were followed. Patients who were imaged before medical or laser treatment were included in the current study. All eyes were newly diagnosed cases.

Acute primary angle closure was defined by the presence of ocular or periorbital pain, nausea or vomiting, and blurred vision with haloes; a presenting IOP of more than 30 mm Hg; and the presence of at least three of the following: conjunctival injection, corneal epithelial edema, mid-dilated unreactive pupil, and/or shallow anterior chamber.14

In all patients, the fellow eye to the APAC-affected eye was evaluated and grouped by clinical findings. Eyes with appositional contact between the peripheral iris and the posterior trabecular meshwork of greater than 270° were included in the primary angle closure suspect (PACS) group.15 Eyes with an occludable angle and exhibiting features indicating trabecular obstruction by the peripheral iris were considered to have primary angle closure (PAC). Such features included elevated IOP, the presence of peripheral anterior synchiae (PAS), iris whirling (distortion of radially orientated iris fibers), “glaukomflecken” lens opacity, or excessive pigment deposition on the trabecular surface, but without the development of a glaucomatous optic disc or any VF change.15 Primary angle closure 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 standard deviation < 5% and values outside the normal limits in the glaucoma hemifield test) were considered to have PACG.15 Only reliable VF test results (false-positive errors < 15%, false-negative errors < 15%, and fixation loss < 20%) were included in the analysis. We excluded patients with a history or current use of topical or systemic medications that could affect the angle or the pupillary reflex; those with a history of previous intraocular surgery, including cataract surgery, laser trabeculoplasty, laser iridoplasty, and laser iridotomy; and those unable to fixate before the AS OCT examination. Eyes diagnosed with secondary angle closure, such as neovascular or uveitic glaucoma, were also excluded. Bilateral acute attack cases were excluded in our current study.

Slit-Lamp Examination and Gonioscopy

Before AS OCT imaging, subjects underwent slit-lamp examination and gonioscopy by an independent observer (KRS) with extensive experience in performing gonioscopy. All subjects were examined with a Sussman lens in a controlled darkened room (0.5 cd/m²).

A 1-mm light beam was reduced to a narrow slit. The vertical beam was offset horizontally to assess nasal and temporal angles, and the horizontal beam was offset vertically for superior and inferior angles. Both static and dynamic gonioscopy were performed by using a Sussman lens, with the eye in the primary position of gaze. Indentation gonioscopy was performed to determine if anterior chamber angle closure was due to apposition or PAS. Care was taken to avoid light falling on the pupil.

Anterior Segment OCT Imaging

Anterior segment OCT imaging was performed under constant dim light (0.5 cd/m²) with the patient in a sitting position. Images were captured at the nasal and temporal angle quadrants (3- and 9-o’clock meridians; nasal–temporal angles at 0° to 180°) by using an AS OCT operating in the enhanced AS single mode (scan length, 16 mm; 256 A-scans). Internal fixation was used in all subjects, and all scans were conducted by a single well-trained operator who was blinded to other clinical findings to minimize operator-related measurement variability. Three images were acquired from each eye, and the highest-quality image, defined as showing good visibility of the scleral spur, was selected for analysis. A single examiner (JRL), who was blinded to other test results and all clinical information of the participants, analyzed all images. The ImageJ software (version 1.46, http://imagej.nih.gov/ij/, provided in the public domain by the National Institutes of Health, Bethesda, MD, USA) was used to measure anterior chamber depth (ACD), iris cross-sectional area (IA), iris thickness at 750 μm from the scleral spur (IT750), iris curvature (IC), lens vault (LV), anterior chamber width (ACW), pupillary distance (PD), and anterior chamber area (ACA) (Fig. 1). Anterior chamber depth was defined as the distance from the corneal endothelium to the anterior surface of the lens. The scleral spur was defined as the point at which a change in curvature of the inner surface of the angle wall became apparent, often presenting as an inward protrusion of the sclera.16 After locating the scleral spur, IT750 was measured at 750 and 1500 μm from the spur17; 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; LV was defined as the perpendicular distance between the anterior pole of the crystalline lens and the horizontal line joining the two scleral spurs (ACW).8 The image acquisition procedure and analysis method are described elsewhere in detail.12,13,18

Analysis

Continuous variables are expressed as means ± standard deviations (SDs) after confirming normality of the data distribution. The anterior segment parameters were compared between APAC-affected eyes and fellow eyes by using a paired t-test. The anterior segment parameters were also compared among different groups of fellow eyes by the Mann-Whitney test. Univariate and multivariate conditional logistic regression analyses were performed to find predictive factors associated with APAC. Variables with P value less than 0.2 in the univariate outcome were incorporated in the multivariate analysis and backward variable selection approach was adopted to obtain the final multivariable model. Statistical analyses were performed by using SPSS version 15.0 (SPSS, Inc., Chicago, IL, USA) and R software version 2.13 (www.
RESULTS

Three eyes were excluded owing to difficulty in the assignment of scleral spur. Thirty-six participants were included in the final analysis. The mean age of the patients was 67.8 ± 8.2 years, and all were Asians (Koreans). Of the 36 participants, 14 were men and 22 were women. Of the 36 fellow eyes, 22 were diagnosed with PACS, 9 with PAC, and 5 with PACG. Demographics of the participants and baseline IOP are summarized in Table 1.

When compared to fellow eyes, affected eyes showed significantly greater CCT (546.7 ± 33.9 vs. 589.7 ± 91.8 μm, P = 0.011), shallower ACD (1.90 ± 0.24 vs. 1.55 ± 0.30 mm, P < 0.001), smaller ACA (12.96 ± 2.38 vs. 10.41 ± 2.34 mm², P < 0.001), and greater LV (1.06 ± 0.31 vs. 1.26 ± 0.36 mm, P = 0.017). In affected eyes compared to fellow eyes, IC was less in both the nasal and temporal sides and IA was smaller (P = 0.011, 0.010, and 0.033, respectively), whereas there was no significant difference in IT between eyes on either side (P = 0.072 [nasal side] and 0.124 [temporal side]). Anterior chamber width and PD did not significantly differ between the affected and fellow eyes (P = 0.459 and 0.525, respectively; Table 2).

We categorized fellow eyes into two groups: one consisting of eyes with PACS, and another consisting of eyes with either PAC or PACG. Primary angle closure and PACG eyes showed higher untreated IOP compared to PAC eyes (20.1 ± 12.6 and 14.5 ± 3.5 mm Hg, respectively; P = 0.046), but other parameters determined by AS OCT did not significantly differ (Table 3).

Table 2. Comparison of AS OCT Parameters Between PAC-Affected Eyes and Fellow Eyes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fellow Eyes, N = 36</th>
<th>APAC Eyes, N = 36</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCT, μm</td>
<td>546.7 ± 33.9</td>
<td>589.7 ± 91.8</td>
<td>0.011</td>
</tr>
<tr>
<td>ACD, mm</td>
<td>1.90 ± 0.24</td>
<td>1.55 ± 0.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACA, mm²</td>
<td>12.96 ± 2.38</td>
<td>10.41 ± 2.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IC, nasal, mm</td>
<td>0.17 ± 0.10</td>
<td>0.11 ± 0.09</td>
<td>0.011</td>
</tr>
<tr>
<td>IC, temporal, mm</td>
<td>0.22 ± 0.11</td>
<td>0.15 ± 0.12</td>
<td>0.010</td>
</tr>
<tr>
<td>IT750, nasal, mm</td>
<td>0.48 ± 0.09</td>
<td>0.44 ± 0.10</td>
<td>0.072</td>
</tr>
<tr>
<td>IT750, temporal, mm</td>
<td>0.45 ± 0.08</td>
<td>0.41 ± 0.11</td>
<td>0.124</td>
</tr>
<tr>
<td>IA, nasal + temporal, mm²</td>
<td>3.35 ± 0.42</td>
<td>2.95 ± 0.60</td>
<td>0.035</td>
</tr>
<tr>
<td>ACW, mm</td>
<td>11.05 ± 0.60</td>
<td>10.94 ± 0.40</td>
<td>0.459</td>
</tr>
<tr>
<td>LV, mm</td>
<td>1.06 ± 0.31</td>
<td>1.26 ± 0.36</td>
<td>0.017</td>
</tr>
<tr>
<td>PD, mm</td>
<td>3.9 ± 0.7</td>
<td>3.7 ± 1.4</td>
<td>0.525</td>
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</table>

DISCUSSION

As expected, acute attack–affected eyes presented substantially high IOP (mean, 47.9 mm Hg) as compared to fellow eyes. Some of the fellow eyes revealed high IOP of up to 31 mm Hg, but the mean IOP of the fellow eyes (16.9 mm Hg) was within the normal range (Table 1). All of the fellow eyes had various degrees of angle closure in our current analysis, with PACS being the most frequent diagnosis. Interestingly, although none of the patients had been previously diagnosed with glaucoma, five were diagnosed with PACG in the fellow eye because they had evidence of iridotrabecular contact in the anterior chamber angle and either glaucomatous optic disc or VF. This finding was in line with previous reports. Since all the fellow eyes of APAC-affected eyes showed a degree of angle closure, APAC can be assumed to be one manifestation of PAC and should thus be considered within the spectrum of PAC.

Our original study objective was to analyze and compare anterior segment features determined by AS OCT between affected and fellow eyes before any medical or laser treatment, such as laser peripheral iridotomy (LPI), for the acute attack. When assessed by AS OCT, one of the most remarkable morphologic differences was the greater LV, less ACD, and thus ACA, in the affected eye. Anterior chamber depth is determined by LV and posterior corneal surface height. Increased CCT, which can be caused by corneal edema due to sudden IOP elevation, can cause decreases in ACD. Our result showed increased CCT and LV in the affected eyes compared with fellow eyes. Thus, both increased LV and CCT seemed to induce a shallow anterior chamber and reduced ACA in our result.

In the present study, the irides of affected eyes were flatter than those of fellow eyes. Usually, relative pupillary block, which is known as the primary cause of PAC, induces iris bombe, resulting in increased IC. Lower IC in affected eyes compared to fellow eyes may be explained by high LV. Owing
to the increase in LV, the central portion of the iris is pushed forward, thus causing the iris to flatten. In addition, fixed pupils due to extremely high IOP may affect iris shape in the affected eye. Figure 2 illustrates the relatively flatter iris configuration with elevated LV in an affected eye compared to its fellow eye. Iris cross-sectional area was smaller in affected eyes, which may be due to iris atrophy caused by the acute attack. These iris-related parameters may vary according to PD; however, PD was not found to be different between affected and fellow eyes. Anterior chamber area is mainly determined by ACD and IC. Hence, in this study, because of the elevated LV and subsequent reduction in ACD, ACA was lower in attack-affected eyes despite lower IC, compared to fellow eyes. Logistic analysis outcome also supported this explanation. Greater LV was a predictive factor for APAC with high OR (66.7).

Increase of LV, and subsequent reduction of IC and less IT due to iris atrophy, may be findings in APAC eyes. Lens-induced mechanism has been continuously addressed in the development of PAC. Previous reports that angle closure progresses despite LPI suggest that the nonpupillary block mechanism plays an important role in the pathogenesis of chronic angle closure. Increased LV may be one cause of nonpupillary block mechanism. Our analysis result may suggest that greater LV is a pathogenic mechanism in APAC as well as in chronic angle closure.

The reason for the greater LV in affected eyes remains unknown. Increases in LV with increasing age have been reported. Aging can increase lens thickness, which can cause increased LV. However, this raises another question as to the other causes of greater LV in the affected eye compared to the fellow eye within the same patient. Some pressure from the vitreous cavity may push the lens anteriorly and damage the lens zonule, thereby causing an increase in LV. Investigators have proposed chorioidal volume expansion as a possible mechanism for anterior lens movement. Anterior segment OCT is not an optimal device to image the ciliary body and choroid because the light source cannot penetrate the iris and corneo-sclera junction. However, in 3 of the 36 eyes, some gaps were noted under the ciliary body, which may reflect chorioidal effusion (Fig. 3). This may partially support the idea that chorioidal volume expansion may contribute to sudden increases in LV and subsequent acute attack. Iris volume increment after pupil dilation in narrow angle eye, or unchanged iris volume according to physiologic mydriasis, have been suggested as possible mechanisms for acute attack. Dynamic changes of volume in uveal structure may provide an explanation for acute attack.

Our study had several limitations. The small sample size was one of these limitations. Also, our observation was a cross-sectional one, not the change obtained at different time points; thus, the result should be interpreted with caution.

In summary, our data revealed increased LV as the most distinguishing feature of acute attack–affected eyes compared to fellow eyes. Flatter iris despite pupillary block may be due to pushing of the central portion of the iris due to increased LV. Thus, pupillary block and elevated LV may play a combined role in inducing acute attack. Furthermore, increased LV may aggravate pre-existing relative papillary block. Considering that both mechanisms contribute to the development of acute attack in PAC, resolving two issues, that is, the increase in LV and pupillary block, is necessary to treat acute attack in patients with angle closure. In case of persistent IOP elevation despite LPI, careful extraction of the lens might be a therapeutic option in APAC eyes when increment of LV is observed.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Univariate Model</th>
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<th>Multivariate Model</th>
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</tr>
</thead>
<tbody>
<tr>
<td>ACD*100, mm</td>
<td>0.912 (0.855, 0.972)</td>
<td>0.005</td>
<td>0.339</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>ACA, mm²</td>
<td>0.386 (0.193, 0.774)</td>
<td>0.007</td>
<td>0.283</td>
<td>0.394 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>IC*100, temporal + nasal, mm</td>
<td>0.935 (0.894, 0.979)</td>
<td>0.004</td>
<td>0.171</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>IT₇₅₀, temporal + nasal, mm</td>
<td>0.904 (0.829, 0.987)</td>
<td>0.024</td>
<td>0.126</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>IA, temporal + nasal, mm</td>
<td>0.102 (0.017, 0.609)</td>
<td>0.012</td>
<td>0.132</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>ACW, mm</td>
<td>0.465 (0.114, 1.887)</td>
<td>0.284</td>
<td>0.017</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>LV, mm</td>
<td>66.744 (2.529, 1761.3)</td>
<td>0.012</td>
<td>0.145</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
<tr>
<td>CCT*100, mm</td>
<td>2.100 (1.245, 3.542)</td>
<td>0.005</td>
<td>0.275</td>
<td>2.568 (1.015, 6.500)</td>
<td>0.047</td>
<td>0.394</td>
</tr>
<tr>
<td>PD, mm</td>
<td>0.829 (0.497, 1.383)</td>
<td>0.472</td>
<td>0.007</td>
<td>0.417 (0.184, 0.948)</td>
<td>0.037</td>
<td>0.394</td>
</tr>
</tbody>
</table>

CI, confidence interval.

FIGURE 2. Acute attack–affected eye (A) with high LV, low ACD, and relatively flat iris (low IC) compared to the fellow eye (B). Owing to elevated LV, the central portion of the iris was pushed forward, causing a reduction in IC.
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