Japanese Journal of Ophthalmology (2019) 63:151–157
https://doi.org/10.1007/s10384-019-00651-0

THE OFFICIAL INTERNATIONAL JOURNAL OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

CLINICAL INVESTIGATION

Comparison of pretreatment measurements of anterior segment parameters in eyes with acute and chronic primary angle closure

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Received: 2 April 2018 / Accepted: 21 December 2018 / Published online: 20 January 2019
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Abstract

Purpose To compare pretreatment anterior segment parameters between eyes with acute primary angle closure (APAC) and chronic primary angle closure (CPAC), and to identify the characteristics of eyes with APAC.

Study design Retrospective.

Methods We measured pretreatment anterior chamber depth (ACD), iris convexity (IC), and pupil diameter in eyes with APAC and CPAC using anterior segment optical coherence tomography. The risk of APAC associated with anterior segment parameters was investigated using multiple logistic regression. Eyes with APAC were discriminated from eyes with CPAC using the receiver-operating characteristic (ROC) curve and area under the curve (AUC). The best cutoff for these variables was determined.

Results Thirty-four eyes with APAC and 60 eyes with CPAC were included. The mean intraocular pressure was 52.3 ± 12.6 mmHg in APAC and 15.5 ± 3.5 mmHg in CPAC ($P < .001$). Eyes with APAC had a shallower ACD (1.407 ± 0.301 mm vs. 1.960 ± 0.205 mm, $P < .001$) and less IC (0.233 ± 0.087 mm vs. 0.294 ± 0.068 mm, $P < .001$) than eyes with CPAC. In multivariate analysis, significant variables associated with APAC were ACD ($P < .001$) and IC ($P = .001$). The AUC for ACD was 0.931 and for IC, 0.742. The best cutoff for ACD was 1.699 mm (sensitivity 0.824, specificity 0.917) and for IC, 0.282 mm (sensitivity 0.853, specificity 0.533).

Conclusions Eyes with APAC had a shallower ACD and less IC. Eyes with an ACD < 1.7 mm may be at risk for APAC.

Keywords Acute primary angle closure · Angle closure · Anterior chamber depth · Anterior segment optical coherence tomography · Iris convexity

Introduction

Primary angle closure glaucoma (PACG) is a major cause of blindness, particularly in East Asia. Acute primary angle closure (APAC) is a severe form of glaucoma considered to be a medical emergency because, left untreated it can progress rapidly to blindness. Identifying factors rendering eyes with angle closure prone to APAC is clinically important for both prevention and treatment.

Anterior segment optical coherence tomography (AS-OCT) is a recently developed technology that enables non-contact, non-invasive, rapid analysis of the anterior segment. Several studies use AS-OCT to compare the morphology of the anterior segment in eyes that have APAC with fellow eyes, or with eyes that have chronic primary angle closure (CPAC) [1–3]. These studies show that eyes with APAC have a shallower anterior chamber depth (ACD), exaggerated lens vault, and less iris convexity (IC).

However, the images of eyes with APAC in the above studies were captured when the APAC had resolved after treatment with medication or laser peripheral iridotomy (LI). Anterior segment parameters measured after treatment might be different from those before treatment. Therefore, images

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of eyes with APAC captured before treatment may be more useful when investigating the etiology of APAC. One study analyzed images of eyes with APAC in its onset and fellow eyes [4] and shows that the 2 main anterior segment parameters associated with the onset of APAC are shallower ACD and less IC. Another study shows that eyes with APAC in its onset have a shallower ACD, less IC, and a greater lens vault than fellow eyes [5]. The aims of this study were to examine and compare the anterior segment parameters in eyes with APAC with those with CPAC, and to identify the characteristics of eyes with APAC.

Patients and methods

Study participants

The Institutional Review Board of Kobe City Medical Center General Hospital reviewed and approved this retrospective study and waived the requirement of informed consent. This study was performed in accordance with the Declaration of Helsinki.

We examined 38 eyes of 38 consecutive patients with APAC in its onset and 70 eyes of 70 patients with CPAC who visited the Department of Ophthalmology of Kobe City Medical Center General Hospital from August 2011 to August 2015. All patients were Japanese. Whenever both eyes fulfilled the inclusion criteria in a patient with CPAC, the right eye was chosen for the study. Although the main purpose of our study was to compare eyes with APAC and CPAC, we also measured untreated fellow eyes of APAC with no previous attack for additional information.

APAC was defined by the following criteria [6, 7]: at least 2 symptoms (ocular or periocular pain, nausea and/or vomiting, an antecedent history of intermittent blurred vision with haloes); intraocular pressure (IOP) > 21 mmHg (measured by Goldman applanation tonometry); and the presence of at least 3 further signs (conjunctival injection, corneal edema, mid-dilated unreactive pupil, and a shallow anterior chamber).

Eyes with CPAC were classified as primary angle closure suspect (PACS), primary angle closure (PAC), or primary angle closure glaucoma (PACG). PACS was defined as eyes with occludable angles, i.e., invisible posterior trabecular meshwork in not less than two quadrants by non-indentation gonioscopy in the primary position. PAC was defined as PACS and either peripheral anterior synechiae or an IOP rise above 21 mmHg. PACG was defined as PAC and glaucomatous optic neuropathy [8].

In several eyes with CPAC, the finding of angle closure in AS-OCT was different from that in gonioscopy. Among the eyes with CPAC, those that had closed angles in both nasal and temporal quadrants in AS-OCT were also compared with eyes with APAC, to match the findings of angle closure in the two groups.

Subjects with a history of any intraocular surgery, e.g., lens extraction or glaucoma surgery (including laser iridotomy and laser gonioplasty) and subjects who had used any miotic or mydriatic medication before examination were excluded from the study. We also excluded subjects in whose eyes the posterior cornea surface, the surfaces of the anterior and posterior iris, and the angle's recess were difficult to detect.

Ophthalmic examinations and measurements

All subjects underwent detailed ophthalmic examination using slit-lamp biomicroscopy, gonioscopy, measurement of IOP by Goldmann applanation tonometry, fundus examination, and AS-OCT imaging. Systemic and topical treatment was started immediately after the examination was completed.

We used a swept-source AS-OCT system (CASIA SS-1000; Tomey) to capture anterior segment images under dark conditions.

ACD was defined as the distance between the corneal endothelium at the corneal apex and the anterior pole of the crystalline lens. Pupil diameter (PD) was defined as the distance between the two tips of the iris.

A software program automatically calculated the ACD and PD. IC was defined as the maximum distance from the posterior boundary of the iris to the iris plane passing through the pupillary margin of the iris and iris root [9]. IC was analyzed as the average of the nasal and temporal quadrants (Fig. 1).

Statistical analysis

Statistical analysis was performed using commercial software (SPSS version 22.0; SPSS Japan, Inc.). For continuous variables, we used Mann–Whitney test for comparing two groups and the analysis of variance (ANOVA) for comparing more than two groups. Whenever the test of homogeneity of variance was passed, post hoc test was analyzed using Tukey test, otherwise Games Howell test was used. We used the chi-square test for categorical variables. Statistical significance was assumed at $P < .05$. Multiple logistic regression analysis was used to estimate the risk of APAC against CPAC associated with the anterior segment parameters (ACD, PD, and IC). We used a forward stepwise entry method. For each significant parameter, we calculated the odds ratio of the risk of APAC as a 0.1-mm decrease of each parameter. The receiver-operating characteristic (ROC) curve and the area under the ROC curve (AUC) were used to discriminate eyes with APAC from eyes with CPAC. Based

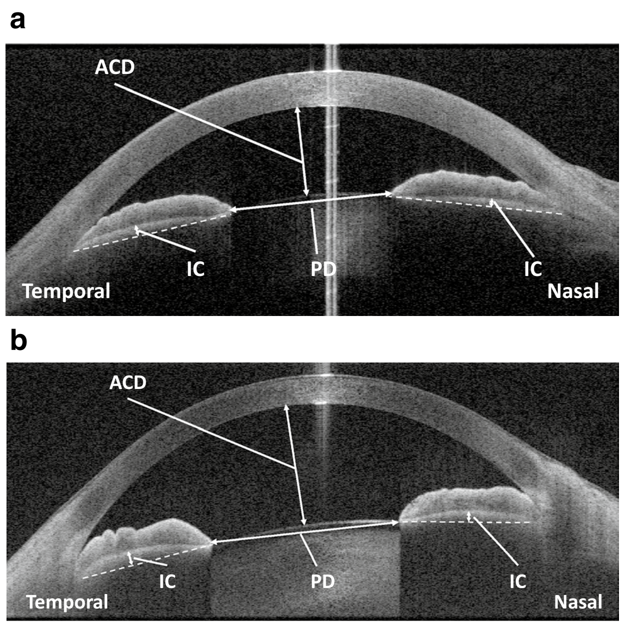

Fig. 1 Determination of pupil diameter (PD), anterior chamber depth (ACD), and iris convexity (IC) in an anterior segment optical coherence tomographic image in an eye with acute and chronic primary angle closure. The dashed lines show the iris plane passing through the pupillary margin of the iris and iris root. a acute primary angle closure. b chronic primary angle closure

on Youden's index, the best cutoff value for each parameter was determined [10].

Results

Four eyes in the APAC group and 10 eyes in the CPAC group were excluded because of poor images, leaving 34 eyes in the APAC group (34 patients; mean age 71.2 ± 8.7 years; 9 men, 25 women) and 60 eyes in the CPAC group (60 patients; mean age 71.2 ± 8.0 years; 8 men, 52 women) for inclusion in the study. The images of untreated fellow eyes of APAC were obtained in 26 eyes. Thirty-eight of the eyes with CPAC had PACS, 19 eyes had PAC, and 3 eyes had PACG. On gonioscopy 21 eyes had angle closure in 4 quadrants, 26 eyes in 3 quadrants, and 13 eyes in 2 quadrants. Only narrow and a few peripheral anterior synechiae were found in eyes with PAC and PACG. The mean IOP was 52.3 ± 12.6 mmHg in eyes with APAC and 15.5 ± 3.5 mmHg in eyes with CPAC ($P < .001$). The baseline patient characteristics are summarized in Table 1.

Eyes with APAC had shallower ACD (1.407 ± 0.301 mm, 1.960 ± 0.205 mm, 1.851 ± 0.264 mm) and less IC (0.233 ± 0.087 mm, 0.294 ± 0.068 mm, 0.327 ± 0.095 mm) than eyes with CPAC and fellow eyes of APAC (Table 2).

Table 1 Baseline patient characteristics

	APAC (n = 34)	CPAC (n = 60)	P-value
Sex (men/women)	9/25	8/52	.112
Age (years)	71.2 ± 8.7	71.2 ± 8.0	.804
IOP (mmHg)	52.3 ± 12.6	15.5 ± 3.5	< .001

Eyes with CPAC: primary angle closure suspect, 38 eyes; primary angle closure, 19 eyes; primary angle closure glaucoma, 3 eyes. The data are shown as the mean ± standard deviation. Sex differences were investigated by the chi-square test. Age and IOP differences were investigated using the Mann–Whitney test

APAC, acute primary angle closure; CPAC, chronic primary angle closure; IOP, intraocular pressure

ACD and IC were identified to be significant parameters in univariate analysis ($P < .001$ and $P = .001$, respectively). In multivariate analysis, ACD and IC remained significant ($P < .001$ and $P = .001$, respectively).

As ACD and IC decreased by 0.1 mm, the odds ratio for the risk of APAC was 3.288 (95% confidence interval [CI]

Table 2 Anterior segment parameters

	APAC (a) (n = 34)	CPAC (b) (n = 60)	Fellow (c) (n = 26)	P-value
PD (mm)	4.52 ± 0.85	4.40 ± 0.83	3.88 ± 0.74	.008: overall .781: (a)-(b) .009: (a)-(c) .020: (b)-(c)
ACD (mm)	1.407 ± 0.301	1.960 ± 0.205	1.851 ± 0.264	< .001: overall < .001: (a)-(b) < .001: (a)-(c) .157: (b)-(c)
IC (mm)	0.233 ± 0.087	0.294 ± 0.068	0.327 ± 0.095	< .001: overall .002: (a)-(b) < .001: (a)-(c) .185: (b)-(c)

The data are shown as the mean ± standard deviation. All parameters were investigated using the analysis of variance (ANOVA). Post hoc test was analyzed using Tukey test if the test of homogeneity of variance is passed (PD, IC), otherwise Games Howell test was used (ACD)

ACD, anterior chamber depth; APAC, acute primary angle closure; CPAC, chronic primary angle closure; IC, iris convexity; PD, pupil diameter

1.863–5.803) and 14.773 (95% CI 3.209–67.997), respectively (Table 3).

The AUCs for the ability of ACD (Fig. 2 a) and IC (Fig. 2 b) to discriminate eyes with APAC from eyes with CPAC were 0.931 and 0.742, respectively. The best cutoff value for ACD was 1.699 mm (sensitivity 0.824, specificity 0.917). For IC, the best cutoff value was 0.282 mm (sensitivity 0.853, specificity 0.533). The distribution of ACD and IC in the two groups is shown in Fig. 3.

Among the 60 eyes with CPAC, 14 eyes had closed angles in both nasal and temporal quadrants in AS-OCT. Thirty-four eyes with APAC and the 14 eyes with CPAC, in which the findings of angle closure were matched, were compared. Eyes with APAC had shallower ACD (1.407 ± 0.301 mm, 1.884 ± 0.259 mm) and less IC (0.233 ± 0.087 mm, 0.301 ± 0.088 mm) than eyes with CPAC ($P < .001$ and $P = .019$, respectively). The AUCs for the ability of ACD and IC to discriminate eyes with APAC from eyes with CPAC changed slightly (from 0.931 and 0.742 to 0.886 and 0.706, respectively). The best cutoff value for ACD was 1.699 mm (sensitivity 0.824, specificity 0.786). For IC, the best cutoff value was 0.222 mm (sensitivity 0.500, specificity 0.929).

Table 3 Discrimination of eyes with APAC from eyes with CPAC: results of multiple logistic regression analysis

Univariate model			
	Partial regression coefficient	P-value	Non-adjusted odds ratio (95% CI, as a 0.1-mm decrease)
PD	-0.0172	.510	0.983 (0.934–1.035)
ACD	0.8311	< .001	2.296 (1.642–3.210)
IC	1.1596	.001	3.189 (1.595–6.375)
Multivariate model			
	Partial regression coefficient	P-value	Adjusted odds ratio (95% CI, as a 0.1-mm decrease)
ACD	1.1903	< .001	3.288 (1.863–5.803)
IC	2.6928	.001	14.773 (3.209–67.997)

ACD, anterior chamber depth; CI, confidence interval; IC, iris convexity; PD, pupil diameter

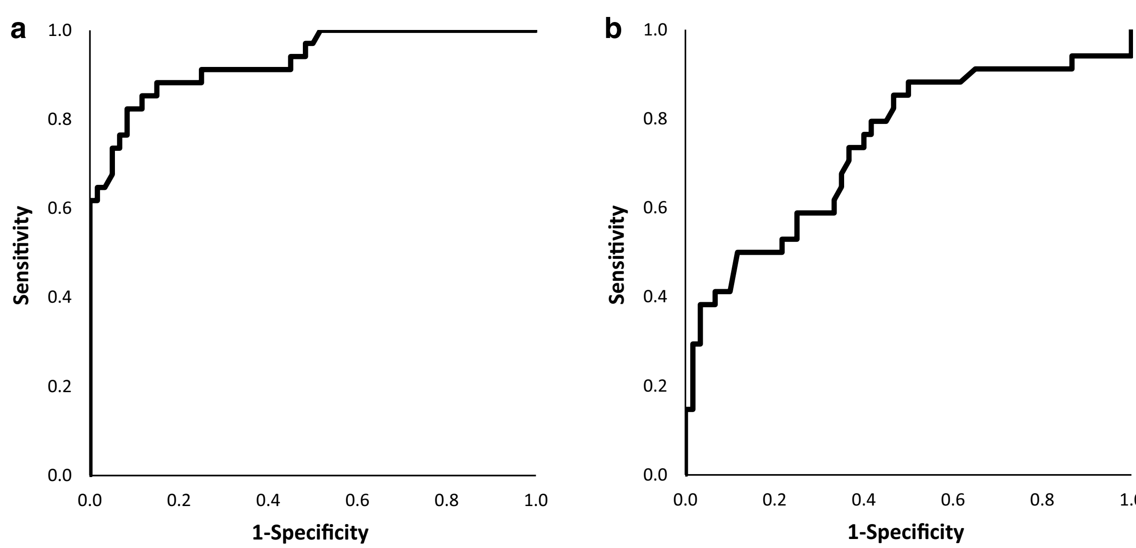

Fig. 2 Receiver operating characteristic (ROC) curves and areas under the curve (AUCs) discriminating eyes with acute primary angle closure from eyes with chronic primary angle closure. a ROC curve by anterior chamber depth. b ROC curve by iris convexity. We calculated the best cutoff value based on Younden's index and the sensitivity and specificity in that criteria

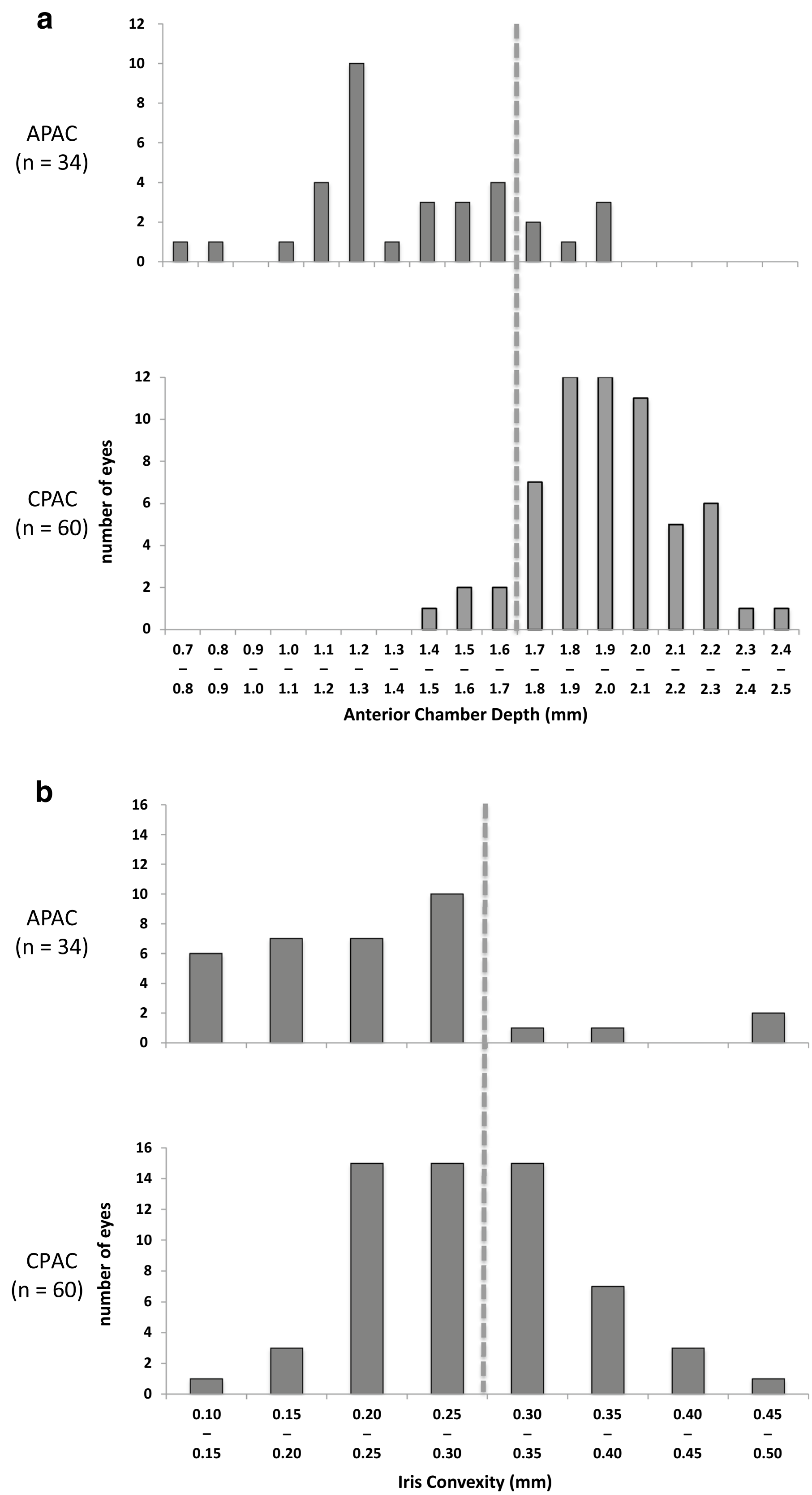

Fig. 3 Distribution of anterior segment parameters in eyes with acute primary angle closure (APAC) and eyes with chronic primary angle closure (CPAC). a anterior chamber depth. b iris convexity. The dashed lines show the best cutoff value

Discussion

We compared the anterior segment parameters between eyes with APAC, eyes with CPAC, and fellow eyes of APAC. Images of eyes with APAC were captured before treatment. APAC is a painful eye disease that needs immediate treatment to prevent blindness. However, the onset of APAC is often during the night, when emergency treatment can be difficult for both patients and medical staff. Therefore, appropriate prophylaxis is needed. Surgical lens extraction or LI are performed to prevent APAC. However, although these treatments are useful, some complications may occur. Complications of LI include IOP spikes, dysphotopsia, anterior chamber bleeding, cataract progression and changes in endothelial cell count [11]. Several serious complications including posterior capsule rupture, corneal edema and malignant glaucoma are reported in surgical lens extraction [12]. Therefore, it is important to assess the risk of APAC before its onset in eyes with angle closure and to evaluate the indication for prophylaxis.

ACD (AUC 0.931) and IC (AUC 0.742) proved efficient in the discrimination between eyes with APAC and those with CPAC. In general, an AUC > 0.90 indicates high accuracy, an AUC of 0.70–0.90 indicates moderate accuracy, an AUC of 0.50–0.70 indicates low accuracy, and an AUC of 0.50 indicates chance-level accuracy [10]. Therefore, our study suggests that these two parameters, especially ACD, would be useful for evaluating the risk of APAC.

It is reported that eyes with APAC have a shallower ACD. A previous study comparing eyes with APAC in its onset and fellow eyes also reports that a shallower ACD and less IC were the most important AS-OCT parameters associated with occurrence of APAC [4]. Another study comparing eyes with treated APAC with fellow eyes and eyes with PACS shows that eyes with APAC had the shallowest ACD, the least IC, and the greatest lens vault when compared with the other two groups [13]. In our previous study, ACD was the major predictor of anterior chamber angle width in eyes with angle closure [14]. Consistent with these findings, we found that ACD was an important determinant of the risk of APAC and that the best cutoff value for ACD was 1.7 mm. In eyes with a shallower ACD, especially less than 1.7 mm, the risk of complications might be tolerated and prophylaxis might be recommended to deepen the angle closure and avoid onset of APAC.

In this study, eyes with APAC had not only a shallower ACD but also less IC. Pupillary block has been considered as the dominant mechanism for development of APAC. The more the pupillary block increases, the more arched the iris becomes. Although our findings seem to be controversial, less IC is reported in previous studies [3, 4, 13]. It is uncertain if less IC is a result of APAC, that is, that the iris was not flattened before the onset of APAC, or if the shape of the iris has already been flat before the onset of APAC. If less IC is a consequence of APAC, increases in the IOP may result in increases in the pressure both in the anterior and posterior chambers which may compress the iris on both sides, leading to a flattened iris. One hypothesis is that as IOP increases in eyes with APAC, the pressure in the anterior chamber is expected to rise, thereby reducing the differential pressure between the anterior and posterior chambers that usually increases IC [4]. If, however, less IC is not a consequence of APAC, the etiology of APAC may involve not only a typical pupillary block mechanism but also a non-pupillary block mechanism, in particular an exaggerated lens vault. Thus, APAC might be provoked not only by an excessively arched iris but also an anterior forward or thickened lens. Because of the anterior forward or thickened lens, the surface of the lens would move anteriorly, push the iris, and make the angle more crowded.

Our study has several limitations. First, the study design was retrospective and included a small sample size. A prospective study with a larger number of patients would yield more reliable results. Further, all patients in this study were Japanese, so the results might not be applicable to other ethnic groups, especially non-Asians.

Third, the images of eyes with APAC were captured after onset of the disease, thus the structure of the anterior segment might be different from the structure that would be captured prior to onset of APAC. Uveal effusion after APAC and a shallow anterior chamber due to uveal effusion are reported [15]. It is known that fragile ciliary zonule is often observed in eyes with APAC and sometimes it provokes APAC. These findings could change the anterior segment parameters.

Due to the retrospective design of the study, we could not analyze the images before onset of APAC. Therefore, we might not be able to apply our cutoff value directly to patients with angle closure for assessment of risk. It would be helpful to research the etiology of APAC by analyzing images of eyes with angle closure, which subsequently develop APAC. Such research may be difficult for ethical reasons, but may be possible in patients with angle closure who refuse preventive treatment and go on to develop APAC. As an alternative, comparing the images during the attack and after alleviating the attack with medication may improve the understanding of APAC pathogenesis.

A limited number of parameters was included in this study because the images' quality in some eyes was too poor to detect the scleral spurs. Therefore, we could not analyze the parameters that would affect the angle closure mechanism, i.e., the angle opening distance, trabecular-iris space area, iris thickness and lens vault. Although we could not analyze lens vault, it is reported that it was independently associated with narrow angles and showed good diagnostic performance in detecting eyes with narrow angles [16]. Patients with APAC had difficulty in opening their eyelids sufficiently because of severe eye pain, nausea, and fatigue and were thus unable to avoid upper and lower lid interference with acquisition of images. Therefore, we analyzed only the horizontal meridian images.

The finding of angle closure in AS-OCT was different from that in gonioscopy. Therefore, 14 eyes with CPAC which had closed angles in both nasal and temporal quadrants in AS-OCT were also compared with eyes with APAC to match the findings of angle closure in the two groups. As with the comparison in all 60 eyes with CPAC, eyes with APAC had shallower ACD and less IC than the 14 eyes with CPAC. Although the best cutoff value for IC changed from 0.282 mm to 0.222 mm, that for ACD remained at 1.699 mm.

In conclusion, eyes with APAC had a shallower ACD and less IC than eyes with CPAC. An ACD of less than 1.7 mm may be at risk for APAC and would be recommended for prophylaxis. A further study in a larger patient population with long-term follow-up is needed.

Conflicts of interest S Yoshimizu, None; F. Hirose, None; S. Takagi; None, M. Fujihara; None, Y. Kurimoto; Grant (Alcon, AMO, Bayer, Canon, HOYA, Kowa, Novartis, Otsuka, Pfizer, Santen, Senju).

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