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ORIGINAL RESEARCH

Evaluation of Multimodal Biometric Parameters for Diagnosing Acute Angle Closure Secondary to Lens Subluxation

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ABSTRACT

Introduction: To evaluate the clinical characteristics and multimodal biometric parameters from ultrasound biomicroscopy (UBM) and IOL Master biometry of patients with acute secondary angle-closure due to lens subluxation (ASAC-LS), acute primary angle-closure (APAC), and cataract.

Methods: This retrospective study included 22 eyes with ASAC-LS, 27 eyes with APAC, and 39 eyes with cataract. Gender, age, affected eye, best corrected visual acuity, axial length, central corneal thickness, and anterior chamber depth (ACD) assessed by UBM and IOL Master were measured and compared between the three groups. In addition, we compared the ratio of ACD (ACD ratio) and the difference of ACD (ACD difference) measured by the two instruments. Logistic regression analysis was conducted to evaluate the predictive factors for lens subluxation. Receiver operating characteristic (ROC) curves were plotted to obtain a suitable cutoff value of biometric parameters to separate ASAC-LS cases from APAC and cataract cases.

Results: In the ASAC-LS group, the median (interquartile range [IQR]) ACD measured by IOL Master was 2.47 (IQR 1.85–2.92) mm while the median ACD measured by UBM was 3.11 (IQR 2.60–3.76) mm. The difference of ACD measured by the two instruments was statistically significant in the ASAC-LS group ($P < 0.001$) whereas the differences were not statistically significant in the APAC group ($P = 0.521$) and cataract group ($P = 0.204$). Subsequent pairwise comparison revealed that only the ACD difference (0.40 [IQR 0.22–1.08] mm) and ACD ratio (1.18 [IQR 1.07–1.40]) in the ASAC-LS group were significantly different from those in the APAC group (ACD difference 0.02 [IQR 0.01–0.07] mm; ACD ratio 1.01 [IQR 1.00–1.04]) and cataract group (ACD difference 0.09 [IQR 0.01–0.14] mm; ACD ratio 1.03 [IQR 1.00–1.04]) (all $P < 0.001$). The ACD difference and ACD ratio were significantly associated with lens subluxation in the multivariate logistic regression analysis ($P < 0.001$ and $P = 0.001$, respectively). Additionally, the ROC curve analysis showed that the ACD difference at 0.235 mm and the ACD ratio at 1.080 were the respective cut-off values

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for lens subluxation, with a sensitivity of 77.3% and specificity of 100.0%.

Conclusion: Our findings provide a new option for identifying lens subluxation. Specifically, combining the ACD from UBM and IOL Master may be helpful for differential diagnosis of ASAC-LS.

Keywords: Biometric parameters; Acute secondary angle closure due to lens subluxation; Acute primary angle closure; Anterior chamber depth; UBM; IOL Master

Key Summary Points

Why carry out this study?

It is not uncommon that acute secondary angle-closure due to lens subluxation (ASAC-LS) is initially misdiagnosed as acute primary angle-closure (APAC). Differential diagnosis of ASAC-LS is important and challenging in clinical practice.

The aim of our study was to explore the new, straightforward, and sensitive indicators for identifying lens subluxation by evaluating the clinical characteristics and multimodal biometric parameters from ultrasound biomicroscopy (UBM) and IOL Master of patients with ASAC-LS, APAC, and cataract.

What was learned from the study?

This study found that anterior chamber depth (ACD) difference measured by UBM and IOL Master at 0.235 mm and the ACD ratio measured by UBM and IOL Master at 1.080 were the cut-off values for lens subluxation, with the same sensitivity of 77.3% and specificity of 100.0%.

The study results suggest that combining the ACD from UBM and IOL Master may be helpful for differential diagnosis of ASAC-LS.

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide [1]. It can be classified into different subtypes according to distinct pathophysiologic mechanisms, including primary open-angle glaucoma (POAG), primary angle-closure glaucoma (PACG), and other subtypes (e.g., secondary glaucoma). As different subtypes of glaucoma should be treated with different regimens, inappropriate therapeutic methods may be chosen with misdiagnosis of the subtype of glaucoma.

Lens subluxation from trauma or arising spontaneously can result in a shallow anterior chamber and crowding of the angle, which is caused by the forward movement of the displaced lens [2]. Pupillary block also may occur due to the filling of the pupil with the lens, vitreous, or both [3]. This condition can lead to intraocular pressure (IOP) elevation and acute secondary angle closure (ASAC) attack. The frequent symptoms and signs of ASAC due to lens subluxation (ASAC-LS) are severe ocular pain, headache, elevated IOP, and shallow anterior chamber, all of which are remarkably similar to those of acute primary angle-closure (APAC) attack. It is not uncommon that ASAC-LS is initially misdiagnosed as APAC, especially in East Asia where PACG has the higher prevalence rate [2, 4–6]. Conventional anti-glaucoma treatment for APAC, such as topical pilocarpine, YAG peripheral iridectomy, and trabeculectomy, may be the treatments administered when ASAC-LS cases are misdiagnosed. Because of vitreous herniation and intractable shallow anterior chamber from lens subluxation, the conventional treatments for APAC rarely provide effective IOP control, which lead to irreversible optic nerve damage in patients with ASAC-LS [2, 4]. Therefore, differential diagnosis of ASAC-LS is both important and challenging in clinical practice.

The routine procedure in clinical diagnosis is to observe the signs of lens subluxation, including iridodonesis, phacodonesis, visibility of the lens equator, decentration of the lens, and vitreous prolapse in the anterior chamber[7–9]. However, the clinical manifestations of ASAC-LS may be atypical, and these signs may be neglected due to corneal edema caused by an elevated IOP [10]. Effective methods for diagnosing lens subluxation have been explored by clinicians. Some studies have reported several indicators for the diagnosis of lens subluxation through qualitative and quantitative analysis of ultrasound biomicroscopy (UBM) imaging features or the biometric parameters from ocular biometry [7, 8, 10–12]. Nevertheless, most of these studies involved complex measurements and complicated formulas, making them difficult to apply in clinical practice.

Lens subluxation that has not been detected with the patient in the sitting position in the clinic is sometimes detected when the patient is in the supine position in the operating room as the position of the lens may change depending on the body posture [5]. In the present study, we explored the new, straightforward, and sensitive indicators that reflect posture-related change of lens position for identifying lens subluxation by evaluating anterior chamber depth (ACD) of patients with ASAC-LS, APAC, and cataract. The ACD was measured by two different instruments, the Zeiss IOL Master, with the patient in a sitting position, and UBM, with the patient in a supine position. The evaluation of multimodal biometric parameters may be helpful for the differential diagnosis of patients with ASAC-LS.

METHODS

This retrospective study was performed in the First Affiliated Hospital of Nanjing Medical University and the First Affiliated Hospital of Kunming Medical University.

The ethics committee of the First Affiliated Hospital with Nanjing Medical University reviewed and approved this retrospective study (2020-SR-340). The study adhered to the tenets of the 1964 Declaration of Helsinki and its subsequent amendments.

The medical records of patients with ASAC-LS, APAC, and cataract attending the two hospitals from September 2019 to February 2022 were consecutively reviewed. We applied the following inclusion criteria of ASAC-LS [7, 8]: (1) patients with sudden ocular pain, blurred vision, nausea, vomiting, and elevated IOP; (2) silt-lamp microscopy revealing conjunctival hyperemia, corneal edema, shallow and/or uneven anterior chamber, with/without iridodonesis, phacodonesis, or vitreous herniation into the anterior chamber; and (3) lens subluxation confirmed by either (a) displacement of the lens equator after full dilation of pupil by slit-lamp examination before surgery, or (b) rupture or disappearance of the zonule and the displacement of lens equator in some quadrants in the operative setting and ruling out of the possibility of iatrogenic trauma to the zonule by two experienced surgeons. The inclusion criteria of APAC were as follows [7, 13–16]: (1) the presence of at least two of the following symptoms: ocular or periocular pain, nausea and vomiting, and an antecedent history of intermittent blurring of vision with haloes; (2) IOP $>$ 21 mm Hg; (3) presence of conjunctival injection, shallow anterior chamber, and mid-dilated fixed pupil with or without corneal epithelial edema; (4) presence of an occludable angle in the affected eye; and (5) patients without lens subluxation. The inclusion criteria of cataract were: (1) lens opacities of more than N2, C2, or P2 according to the Lens Opacities Classification System II; (2) patients with open angle and IOP $\leq$ 21 mmHg; and (3) patients without lens subluxation. Patients with the following conditions were excluded: (1) patients who are unable to participate in the ocular examinations; (2) patients with intumescent swelling or hyper mature lens; (3) patients with a history of corneal disease, uveitis, corneal surgery, and intraocular surgery; (4) patients with zonular laxity but without definite signs of lens subluxation; and (5) patients with definite ocular trauma history.

All patients were asked about their medical history, including history of trauma, and underwent a detailed ophthalmologic examination, including best corrected visual acuity (BCVA), slit-lamp microscopy, tonometry, specular microscope, UBM (model SW-3200L; SUOER, Tianjin, China), and the IOL Master 500/IOL Master 700 (Carl Zeiss Meditec, Jena, Germany). The IOL Master 700 biometer was used in the First Affiliated Hospital of Nanjing Medical University and the IOL Master 500 biometer was used in the First Affiliated Hospital of Kunming Medical University. The demographic and clinical data of patients were retrieved from the patient's medical records. Ocular biometric parameters included axial length (AL), central corneal thickness (CCT), and ACD. ACD was taken as the depth from the epithelium of the cornea to the anterior surface of the lens in this study, and was detected using both IOL Master and UBM. ACD-I and ACD-U were used to denote the value of ACD measured by the IOL Master and UBM, respectively. All enrolled eyes underwent lens extraction surgery by two experienced surgeons. The type of lens extraction surgery for each patient was determined according to the extent of zonular dehiscence. Phacoemulsification with capsular tension ring and intraocular lens (IOL) implantation was performed in patients with zonular dehiscence of < 6 h. Intracapsular cataract extraction with intrascleral fixation of IOL was chosen for patients with zonular dehiscence of > 6 h. All data were collected after the corneas were clear before surgery.

Statistical Analysis

SPSS version 21.0 software (IBM Corp, Armonk, NY, USA) was used for the statistical analyses. The artwork was created using GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA). Quantitative data with a normal distribution were expressed as mean ± standard deviation (SD), and quantitative data with no normal distribution were expressed as median deviation with interquartile range (IQR). Quantitative data were subject to one-way analysis of variance (ANOVA) or Kruskal–Wallis *H*-test, depending on data distribution. Categorical data were analyzed using the Chi-squared test. The Bonferroni method was used to correct for post hoc pairwise comparisons of significance levels. Repeated measurement data were analyzed by repeated-measures ANOVA. Univariate logistic regression analysis was conducted to evaluate the predictive factors for lens

Table 1 The demographic characteristics and ocular biometric parameters of the patients enrolled in the study

Characteristics/parameters	ASAC-LS	APAC	Cataract	*P* value
Cases (*n*, eyes)	22	27	39	/
Gender (*n*, male/female)	11/9	7/17	17/13	0.095
Age (years)	54.50 (44.75–62.50)	61.00 (59.00–64.00)	61.00 (53.00–66.00)	0.078
OD/OS (*n*, eyes)	13/9	17/10	21/18	0.756
BCVA (Log MAR)	0.82 (0.49–1.40)	1.00 (0.60–2.00)	0.70 (0.52–1.30)	0.145
AL (mm)	23.36 ± 1.32	22.45 ± 0.80	23.32 ± 0.98	0.002[a]
CCT (μm)	537.14 ± 34.18	530.74 ± 45.74	514.62 ± 39.13	0.080
ACD-I (mm)	2.47 (1.85–2.92)	2.15 (1.94–2.27)	3.32 (3.12–3.62)	< 0.001[b]
ACD-U (mm)	3.11 (2.60–3.76)	2.17 (1.96–2.29)	3.40 (3.18–3.75)	< 0.001[c]

Values are presented as the mean ± standard deviation (SD) or as the median with the interquartile range (IQR) in parentheses

ASAC-LS Acute secondary angle closure due to lens subluxation, *APAC* acute primary angle-closure, *OD* right eye, *OS* left eye, *BCVA* best corrected visual acuity, *AL* axial length, *CCT* central corneal thickness, *ACD-I* anterior chamber depth measured by the IOL Master biometric system , *ACD-U* anterior chamber depth measured by ultrasound biomicroscopy

[a]Significance pairwise comparison: $P = 0.008$ for ASAC-LS vs. APAC; $P = 0.003$ for APAC vs. cataract

[b]Significance pairwise comparison: $P < 0.001$ for ASAC-LS vs. cataract; $P < 0.001$ for APAC vs. cataract

[c]Significance pairwise comparison: $P < 0.001$ for ASAC-LS vs. APAC; $P < 0.001$ for APAC vs. cataract

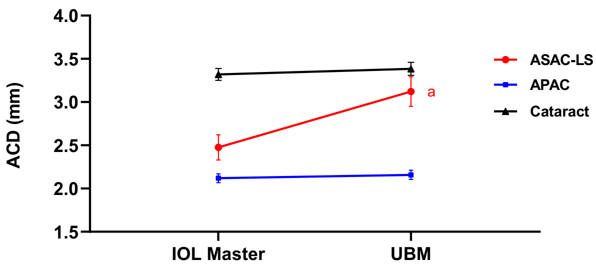

Fig. 1 Comparison of the differences in anterior chamber depth (*ACD*) measured by the IOL Master biometer and ultrasound biomicroscopy (*UBM*) in the ASAC-LS group, APAC group, and cataract group. *ASAC-LS* Acute secondary angle closure due to lens subluxation, *APAC* acute primary angle-closure. Lowercase a indicates a significant difference at $P < 0.001$, repeated-measures analysis of variance (ANOVA) with SIDAK correction

subluxation. Variables with $P < 0.2$ were included in the multivariate logistic regression analyses. Receiver operating characteristic (ROC) curves were plotted to obtain a suitable cutoff value of biometric parameters to separate ASAC-LS cases from APAC and cataract cases. A P value < 0.05 was considered statistically significant.

RESULTS

Twenty-two eyes of 20 patients with ASAC-LS, 27 eyes of 24 patients with APAC, and 39 eyes of 30 patients with cataract were included in this study. The demographic characteristics and ocular biometric parameters of all enrolled patients are summarized in Table 1. Gender, age, affected eye, preoperative BCVA and CCT were not significantly different among the three groups ($P = 0.095$, $P = 0.078$, $P = 0.756$, $P = 0.145$, and $P = 0.08$, respectively). There were statistically significant differences in AL, ACD-I, and ACD-U among the groups ($P = 0.002$, $P < 0.001$, and $P < 0.001$, respectively). However, further pairwise comparisons revealed that the above biometric parameters in the ASAC-LS group were not significantly different from those in the APAC group and cataract group.

As determined by repeated-measures ANOVA, the main effects on ACD were significant according to group ($F = 52.091$, $P < 0.001$) and measurement method ($F = 52.091$, $P < 0.001$). The interaction effects of group and measurement method on ACD were also significant ($F = 29.440$, $P < 0.001$). The simple effects analysis is shown in Fig. 1. The differences in ACD measured by the two instruments were not statistically significant in the APAC group ($P = 0.521$) and cataract group ($P = 0.204$), but there was a statistically significant difference between the two instruments for ACD measurements in the ASAC-LS group ($P < 0.001$).

Based on the above finding, we chose the ratio of ACD (ACD-U/ACD-I) and the difference in ACD (ACD-U − ACD-I) measured by the two instruments as new parameters to reflect the

Table 2 Anterior chamber depth difference and Anterior chamber depth ratio of the enrolled patients

Parameters[a]	ASAC-LS	APAC	Cataract	*P* value
ACD difference (mm)	0.40 (0.22–1.08)	0.02 (0.01–0.07)	0.09 (0.01–0.14)	< 0.001[b]
ACD ratio	1.18 (1.07–1.40)	1.01 (1.00–1.04)	1.03 (1.00–1.04)	< 0.001[c]

Values are presented as the median with IQR in parentheses

[a]ACD difference is the ACD measured by UBM − ACD measured by the IOL Master biometer. ACD ratio is the ACD measured by UBM/ACD measured by the IOL Master biometer

[b]Significance pairwise comparison: $P < 0.001$ for ASAC-LS vs. APAC; $P < 0.001$ for ASAC-LS vs. Cataract; $P = 0.240$ for APAC vs. Cataract

[c]Significance pairwise comparison: $P < 0.001$ for ASAC-LS vs. APAC; $P < 0.001$ for ASAC-LS vs. Cataract; $P = 1.000$ for APAC vs. Cataract

Table 3 Univariate and multivariate logistic regression models

Variables	Univariate logistic regression model		Multivariate logistic regression model 1[a]		Multivariate logistic regression model 2[a]	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Gender						
Male	1					
Female	0.69 (0.26, 1.83)	0.457				
Age (years)	0.98 (0.94, 1.01)	0.188	0.99 (0.93, 1.05)	0.672	0.98 (0.93, 1.04)	0.516
Affected eye						
OD	1					
OS	0.94 (0.35, 2.50)	0.901				
BCVA (log MAR)	0.84 (0.45, 1.56)	0.582				
AL (mm)	1.41 (0.89, 2.24)	0.140	0.94 (0.45, 1.97)	0.864	1.15 (0.54, 2.43)	0.725
CCT (μm)	1.01 (1.00, 1.02)	0.117	1.00 (0.99, 1.02)	0.662	1.00 (1.00, 1.02)	0.811
ACD difference (mm) × 100[b]	1.19 (1.09, 1.29)	< 0.001	1.18 (1.08, 1.29)	< 0.001		
ACD ratio × 100[b]	1.70 (1.25, 2.31)	0.001			1.67 (1.23, 2.28)	0.001

CI Confidence interval, *OR* odds ratio

[a]Model 1: analysis of ACD difference; model 2: analysis of ACD ratio

[b]The ACD difference and ACD ratio were each multiplied by 100 for the statistical analysis due to minor variations in the range of the variables

difference between the two measurement methods. As shown in Table 2, the differences in ACD difference and ACD ratio among the three patient groups were statistically significant ($P < 0.001$ and $P < 0.001$, respectively). Further pairwise comparison revealed that ACD difference and ACD ratio in the ASAC-LS group were significantly different from those in the APAC group and cataract group, respectively.

Logistic regression models were used to evaluate the association of clinical characteristics and biometric parameters of the patients with lens subluxation; the results are presented in Table 3. Lens subluxation (ASAC-LS group) was considered to be a positive event and no lens subluxation (APAC group and cataract group) was considered to be a negative event. To avoid multicollinearity, variables that correlated significantly with each other were not analyzed simultaneously. Thus, analysis of ACD difference (model 1) and analysis of ACD ratio (model 2) were conducted in separate models. Following univariable analysis, the variables with a P value < 0.20 were included in the multivariate analysis. According to the multivariate models, the ACD difference and ACD ratio were significantly associated with lens subluxation ($P < 0.001$ and $P = 0.001$, respectively).

We selected the ACD difference and the ACD ratio that showed significant differences as the new potential predictors for lens subluxation. The ROC curve was constructed to determine the diagnostic accuracy of the ACD difference and ACD ratio. The results of the ROC curve analysis are presented in Fig. 2. The area under the ROC (AUROC) curve of ACD difference and the ACD ratio was 0.917 and 0.928, respectively. The ACD difference at 0.235 mm was found to be the cut-off value for lens subluxation, with a sensitivity of 77.3% and a specificity of 100.0%. The ACD ratio at 1.080 was found to be the

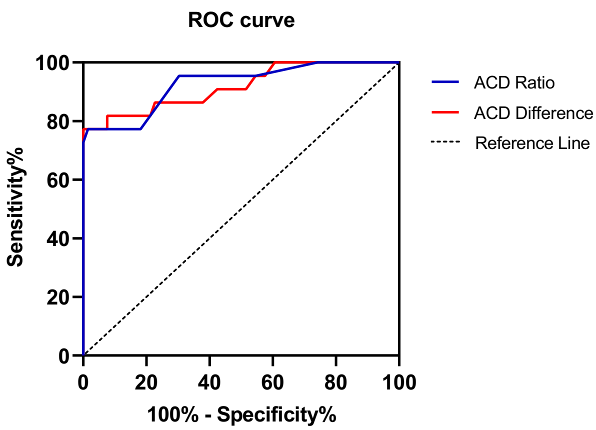

Fig. 2 Receiver operating characteristics (ROC) curve for ACD difference and ACD ratio regarding the diagnosis of lens subluxation. The area under the receiver operating characteristic (AUROC) curve of the ACD difference and ACD ratio was 0.917 and 0.928, respectively. ACD Difference is: ACD measured by UBM − ACD measured by the IOL Master biometer. The ACD Ratio is: ACD measured by UBM/ACD measured by the IOL Master biometer

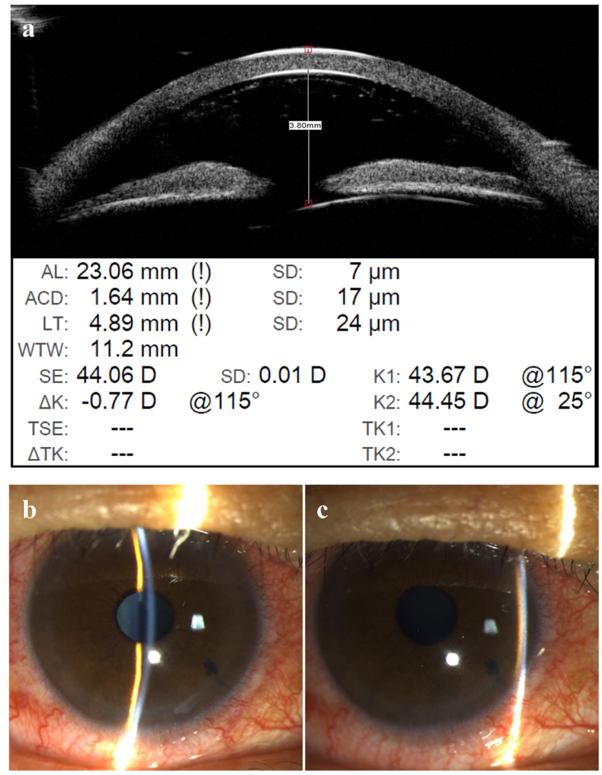

Fig. 3 Case 1 has acute secondary angle closure due to lens subluxation (ASAC-LS group). The patient had a history of acute angle closure attack in his right eye. **a** UBM measured with the patient in a supine position revealed partial displacement of the lens and a normal central and peripheral ACD. The ACD measured by UBM was 3.80 mm (upper figure of **a**), and the ACD measured by the IOL Master biometer was 1.64 mm (lower figure of **a**). **b**, **c** Photograph of the anterior segment of the patient's right eye measured with the patient in a sitting position shows an obvious shallow central ACD and a peripheral ACD of less than one-fourth the corneal thickness

cut-off value for lens subluxation, with a sensitivity of 77.3% and a specificity of 100.0%.

Two representative cases from the ASAC-LS group are shown in Figs. 3 and 4, respectively. Figure 3 shows the clinical data of a patient with a history of acute angle closure attack in his right eye; peak IOP was 42 mmHg. The ACD differed greatly before surgery when measured with the patient in different positions (Fig. 3a–c). The sign of lens subluxation was noted on the UBM image and the ACD-U was 3.80 mm (Fig. 3a). However, ACD-I assessed using the IOL-Master biometer was 1.64 mm (Fig. 3a). The ACD difference was 2.16 mm and the ACD ratio was 2.32, which matched the cut-off value for lens subluxation. Figure 4 shows the clinical data of a second patient who had a history of acute angle closure attack in his right eye; peak IOP was 35 mmHg. The UBM images of both eyes before surgery showed no obvious lens displacement (Fig. 4a, c). Nevertheless, the ACD difference was 0.38 mm (right eye) and 0.41 mm (left eye), and the ACD ratio was 1.27 (right eye) and 1.14 (left eye) in this case. According to the cut-off value for lens subluxation diagnosis, the patient might have had lens subluxation in both eyes. The diagnosis of lens subluxation was confirmed during the subsequent cataract surgery on both eyes.

DISCUSSION

Lens subluxation is a multifactorial disease, with symptoms that can be variable and occult [7, 8]. In the present study, we analyzed clinical characteristics and multimodal biometric parameters of patients with ASAC-LS, APAC, and cataract obtained from UBM and the IOL

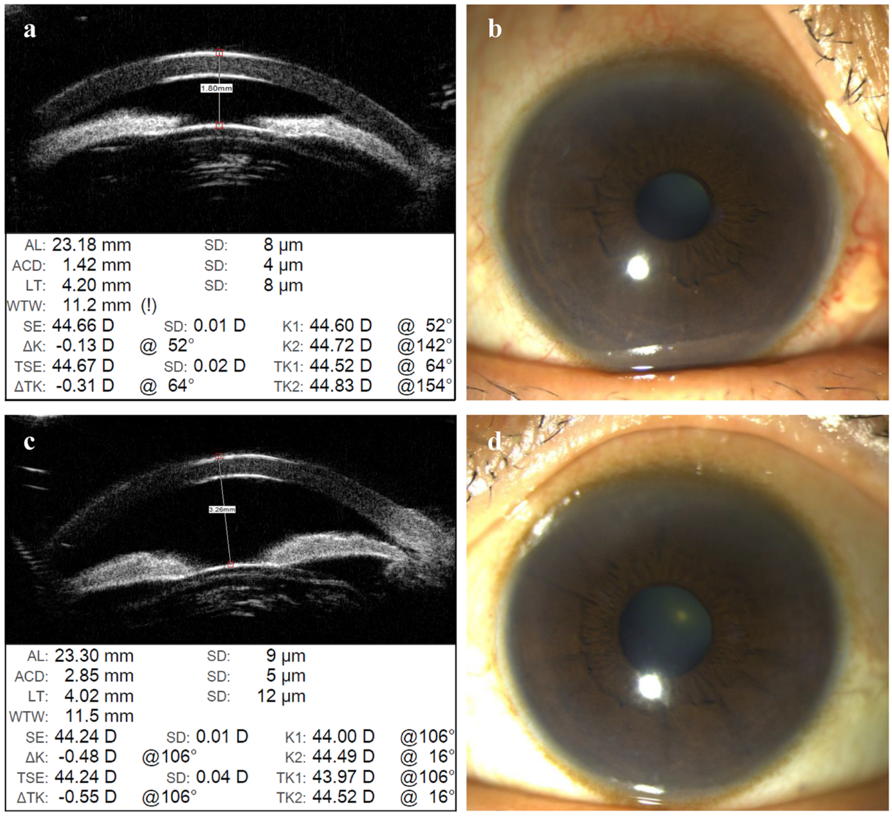

Fig. 4 Case 2 has acute secondary angle closure due to lens subluxation (ASAC-LS group). The patient had a history of acute angle closure attack in his right eye. **a**, **b** Clinical data on his right eye. **a** UBM measured with the patient in a supine position revealed no obvious displacement of the lens. The ACD measured by UBM (ACD-U) was 1.80 mm (upper figure of **a**), and the ACD measured by the IOL Master biometer (ACD-I) was 1.42 mm (lower figure of **a**). **b** Photograph of the anterior segment of the patient's right eye. **c**, **d** Clinical data on the patient's left eye. **c** UBM measured in a supine position revealed no obvious displacement of the lens. The ACD-U was 3.26 mm (upper figure of **c**) and the ACD-I was 2.85 mm (lower figure of **c**). **d** Photograph of the anterior segment of the patient's left eye. As the patient had no history of acute angle closure attack in his left eye, the data on his left eye was not included in this analysis

Master biometer. Our findings suggested that the ACD difference and ACD ratio from UBM and the IOL Master might be new potential predictors for identifying lens subluxation, especially for the differential diagnosis of ASAC-LS.

Epidemiological studies have shown that the prevalence of PACG is highest in East Asia [1, 6]. PACG is more visually debilitating than POAG [17] and is responsible for the vast majority of patients in China with blindness due to bilateral glaucoma [18–20]. Therefore, effective intervention for PACG is the key to prevent blindness caused by glaucoma in East Asia, especially in China. APAC attack is a unique form of PACG which requires the appropriate emergency treatment as glaucomatous optic neuropathy can develop rapidly if patients with high IOP due to APAC do not receive treatment [13, 14]. However, it is not uncommon that ASAC attack due to lens subluxation is initially misdiagnosed as APAC attack in the clinic. For example, two of the largest departments of ophthalmology in China reported similar misdiagnosis rates: 31 eyes (5.89%) with ASAC-LS were misdiagnosed with APAC between March 2003 and March 2009 in Zhongshan Ophthalmic Center [2] and 85 inpatients (4.1%) with lens subluxation were misdiagnosed with PACG between January 2013 and January 2016 in the Eye and ENT Hospital of Fudan University [4]. Such misdiagnoses can lead to inappropriate treatment choices and affect the management of the harmful high IOP. Recently, lens extraction has emerged as first-line therapy for PACG, including APAC attack [5, 20]. Nevertheless, the treatment of ASAC-LS may be complicated, and ciliary sulcus IOL placement, the use of a capsular tension ring, or sclera-fixated IOL according to the extent of zonular weakness have been suggested as treatment options [5]. If the correct diagnosis can be made before the surgery takes place, the appropriate treatments can be applied according to the patient's condition, thereby increasing the success rate of the surgery and the recovery of visual function [8, 9].

Lens subluxation is likely due to the partial zonular dehiscence resulting from trauma or occurring spontaneously [7, 8]. Most patients with lens subluxation can be diagnosed by observation of the common manifestations of lens subluxation (see Introduction). These manifestations are not difficult to observe by slit-lamp examination once the pupil is fully dilated. However, it is challenging to detect lens subluxation in eyes presenting with a sudden onset of symptoms and signs similar to those of APAC attack. Clinicians seldom choose to dilate the pupil of these patients because of a potential risk of exacerbation of pupillary block; rather, pilocarpine is still widely used in Asian countries [21], and miotic therapy, which makes the condition worse, might be used in such patients. Corneal edema due to high IOP also increases the difficulty of diagnosis.

With the continuous development and application of ophthalmic technology, multiple ocular biometric imaging and biometry instruments have been developed to objectively and accurately visualize and evaluate biometric conditions [7, 22]. UBM has been proven to be a helpful method for identifying lens subluxation [7, 10–12, 23, 24]. However, UBM is relatively operator-dependent [14], and there is a significant learning curve before zonules can be accurately diagnosed with UBM. If the examiner is inexperienced, there is the possibility of false-negative results [23]. Sometimes even an experienced operator can not detect occult lens subluxation with UBM, especially when the range of zonula dehiscence is small. Therefore, researchers have been searching for more effective diagnostic methods for lens subluxation. Wang et al. reported that iris lens angle = 0 and nonforward convexity of the iris are sensitive and characteristic indicators that hint at a clinical diagnosis of ASAC-LS [12]. Xing et al. discovered that relative lens position was the most sensitive indicator to distinguish APAC from ASAC-LS [8]. However, these methods involve far too many parameters and complicated formulas, making them difficult to apply in clinical practice.

A number of studies have focused mainly on the difference in ACD between the affected and fellow eye. In one study of patients with ASAC-LS, the affected eye had a narrow angle whereas the unaffected eye had a wide angle while, in contrast, patients with APAC had narrow angles in both eyes [2]. Lin et al. found that an asymmetrical anterior chamber between bilateral eyes is an important feature in lens subluxation-induced acute angle closure [10]. Jing et al. reported that an inter-eye difference in ACD of > 0.63 mm was highly indicative of lens subluxation [7]. However, it is also general knowledge that some East Asians are born with shallow anterior chambers. In some patients, especially in those with lens subluxation occurring spontaneously, lens subluxation may appear in both eyes, such as the case reported in Fig. 4. An inter-eye ACD difference may make it more difficult to diagnose lens subluxation among these individuals.

In our present study, we evaluated clinical characteristics and multimodal biometric parameters from UBM and IOL Master of patients with ASAC-LS, APAC, and cataract. The clinical characteristics and AL of patients presented similar results as reported in previous studies [5, 7, 25]. The patients with ASAC-LS were relatively younger (although the difference was not statistically significant, $P = 0.078$) and normal AL, similar to patients with cataract (Table 1). There was a female preponderance among patients with APAC (although again the difference was not statistically significant, $P = 0.095$) and shorter AL ($P = 0.002$) (Table 1).

However, these results did not provide enough information for a differential diagnosis.

Many instruments based on different techniques are available for measuring ACD [25]. A unique aspect of this study was acquiring ACD measurements by two different instruments. The IOL Master 500 is an ophthalmic biometer based on partial coherence interferometry [26] and the IOL Master 700 is an ophthalmic biometer based on swept source optical coherence tomography [27]. The UBM technique, developed by Pavlin et al. [28], can provide images of the biometric and quantitative assessments of the ocular biometric parameters [25, 29]. It was interesting to note that differences in ACD measured by the two instruments were not statistically significant in the APAC group ($P = 0.521$) and cataract group ($P = 0.204$), whereas they were statistically significant in the ASAC-LS group ($P < 0.001$) (Fig. 1). Based on this result, the difference between these two measurements of ACD may be a potential predictor for diagnosing ASAC-LS; thus, we selected the ACD ratio and the ACD difference as new parameters to reflect the difference between these two measurements. In pairwise comparisons, only the ACD difference and ACD ratio of the ASAC-LS group were statistically different compared with the APAC group and cataract group (Table 2). Moreover, logistic regression models revealed that ACD difference and ACD ratio were significantly associated with lens subluxation ($P < 0.001$ and $P = 0.001$, respectively) (Table 3).

In order to select the indicator with the best diagnostic value, we used ROC curve analysis to determine the potential diagnostic value of the ACD difference and ACD ratio (Fig. 2). The ACD difference at 0.235 mm and the ACD ratio at 1.080 were found to be the cut-off values for lens subluxation, with the same sensitivity of 77.3% and specificity of 100.0%. The value of an ACD difference > 0.235 mm or an ACD ratio > 1.080 must evoke a high level of suspicion for lens subluxation. The AUC of the ACD difference and ACD ratio was 0.917 and 0.928, respectively, demonstrating that the ACD ratio was more valuable in terms of lens subluxation detection.

In addition to the differences in these two diagnostic technologies, there is also a large difference between these two measurement methods in terms of the body posture during the examination. The position of the subluxated lens can also change depending on the body posture [5]. Given our findings, we speculated that the difference for ACD between the two measurement methods might come from the different body postures. For the UBM examination, patients were examined in the supine position, while for the IOL Master biometric measurement, patients were examined in a sitting position. When the lens is subluxated, the lens zonule dehiscence has a large effect on the position of the lens. Thus, changing body position causes the subluxated lens to move, which leads to changes in ACD, such as in the case shown in Fig. 3, who came from the ASAC-LS group. The ACD of this patient differed greatly depending on the body posture during the examination (sitting vs. supine). This alteration in ACD depending on body position could help clinicians identify lens subluxation which may be overlooked by a single examination, such as UBM. Figure 4 is an example of a case also from the ASAC-LS group, but without obvious displacement of lens in the UBM images of both eyes before surgery. However, the diagnosis of lens subluxation was confirmed during the subsequent cataract surgery on both eyes. The ACD difference and ACD ratio of both eyes met the cut-off value for lens subluxation diagnosis. As the specificity obtained from the ROC curve was 100.0%, we should highly suspect lens subluxation when the ACD difference and the ACD ratio are above the cut-off value.

Compared with the previous reports [5, 7, 8, 10, 12], our results provide a new diagnostic method for lens subluxation with high specificity which would be easy to master and convenient to use in the clinic. Our method has many advantages in terms of the differential diagnosis of lens subluxation, especially in patients with shallow anterior chamber or lens subluxation in both eyes. To our knowledge, this is the first study that has focused on combining ACDs from UBM and the IOL Master biometer for diagnosing lens subluxation.

This study has several limitations. First, this was a retrospective study, and the clinical information was collected by reviewing the medical records of the patients enrolled in the study. Therefore, quantitative analysis of the extent of lens subluxation was not performed as the data involving areas of zonular dehiscence were missing. Some patients included in this study did not receive the related ocular examinations for the fellow eyes and, therefore, the data on the fellow eyes were lacking. Second, our sample size was relatively small, and the conclusions drawn need further confirmation in a larger study population. A large-sized study with a prospective design is required to validate our results, as is quantitative analysis of the association between the area of zonular dehiscence and the extent of posture-related lens movement.

CONCLUSION

This study provides a new option for identifying lens subluxation. Specifically, the ACD difference and ACD ratio may be helpful indicators for differential diagnosis of ASAC-LS.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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