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Occult zonulopathy detected during cataract surgery in patients with acute primary angle closure

Jiawei Chen [1, 2, 3], **Xiang-Ling Yuan** [1, 4], **Xinyue Zhang** [1, 2], **Yanjun Huang** [3], **Xiaona Huang** [3], **Xuanchu Duan** [Corresp. 1, 2]

[1] Aier Academy of Ophthalmology, Central South University, Changsha, Hunan, China

[2] Aier Glaucoma Institute, Hunan Engineering Research Center for Glaucoma with Artificial Intelligence in Diagnosis and Application of New Materials, Changsha Aier Eye Hospital, Changsha, Hunan, China

[3] Department of Ophthalmology, The Sixth Affiliated Hospital of South China University of Technology, Foshan, Guangdong, China

[4] Aier Eye Institute, Changsha, Hunan, China

Corresponding Author: Xuanchu Duan
Email address: duanxchu@csu.edu.cn

Background: Whether occult zonulopathy contributes to the development of acute primary angle closure (APAC) remains elusive. This study aimed to determine the association of occult zonulopathy detected during cataract surgery with acute APAC and investigate the biometric characteristics of APAC patients with or without occult zonulopathy.

Methods: Retrospective case-control study. A total of 27 Chinese unilateral APAC subjects and 132 control subjects with comprehensive ophthalmic examinations were recruited. Occult zonulopathy was identified with the intraoperative signs during cataract surgery. The proportion of occult zonulopathy was compared between the APAC and control groups. Multivariate logistic analysis was conducted to determine the association of occult zonulopathy with APAC. The ocular biometric parameters were compared between APAC and the contralateral eyes in APAC patients with or without occult zonulopathy.

Results: APAC patients (63.0%) had a significantly larger proportion of occult zonulopathy than control subjects (1.5%, P < 0.001). In multivariate logistic analysis, occult zonulopathy was significantly associated with APAC after adjusting the axial length (AL) and sex (OR = 126.49, 95% CI: 20.89 - 766.02; P < 0.001). Compared to contralateral eyes, shallower central anterior chamber depth, lens position and relative lens position closer to the anterior were found in APAC eyes both with and without occult zonulopathy (all P < 0.05), but no difference in AL and lens thickness.

Conclusion: A larger proportion of occult zonulopathy was significantly associated with APAC. Occult zonulopathy could be a risk factor for APAC by inducing a forward shifting of the lens.

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Jiawei Chen[1,2,3], Xiang-Ling Yuan[1,4], Xinyue Zhang[1,2], Yanjun Huang[3], Xiaona Huang[3], Xuanchu Duan[1,2#]

[1] Aier Academy of Ophthalmology, Central South University, Changsha, Hunan, China.

[2] Aier Glaucoma Institute, Hunan Engineering Research Center for Glaucoma with Artificial Intelligence in Diagnosis and Application of New Materials, Changsha Aier Eye Hospital, Changsha, Hunan, China.

[3] Department of Ophthalmology, The Sixth Affiliated Hospital of South China University of Technology, Foshan, Guangdong, China.

[4] Aier Eye Institute, Changsha, Hunan, China.

#Corresponding author:

Xuanchu Duan, M.D., Ph.D.

Aier Glaucoma Institute, Hunan Engineering Research Center for Glaucoma with Artificial Intelligence in Diagnosis and Application of New Materials, Changsha Aier Eye Hospital, No.188 South Furong Road, Changsha, Hunan Province, 410015, P.R. China. Email: duanxchu@csu.edu.cn; Phone: +86-0731 85229669; Fax: +86-0731 85229669; ORCID: 0000-0002-3148-1703.

Abstract

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Introduction

Glaucoma, a leading cause of irreversible blindness, brings about an increasing burden worldwide.(GBD & Group 2021; Lin et al. 2023) Primary angle-closure glaucoma (PACG) is one of its essential subtypes, characterized by an anatomically closed angle resulting in intraocular pressure (IOP) elevation.(Weinreb et al. 2014) PACG is responsible for approximately 50% of blindness attributed to glaucoma. (Quigley & Broman 2006) It was estimated that PACG would affect more than 32 million individuals globally by 2040, with about 80% of these cases in Asia. (Tham et al. 2014) According to the protocol of the International Society of Geographic and Epidemiologic Ophthalmology (ISGEO), primary angle closure was categorized into three types: primary angle-closure suspect (PACS), primary angle closure (PAC), and primary angle-closure glaucoma (PACG). (Foster et al. 2002) Acute primary angle closure (APAC) is considered an ophthalmic emergency with a rapid increase in IOP, which could induce acute optic nerve injury and potentially lead to permanent visual loss or blindness. (Gedde et al. 2021)

Studies have shown that short axial length (AL), shallow anterior chamber depth (ACD), and thick lens thickness (LT) are the collective anatomical risk factors for PACG.(Marchini et al. 2015) Pupillary block, plateau iris, abnormal lens position, and choroidal effusion are taken for the main mechanisms of closed angle in PACG. (Sun et al. 2017) Among patients diagnosed with unilateral APAC, only 6.5% of them developed glaucoma in their contralateral eyes during a follow-up period of 4 to 10 years. (Friedman et al. 2006) It remains confusing that some unilateral APAC patients could avoid acute angle-closure attacks on their contralateral eyes for years without any treatment. Rather than acute angle closure, most angle closure developed chronically wanting in signs and symptoms, which is still difficult to fully interpret by the available evidence.(Wilensky et al. 1993) With the comprehensive application of phacoemulsification in cataract extraction, a significant incidence of occult zonulopathy in PACG patients was observed during cataract surgery.(Kwon & Sung 2017; Zhang et al. 2023) However, limited studies were conducted to demonstrate the association between occult zonulopathy and APAC. Additionally, previous studies have shown inconsistent findings on the association between a relatively longer axial length and zonulopathy.(Kwon & Sung 2017; Zhang et al. 2023) For the critical function of lens zonules and lens position in PACG, clarifying the impact of occult zonulopathy on acute angle closure would help elucidate the unpredictable occurrence of APAC. Hence, this study aimed to investigate the association of occult zonulopathy with APAC and to determine the biometric characteristics of APAC patients with or without occult zonulopathy.

Materials & Methods

Participants

This was a retrospective, case-control study following the tenets of the Declaration of Helsinki.

Approval was granted by the Medical Ethics Committee of the Sixth Affiliated Hospital of South China University of Technology (Foshan Nanhai District People's Hospital; approval number: 2023008). After an explanation of the nature and possible consequences of the study, written informed consent was obtained from all the subjects. This study was registered in the Chinese Clinical Trial Registry (registration number: ChiCTR2300077395).

A total of 27 unilateral APAC subjects and 132 control subjects were recruited from April 1, 2022, to June 1, 2023 (**Fig. 1**). APAC was diagnosed according to the following criteria:(Aung et al. 2004; Li et al. 2023) (1) at least two of the following symptoms: ophthalmalgia or periocular pain, nausea and/or vomiting, an antecedent history of intermittent blurring of vision with halos; (2) acute increase in IOP (＞30 mmHg); (3) presenting at least one of the three signs: conjunctival injection, corneal epithelial edema, glaucomatous flecks, and mild-dilated unreactive pupil; (4) presenting shallow anterior chamber in both eyes, with a closed angle in APAC eye and a narrow-angle in the fellow eye under gonioscopy. APAC patients who were accompanied by age-related cataract with best-corrected visual acuity (BCVA) worse than 0.3 logarithms of the minimum angle of resolution (logMAR) were included in this study. The control subjects were enrolled as follows: (1) age above 50 years; (2) diagnosed as age-related cataract with BCVA worse than 0.3 logMAR; (3) open-angle in gonioscopy with IOP≤21mmHg without medications; (4) absent of glaucomatous optic neuropathy or visual field damage.

Patients with one of the following situations were excluded: (1) history or signs of acute angle closure in the contralateral eyes of APAC eyes; (2) history of surgical or laser peripheral iridectomy, trabeculectomy, vitrectomy, pterygium excision, and so on; (3) history or signs of ocular trauma and traumatic surgery in the eye; (4) history of high myopia (axial length ≥26mm), chronic PACG, primary open-angle glaucoma, secondary glaucoma, pseudoexfoliation syndrome, uveitis, retinal detachment, retinitis pigmentosa, diabetic retinopathy, hyper-mature cataract, ocular tumor, Marfan syndrome, Marchesani syndrome, etc.; (5) diagnosis or signs of lens subluxation or luxation (iridodonesis, phacodonesis, visibility of lens equator). Occult zonulopathy was defined by the sign NO.1 combined with the sign NO.2, or the sign NO.1 combined with the sign NO.3 among the following intraoperative signs during cataract surgery:(Qiao et al. 2022; Zhang et al. 2023) (1) wrinkling of anterior lens capsules while making continuous curvilinear capsulorhexis; (2) distorted anterior lens capsules opening or a floppy capsular bag after cortical removal; (3) visualization of the capsular equator during or after nuclear/cortical removal (**Fig. 2**).

Ophthalmic examinations

All participants underwent detailed ophthalmologic examinations before surgery, including lamp biomicroscope examination, best-corrected visual acuity measurement, IOP measurement, optical coherence tomography measurement (Zeiss Cirrus HD-OCT 500, Carl Zeiss; Jena, Germany), visual field test (Humphrey Field analyzer II, Carl Zeiss Humphrey 750i; Jena, Germany), and ocular biometric measurement (IOL master 700, Carl Zeiss; Jena, Germany). Anti-glaucoma medications (brimonidine, brinzolamide, timolol, mannitol, pilocarpine) were prescribed for lowering IOP when patients came to the ophthalmic emergency room. All the ophthalmological examinations were performed under a transparent cornea and IOP ≤ 30 mmHg.

Data collection

The data of age, sex, medical histories, diagnosis, and surgical records of all subjects were derived from the medical record system. Ocular biometric data of AL, flat keratometry, steep keratometry, central ACD, LT (lens thickness), central corneal thickness (CCT), corneal diameter, pupil diameter, angle alpha, degree of alpha, angle kappa, and degree of kappa were collected from ocular biometric measurement. The value of ACD did not contain CCT. Lens position (LP = ACD + 1/2 LT) and relative lens position (RLP = (ACD +1/2 LT) / AL) were calculated.

Statistical analyses

Only the primary surgical eye of each bilateral control subject was included to compare biometric parameters with APAC eyes. Shapiro-Wilk test was used for assessing the data distribution of normality. Continuous variables were described as mean with standard deviation (mean ± SD) or median with interquartile range (IQR: Q1, Q3). An independent t-test was used to compare the normality-distributed continuous data between groups, and the Mann-Whitney U test was applied to compare disnormality-distributed continuous data. The paired t-test or Wilcoxon-matched rank test was performed to compare the biometric parameters between APAC and contralateral eyes. Categorical variables were presented as frequency with percentage and compared by χ^2 test or Fisher's exact test. Univariate and multivariate logistic analyses were applied to explore the association of biometric parameters and occult zonulopathy with APAC.

The difference was considered statistically significant with $P < 0.05$ or $P < 0.05 / 3 = 0.0167$ in multiple comparisons after Bonferroni's correction. All statistical analyses were performed using SPSS STATISTICS 26.0 (IBM SPSS Inc., Chicago, IL, USA).

Results

Twenty-seven APAC eyes with 27 contralateral eyes and 264 eyes of 132 control subjects were embraced in the present study. Thereinto, 27 APAC eyes, six contralateral eyes, and 264 eyes of control subjects received phacoemulsification cataract extraction and intraocular lens implantation (or combined with goniosynechialysis in APAC) conducted by three specialist surgeons. There was no significant difference in occult zonulopathy among surgeons ($P = 0.100$). No significant difference in age was found between the APAC group (67.26 ± 9.24 years) and the control group (70.58 ± 7.88 years, $P = 0.054$) (***Table 1***). The APAC group (85.2%) had significantly more females than the control group (61.4%, $P = 0.025$). APAC eyes showed significantly shorter AL (22.54 ± 0.73 mm, $P < 0.001$), shallower central ACD (1.57 ± 0.26 mm, $P < 0.001$), thicker LT (5.09 ± 0.37 mm, $P < 0.001$), both LP (4.12 ± 0.21 mm, $P < 0.001$) and RLP (18.29 ± 0.91 %, $P < 0.001$) closer to anterior, thicker CCT (571.33 ± 62.11 μm, $P = 0.002$), and smaller corneal diameter (11.24 ± 0.46 mm, $P = 0.001$) than control eyes. Contralateral eyes of APAC eyes had significantly shorter AL, shallower central ACD, thicker LT, LP and RLP closer to anterior compared to the control group (all $P < 0.001$). As compared to contralateral eyes (central ACD: 1.72 ± 0.27 mm; LP: 4.26 ± 0.21 mm; RLP: 18.98 ± 0.99 %), APAC eyes showed significantly shallower central ACD (1.57 ± 0.26 mm, $P = 0.008$), lower LP (4.12 ± 0.21

mm, $P = 0.007$) and RLP (18.29 ± 0.91 %, $P = 0.006$), but no significant difference in AL and LT.

APAC eyes (0.62 ± 0.46 mm) had significantly greater angle kappa than the control (0.34 ± 0.27 mm, $P < 0.001$) and the contralateral eyes (0.36 ± 0.30 mm, $P = 0.011$) (***Table 1***). No significant difference was observed in angle kappa between the contralateral eyes of APAC eyes and control eyes ($P = 0.713$). The distribution of angle alpha and angle kappa of APAC, contralateral, and control eyes were displayed in **Figure 3**. The percentage of occult zonulopathy was significantly larger in APAC eyes (63.0%) than in control eyes (1.5%, $P < 0.001$) and the contralateral eyes ($P = 0.007$). There was no significant difference in occult zonulopathy between the contralateral eyes and control eyes ($P = 1.00$). In multivariate logistic analysis, occult zonulopathy was significantly associated with APAC after adjusting sex and AL (odds ratio (OR) = 126.49, 95% confidence interval (CI): 20.89 - 766.02; $P < 0.001$) (***Table 2***). The ACD, LT, LP and RLP were excluded from multivariate logistic analysis because of their potential correlation with AL. Compared to contralateral eyes, shallower central ACD, thicker CCT, LP and RLP closer to the anterior were observed in both APAC eyes with occult zonulopathy and without occult zonulopathy (all $P < 0.05$) (***Table 3***) For APAC patients, eyes with occult zonulopathy showed no significant difference in biometric parameters compared to eyes without occult zonulopathy (all $P > 0.05$) (**Fig. 4**).

For the binocular differences in ocular biometric parameters, APAC patients showed significantly larger variations in steep keratometry ($P < 0.001$), LP ($P < 0.001$), RLP ($P < 0.001$), CCT ($P < 0.001$), corneal diameter ($P = 0.005$), pupil diameter ($P < 0.001$), and angle kappa ($P < 0.001$) than control subjects, but the more minor binocular difference in LT ($P = 0.016$) (***Table 4***). The binocular difference in LT of APAC subjects with occult zonulopathy (median: 0.070, IQR: 0.035 to 0.150) was significantly greater than that of APAC eyes without occult zonulopathy (median: 0.025, IQR: 0.018 to 0.073; $P = 0.046$). No binocular differences were detected in AL, keratometry, central ACD, LP, RLP, CCT, corneal diameter, pupil diameter, angle alpha, and angle kappa between APAC eyes with and without occult zonulopathy (all $P > 0.05$).

Discussion

Lens zonules were the most critical anatomic structures for lens stabilization. Severe zonulopathy could result in lens luxation or subluxation with typical signs, such as iridodonesis, phacodonesis, asymmetric ACD in both eyes, and even lens sinking.(Jing et al. 2021; Zhang et al. 2019) Lens luxation or subluxation is the common cause of secondary angle-closure glaucoma.(Chen et al. 2023b; Tang et al. 2024; Xing et al. 2020) Occult zonulopathy is a result of weakness or partial damage in lens zonules, which lack preoperative signs of lens luxation or subluxation. Our study showed that only a very small part of normal cataract patients would be affected by occult zonulopathy. Zhang, et al. found that 10.9% of patients with age-related cataract were diagnosed with zonulopathy intraoperatively, which was obviously higher than our finding on occult zonulopathy (1.5%) because they included the patients with visualization of the equator of the lens with fully dilated pupil and out of shape or deviation of the anterior capsular opening after the cortex removed. (Zhang et al. 2024) The findings of this study also revealed a significantly higher incidence of occult zonulopathy in APAC eyes (63.0%) than the normal eyes with age-related cataract, which was close to the reported incidence in a previous study (69%). (Zhang et al. 2023) Twenty-one percent of APAC patients had zonular instability intraoperatively in a Korean study. (Kwon & Sung 2017) This study may have reported a lower incidence of occult zonulopathy due to excluding APAC patients with intraoperative zonular damage. Furthermore, the proportion of occult zonulopathy in APAC eyes was remarkably higher than in the control and contralateral eyes (***Table 1***), which was consistent with the prior study. (Zhang et al. 2023) Our study showed that people with occult zonulopathy had over 126 times higher risk of APAC than those without occult zonulopathy despite having the same AL, but it has a relatively high confidence interval range. Overall, the findings of our study suggest that occult zonulopathy could be a crucial risk factor for APAC.

This study revealed that APAC eyes with occult zonulopathy had longer AL, smaller keratometry, thinner LT, and RLP closer to anterior than that of APAC eyes without occult zonulopathy, though the differences were not statistically significant (***Table 3***). Another study found that shallower ACD and thicker LT, but not AL and RLP, were uncovered in APAC patients with zonulopathy. (Zhang et al. 2023) Kwon, Junki, *et al.*(Kwon & Sung 2017) reported longer AL and higher lens vault (LV) in APAC eyes with zonular instability but no difference in ACD, anterior chamber width (ACW), angle opening distance (AOD) 750, and trabecular iris space area (TISA) 750. In the study by Chen, Hailiu, *et al.*(Chen et al. 2023a), APAC eyes with zonular laxity significantly had shallower ACD, higher LV, less RLP, thinner iris thickness (IT), smaller anterior chamber area (ACA) and AOD500, and no significant differences in AL, LT, ACW, anterior placement of the ciliary body (APCB), and ciliary body thickness (CBT) were found. The results widely varied among studies due to the differences in inclusion criteria, sample sizes, and included populations. Regardless, those inconsistent results seem to imply an anteriorly placed and thicker lens, shallower anterior chamber, and longer AL in APAC eyes with occult zonulopathy. Further multicentric research with a larger sample size and unitive inclusion criteria is warranted to confirm the discrepancy in ocular biometric parameters between APAC eyes with and without occult zonulopathy.

Several investigations have demonstrated shallower central ACD, LP and RLP closer to the anterior in APAC eyes compared to the contralateral eyes, which was also found in this study.(Li et al. 2018; Senthilkumar et al. 2022; Zhang et al. 2010) The smaller values of ACA, AOD, CBT, APCB, TISA, iris area, and iris curvature were found in APAC eyes.(Li et al. 2018; Senthilkumar et al. 2022) Our study showed no significant difference in AL and LT between the bilateral eyes in APAC patients, aligning with previous findings.(Li et al. 2018; Moghimi et al. 2014) Therefore, it seems that a forward movement of the lens could be a reasonable explanation for the crowded anterior structures in APAC eyes under the circumstance of having a similar dimension of eyeball with contralateral eyes. In the present study, APAC eyes were found to have a greater angle alpha and kappa than normal eyes and a greater angle kappa than fellow eyes (***Table 1***). Both greater angle alpha and angle kappa have been demonstrated to be associated with crystalline lens decentration and tilt.(Li et al. 2021; Shen et al. 2023) As the crystalline lens decentration and tilt were related to PAC diseases, greater angle alpha and angle kappa may suggest a change of lens stability in APAC eyes. (Wang et al. 2020) Occult zonulopathy could fully explain the forward shifting of the lens and the altered lens stability in APAC.

A slight change of biometric parameters attributed to occult zonulopathy may be challenging to detect for the existing crowded anterior segment in APAC patients. APAC patients with occult zonulopathy showed similar binocular differences in AL, central ACD, LP, RLP, angle alpha, and angle kappa compared to those without occult zonulopathy, but had significant differences in ACD, CCT, LP and RLP. Whereas LP and RLP showed no significant difference in APAC eyes without zonular laxity, and greater binocular differences in LT, LV, RLP, ACD, ACA, AOD500, and IT were discovered in APAC patients with zonular laxity in a study. (Chen et al. 2023a) The different inclusion criteria and sample sizes may account for the inconsistent results. APAC patients demonstrated larger binocular differences in steep keratometry, LP, RLP, corneal diameter, and angle kappa of bilateral eyes than control subjects, suggesting the more asymmetric ocular anterior structures in APAC patients. Anyhow, the binocular differences in APAC patients are too small to recognize under regular examinations before surgery.

Although shallow ACD and higher LV were shown as risk factors for zonular laxity, they could result from the forward shifting of the lens. (Chen et al. 2023a) It's reliable that longer AL (23.23 ± 0.55 mm) is a risk factor for occult zonulopathy in APAC patients, as it was independent of the abnormal lens position. (Kwon & Sung 2017) Occult zonulopathy could promote the development of APAC by causing the anterior shifting of the lens, resulting in a more crowded ocular anterior segment. The iris closely contacts the anterior surface of the lens, making pupillary block prone to happen easily (**Fig. 5**). Rapid IOP elevation could induce acute ischemia in the ciliary body and iris with severe inflammation in the anterior and posterior chamber, leading to lens zonules injury. Alternatively, zonulopathy could be a consequence of overstressing from the heavy lens or increased posterior pressure. (Zhang et al. 2023) In summary, occult zonulopathy contributes to the risk of APAC, and lens zonules would be damaged by an IOP elevation attack, creating a vicious circle. A further prospective study would be helpful to illustrate the association of occult zonulopathy with the duration of high IOP.

There are several limitations in this study. First, this study excluded the bilateral APAC patients, PACS, and PACG patients. Previous reports indicated that 39.1% of PACG patients and 15.3% of PAC and PACS patients were detected with zonulopathy during cataract surgery. (Zhang et al. 2023) They may provide insights into the association of zonulopathy with chronic angle closure. Bilateral APAC patients, despite a minority of all APAC patients, might experience different mechanisms of angle closure from unilateral APAC patients. Second, 21 contralateral eyes of APAC eyes underwent laser peripheral iridectomy (LPI) treatment because of their mild cataract or rejection of surgery. Only six contralateral eyes underwent cataract surgery and accepted assessment of lens zonules during surgery, which might influence the conclusion derived from the inter-eye comparison. Third, the diagnosis of occult zonulopathy was qualitative, depending on the indirect signs intraoperatively, which might be subjective.

Future studies would benefit from new techniques that allow direct examination of lens zonules for a more quantitative evaluation. Fourth, ocular traumatic history was based on the medical history and the possible signs of trauma. Minor ocular trauma in children or teenagers might be omitted, though patients with a history or signs of ocular trauma have been excluded. Finally, IOP-lowering treatments might influence the ACD because of the changes in the IOP level.

Conclusions

APAC eyes exhibited a larger proportion of occult zonulopathy than the contralateral and control eyes. Occult zonulopathy was significantly associated with APAC. Occult zonulopathy could be a risk factor for APAC, as it might result in an anterior shifting of the lens.

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Conflict of interest

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval statement

This study has been approved by the Medical Ethics Committee of the Sixth Affiliated Hospital of South China University of Technology (Foshan Nanhai District People's Hospital; approval number: 2023008). The procedures used in this study adhere to the tenets of the Declaration of Helsinki. This study was registered in the Chinese Clinical Trial Registry (registration number: ChiCTR2300077395). Written informed consent was obtained from all individual participants included in the study.

Data availability statement

Data was available in the supplementary files.

Author contribution

Conceptualization: Jiawei Chen, Xuanchu Duan; Methodology: Jiawei Chen, Xuanchu Duan, Xiang-Ling Yuan, Yanjun Huang, Xiaona Huang; Data curation: Jiawei Chen, Yanjun Huang, Xiaona Huang; Formal analysis and investigation: Jiawei Chen, Xiang-Ling Yuan, Xinyue Zhang, Yanjun Huang, Xiaona Huang; Writing - original draft preparation: Jiawei Chen, Xiang-Ling Yuan, Xinyue Zhang; Writing - review and editing: Xuanchu Duan, Yanjun Huang, Xiaona Huang; Funding acquisition: Xuanchu Duan. All authors read and approved the final manuscript.

References

Aung T, Friedman DS, Chew PTK et al. 2004. Long-term outcomes in asians after acute primary angle closure. *Ophthalmology* 111:1464-1469. doi: 10.1016/j.ophtha.2003.12.061.

Chen H, Ye L, Cheng L et al. 2023a. Ocular Biometric Characteristics in Preoperative Diagnosis of Acute Angle Closure with and without Zonular Laxity. *J Glaucoma* 33:195-205. doi: 10.1097/IJG.0000000000002307.

Chen X, Song Q, Yan W et al. 2023b. Evaluation of Multimodal Biometric Parameters for Diagnosing Acute Angle Closure Secondary to Lens Subluxation. *Ophthalmol Ther* 12:839-851. doi: 10.1007/s40123-022-00638-0.

Foster PJ, Buhrmann R, Quigley HA et al. 2002. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol* 86:238-242. doi: 10.1136/bjo.86.2.238.

Friedman DS, Chew PTK, Gazzard G et al. 2006. Long-term outcomes in fellow eyes after acute primary angle closure in the contralateral eye. *Ophthalmology* 113:1087-1091. doi: 10.1016/j.ophtha.2006.02.016.

GBD D, and Group VLE. 2021. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. *Lancet Glob Health* 9:e144-e160. doi: 10.1016/S2214-109X(20)30489-7.

Gedde SJ, Chen PP, Muir KW et al. 2021. Primary Angle-Closure Disease Preferred Practice Pattern®. *Ophthalmology* 128:P30-P70. doi: 10.1016/j.ophtha.2020.10.021.

Jing Q, Chen T, Chen Z et al. 2021. Ocular Manifestations of Acute Secondary Angle Closure Associated With Lens Subluxation. *Front Med (Lausanne)* 8:738745. doi: 10.3389/fmed.2021.738745.

Kwon J, and Sung KR. 2017. Factors Associated With Zonular Instability During Cataract Surgery in Eyes With Acute Angle Closure Attack. *Am J Ophthalmol* 183:118-124. doi: 10.1016/j.ajo.2017.09.003.

Li X, Wang W, Huang W et al. 2018. Difference of uveal parameters between the acute primary angle closure eyes and the fellow eyes. *Eye (Lond)* 32:1174-1182. doi: 10.1038/s41433-018-0056-9.

Li Z, Fan N, Cheng Y et al. 2023. Factors associated with severe corneal endothelial damage following acute primary angle closure in Chinese subjects. *Graefes Arch Clin Exp Ophthalmol* 261:2927-2934. doi: 10.1007/s00417-023-06109-x.

Li Z, Zhu Z, Li X et al. 2021. Age-related changes in crystalline lens tilt and decentration: swept-source OCT study. *J Cataract Refract Surg* 47:1290-1295. doi: 10.1097/j.jcrs.0000000000000632.

Lin Y, Jiang B, Cai Y et al. 2023. The Global Burden of Glaucoma: Findings from the Global Burden of Disease 2019 Study and Predictions by Bayesian Age-Period-Cohort Analysis. *J Clin Med* 12:1828. doi: 10.3390/jcm12051828.

Marchini G, Chemello F, Berzaghi D et al. 2015. New findings in the diagnosis and treatment of primary angle-closure glaucoma. *Prog Brain Res* 221:191-212. doi: 10.1016/bs.pbr.2015.05.001.

Moghimi S, Zandvakil N, Vahedian Z et al. 2014. Acute angle closure: qualitative and quantitative evaluation of the anterior segment using anterior segment optical coherence tomography. *Clin Experiment Ophthalmol* 42:615-622. doi: 10.1111/ceo.12285.

Qiao CY, Zhang H, Zhang Y et al. 2022. Comparison study for the proportion of underdiagnosed zonulopathy in angle closure glaucoma. *Zhonghua Yan Ke Za Zhi* 58:872-881. doi: 10.3760/cma.j.cn112142-20211226-00608.

Quigley HA, and Broman AT. 2006. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 90:262-267. doi: 10.1136/bjo.2005.081224.

Senthilkumar VA, Pradhan C, Rajendrababu S et al. 2022. Comparison of uveal parameters between acute primary angle-closure eyes and fellow eyes in South Indian population. *Indian J Ophthalmol* 70:1232-1238. doi: 10.4103/ijo.IJO_1561_21.

Shen L, Yang W, Li D et al. 2023. Crystalline lens decentration and tilt in eyes with different axial lengths and their associated factors. *Indian J Ophthalmol* 71:763-767. doi: 10.4103/ijo.IJO_1054_22.

Sun X, Dai Y, Chen Y et al. 2017. Primary angle closure glaucoma: What we know and what we don't know. *Prog Retin Eye Res* 57:26-45. doi: 10.1016/j.preteyeres.2016.12.003.

Tang Y, Gao Y, Yu X et al. 2024. Novel diagnostic indicators for acute angle closure secondary to lens subluxation based on anterior segment and lens parameters. *Heliyon* 10:e25164. doi: 10.1016/j.heliyon.2024.e25164.

Tham Y-C, Li X, Wong TY et al. 2014. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 121:2081-2090. doi: 10.1016/j.ophtha.2014.05.013.

Wang X, Chen X, Tang Y et al. 2020. Morphologic Features of Crystalline Lens in Patients with Primary Angle Closure Disease Observed by CASIA 2 Optical Coherence Tomography. *Invest Ophthalmol Vis Sci* 61:40. doi: 10.1167/iovs.61.5.40.

Weinreb RN, Aung T, and Medeiros FA. 2014. The pathophysiology and treatment of glaucoma: a review. *JAMA* 311:1901-1911. doi: 10.1001/jama.2014.3192.

Wilensky JT, Kaufman PL, Frohlichstein D et al. 1993. Follow-up of angle-closure glaucoma suspects. *Am J Ophthalmol* 115:338-346. doi: 10.1016/s0002-9394(14)73585-8.

Xing X, Huang L, Tian F et al. 2020. Biometric indicators of eyes with occult lens subluxation inducing secondary acute angle closure. *BMC Ophthalmol* 20:87. doi: 10.1186/s12886-020-01355-7.

Zhang H, Zhang Y, Zhang S et al. 2023. Zonulopathy Identified During Cataract Extraction in Patients With Primary Angle Closure Disease. *J Glaucoma* 32:783-791. doi: 10.1097/IJG.0000000000002247.

Zhang HT, Xu L, Cao WF et al. 2010. Anterior segment optical coherence tomography of acute primary angle closure. *Graefes Arch Clin Exp Ophthalmol* 248:825-831. doi: 10.1007/s00417-009-1291-3.

Zhang Y, Zhang H, Song X et al. 2024. Proportion and risk factors of zonulopathy in patients with age-related cataract. *Heliyon* 10:e28644. doi: 10.1016/j.heliyon.2024.e28644.

Zhang Y, Zong Y, Jiang Y et al. 2019. Clinical Features and Efficacy of Lens Surgery in Patients with Lens Subluxation Misdiagnosed as Primary Angle-Closure Glaucoma. *Curr Eye Res* 44:393-398. doi: 10.1080/02713683.2018.1548130.

Figure legends

Figure 1. **Flow diagram showing study design and subject inclusion.**

Figure 2. Diagrams of intraoperative signs of occult zonulopathy. (**a**) Wrinkling of anterior lens capsules while making continuous curvilinear capsulorhexis; (**b**) A distorted anterior lens capsules opening and floppy capsular bag after cortical removal; (**c**) A distorted anterior lens capsules opening, floppy capsular bag and visualization of the capsular equator after cortical removal.

Figure 3. Distribution of angle alpha and angle kappa in control, APAC, and the contralateral eyes. (**a**) APAC eyes showed a significantly greater angle alpha than control eyes ($P = 0.012$), but no difference compared to the contralateral eyes ($P = 0.074$). (**b**) APAC eyes had a significantly greater angle kappa than control eyes ($P < 0.001$) and the contralateral eyes ($P = 0.011$), but no difference between control eyes and the contralateral eyes ($P = 0.713$). (**c-d**) No significant difference in angle alpha and angle kappa was found in the APAC eye with and without occult zonulopathy (both $P > 0.05$).

Figure 4. The difference in biometric parameters between APAC eyes with and without occult zonulopathy. APAC eyes with occult zonulopathy showed longer AL, smaller keratometry, thinner LT, and RLP closer to anterior than that of APAC eyes without occult zonulopathy despite no statistical significance (all $P > 0.05$).

Figure 5. Pupillary block and anteriorly placed lens showed in ultrasound bio-microscope

measurement (UBM). The iris closely contacts the anterior surface of the lens, rising forward with a great iris curve. A shallow anterior chamber depth is present with a lens closing to the anterior.

Table 1 (on next page)

Demographic and biometric parameters of control, APAC eyes and the contralateral eyes

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length; Statistically significant difference defined as $P < 0.05/3 = 0.0167$. * χ^2 test, † Fisher's exact test, ‡ Independent t test., ‡ Mann-Whitney U test, § Paired t test, || Wilcoxon-matched rank test.

Table 1. Demographic and biometric parameters of control, APAC eyes and the contralateral eyes

	Control eyes G1 (n = 132)	APAC eyes G2 (n = 27)	Contralateral eyes G3 (n = 27)	*P* G1 vs G2	*P* G1 vs G3	*P* G2 vs G3
Age (years)	70.58 ± 7.88	67.26 ± 9.24	-	0.054‡	-	-
Sex						
Male (%)	51 (38.6%)	4 (14.86%)	-	0.025*	-	-
Female (%)	81 (61.4%)	23 (85.2%)				
Occult zonulopathy						
No (%)	130 (98.5%)	10 (37.0%)	6	< 0.001†	1.000†	0.007†
Yes (%)	2 (1.5%)	17 (63.0%)	0			
Axial length (mm)	23.49 ± 0.98	22.54 ± 0.73	22.45 ± 0.74	< 0.001‡	< 0.001‡	0.561§
Flat keratometry (diopters)	43.79 ± 1.63	43.75 ± 1.34	43.88 ± 1.28	0.912‡	0.795‡	0.539§
Steep keratometry (diopters)	44.91 ± 1.78	44.97 ± 1.40	44.80 ± 1.32	0.869‡	0.761‡	0.340§
Central ACD (mm)	2.51 ± 0.40	1.57 ± 0.26	1.72 ± 0.27	< 0.001‡	< 0.001‡	0.008§
Len thickness (mm)	4.58 ± 0.48	5.09 ± 0.37	5.07 ± 0.35	< 0.001‡	< 0.001‡	0.364§
Lens position (mm)	4.80 ± 0.30	4.12 ± 0.21	4.26 ± 0.21	< 0.001‡	< 0.001‡	0.007§
Relative lens position (%)	20.43 ± 1.07	18.29 ± 0.91	18.98 ± 0.99	< 0.001‡	< 0.001‡	0.006§
Central corneal thickness (µm)	528.27 ± 32.67	571.33 ± 62.11	528.26 ± 34.36	0.002‡	0.999‡	< 0.001§
Corneal diameter (mm)	11.64 ± 0.52	11.24 ± 0.46	11.40 ± 0.34	0.001‡	0.038‡	0.050§
Pupil diameter (mm)	3.59 ± 0.87	3.82 ± 1.49	2.70 ± 1.06	0.441‡	< 0.001‡	0.001§
Angle alpha (mm)	0.57 ± 0.32	0.73 ± 0.37	0.58 ± 0.30	0.012‡	0.969‡	0.074‖
Angle kappa (mm)	0.34 ± 0.27	0.62 ± 0.46	0.36 ± 0.30	< 0.001‡	0.713‡	0.011‖

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length; Statistically significant difference defined as $P < 0.05/3 = 0.0167$.

* $\chi 2$ test, † Fisher's exact test, ‡ Independent t test., ‡ Mann-Whitney U test, § Paired t test, || Wilcoxon-matched rank test.

Table 2(on next page)

Univariate and multivariate logistic analysis of occult zonulopathy with APAC

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length.

Table 2. Univariate and multivariate logistic analysis of occult zonulopathy with APAC

	Univariate logistic analysis		Multivariate logistic analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (per year)	0.95 (0.90 - 1.00)	0.057	-	
Sex (female)	3.62 (1.18 - 11.08)	0.024	2.55 (0.38 - 16.90)	0.333
Occult zonulopathy (yes)	110.50 (22.31 - 547.38)	< 0.001	126.49 (20.89 - 766.02)	< 0.001
Axial length (mm)	0.32 (0.18 - 0.56)	< 0.001	0.32 (0.14 - 0.72)	0.006
Flat keratometry (diopters)	0.99 (0.76 - 1.28)	0.912	-	
Steep keratometry (diopters)	1.02 (0.80 - 1.29)	0.868	-	
Central ACD (per 0.1mm)	0.43 (0.30 - 0.62)	< 0.001	-	
Len thickness (mm)	11.81 (3.92 - 35.59)	< 0.001	-	
Lens position (per 0.1mm)	0.19 (0.09 - 0.41)	< 0.001	-	
Relative lens position (%)	0.04 (0.01 - 0.14)	< 0.001	-	
Central corneal thickness (μm)	1.02 (1.01 - 1.04)	< 0.001	-	
Corneal diameter (mm)	0.27 (0.12 - 0.64)	0.003	-	
Pupil diameter (mm)	1.24 (0.84 - 1.83)	0.278	-	
Angle alpha (mm)	3.38 (1.14 - 10.08)	0.029	-	
Angle kappa (mm)	9.12 (2.63 - 31.60)	< 0.001	-	

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length.

Table 3(on next page)

Comparison of biometric parameters between APAC eyes with or without occult zonulopathy and the contralateral eyes

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length. ‡ Mann-Whitney U test, || Wilcoxon-matched rank test.

Table 3. Comparison of biometric parameters between APAC eyes with or without occult zonulopathy and the contralateral eyes

	APAC with occult zonulopathy (n = 17)		APAC without occult zonulopathy (n = 10)		$P^{\|\|}$	$P^{\|\|}$	$P^{‡}$
	APAC eyes G1	Contralateral eyes G2	APAC eyes G3	Contralateral eyes G4	G1 VS G2	G3 VS G4	G1 VS G3
Axial length (mm)	22.64 ± 0.80	22.71 ± 0.82	22.37 ± 0.58	22.32 ± 0.51	0.421	0.172	0.175
Flat keratometry (diopters)	43.43 ± 1.36	43.59 ± 1.33	44.30 ± 1.19	44.37 ± 1.09	1.000	0.386	0.050
Steep keratometry (diopters)	44.75 ± 1.28	44.63 ± 1.37	45.35 ± 1.57	45.09 ± 1.25	0.523	0.959	0.248
Central ACD (mm)	1.56 ± 0.29	1.70 ± 0.32	1.59 ± 0.22	1.75 ± 0.14	0.037	0.007	0.880
Len thickness (mm)	5.08 ± 0.44	5.05 ± 0.42	5.11 ± 0.24	5.11 ± 0.21	0.618	0.683	0.782
Lens position (mm)	4.11 ± 0.23	4.23 ± 0.25	4.14 ± 0.18	4.31 ± 0.12	0.019	0.005	0.802
Relative lens position (%)	18.14 ± 0.95	18.79 ± 1.15	18.54 ± 0.84	19.31 ± 0.51	0.019	0.005	0.192
Central corneal thickness (μm)	581.18 ± 72.90	530.53 ± 41	554.60 ± 34.69	524.40 ± 19.87	0.001	0.019	0.393
Corneal diameter (mm)	11.29 ± 0.49	11.42 ± 0.33	11.16 ± 0.41	11.36 ± 0.37	0.161	0.096	0.449
Pupil diameter (mm)	3.95 ± 1.61	2.53 ± 0.76	3.60 ± 1.30	2.98 ± 1.45	0.004	0.343	0.421
Angle alpha (mm)	0.67 ± 0.29	0.63 ± 0.34	0.84 ± 0.49	0.49 ± 0.22	0.435	0.093	0.615
Angle kappa (mm)	0.52 ± 0.28	0.41 ± 0.36	0.79 ± 0.65	0.27 ± 0.14	0.231	0.012	0.461

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length. ‡ Mann-Whitney U test, || Wilcoxon-matched rank test.

Table 4(on next page)

Comparison of the binocular differences in biometric parameters between control and APAC eyes, APAC eyes with and without occult zonulopathy

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length; Data were described as median with interquartile range (Q1, Q3). ‡ Mann-Whitney U test.

Table 4. Comparison of the binocular differences in biometric parameters between control and APAC eyes, APAC eyes with and without occult zonulopathy

	Control (n = 132)	APAC (n = 27)	$P^‡$	APAC with occult zonulopathy (n = 17)	APAC without occult zonulopathy (n = 10)	$P^‡$
Axial length (mm)	0.100 (0.043, 0.210)	0.120 (0.080, 0.170)	0.377	0.120 (0.080, 0.225)	0.115 (0.078, 0.163)	0.473
Flat keratometry (diopters)	0.370 (0.173, 0.588)	0.480 (0.270, 1.060)	0.072	0.450 (0.290, 0.960)	0.585 (0.135, 1.143)	0.941
Steep keratometry (diopters)	0.260 (0.120, 0.500)	0.610 (0.230, 0.930)	< 0.001	0.600 (0.200, 0.990)	0.625 (0.225, 1.065)	0.941
Central ACD (mm)	0.076 (0.037, 0.166)	0.126 (0.058, 0.279)	0.060	0.126 (0.053, 0.307)	0.119 (0.048, 0.240)	0.749
Len thickness (mm)	0.095 (0.040, 0.220)	0.060 (0.020, 0.140)	0.016	0.070 (0.035, 0.150)	0.025 (0.018, 0.073)	0.046
Lens position (mm)	0.059 (0.030, 0.105)	0.101 (0.061, 0.250)	< 0.001	0.148 (0.061, 0.250)	0.100 (0.066, 0.240)	0.749
Relative lens position (%)	0.228 (0.114, 0.442)	0.513 (0.246, 0.107)	< 0.001	0.577(0.220, 1.884)	0.484 (0.359, 1.188)	0.824
Central corneal thickness (μm)	12.0 (5.0, 18.0)	35.0 (20.0, 61.0)	< 0.001	27.0 (15.5, 73.0)	35.5 (28.3, 51.3)	0.786
Corneal diameter (mm)	0.20 (0.10, 0.30)	0.30 (0.20, 0.50)	0.005	0.30 (0.20, 0.45)	0.30 (0.10, 0.53)	0.863
Pupil diameter (mm)	0.30 (0.10, 0.50)	1.50 (0.59, 2.40)	< 0.001	1.90 (0.64, 2.75)	1.25 (0.35, 2.00)	0.264
Angle alpha (mm)	0.14 (0.053, 0.30)	0.24 (0.05, 0.30)	0.404	0.18 (0.04, 0.29)	0.28 (0.10, 0.72)	0.223
Angle kappa (mm)	0.10 (0.00, 0.20)	0.20 (0.10, 0.70)	< 0.001	0.20 (0.15, 0.45)	0.30 (0.08, 0.80)	0.711

APAC: acute primary angle closure; ACD: anterior chamber depth; n: number; Lens position = ACD + 1/2 lens thickness; Relative lens position = lens position / axial length; Data were described as median with interquartile range (Q1, Q3). ‡ Mann-Whitney U test.

Figure 1

Flow diagram showing study design and subject inclusion.

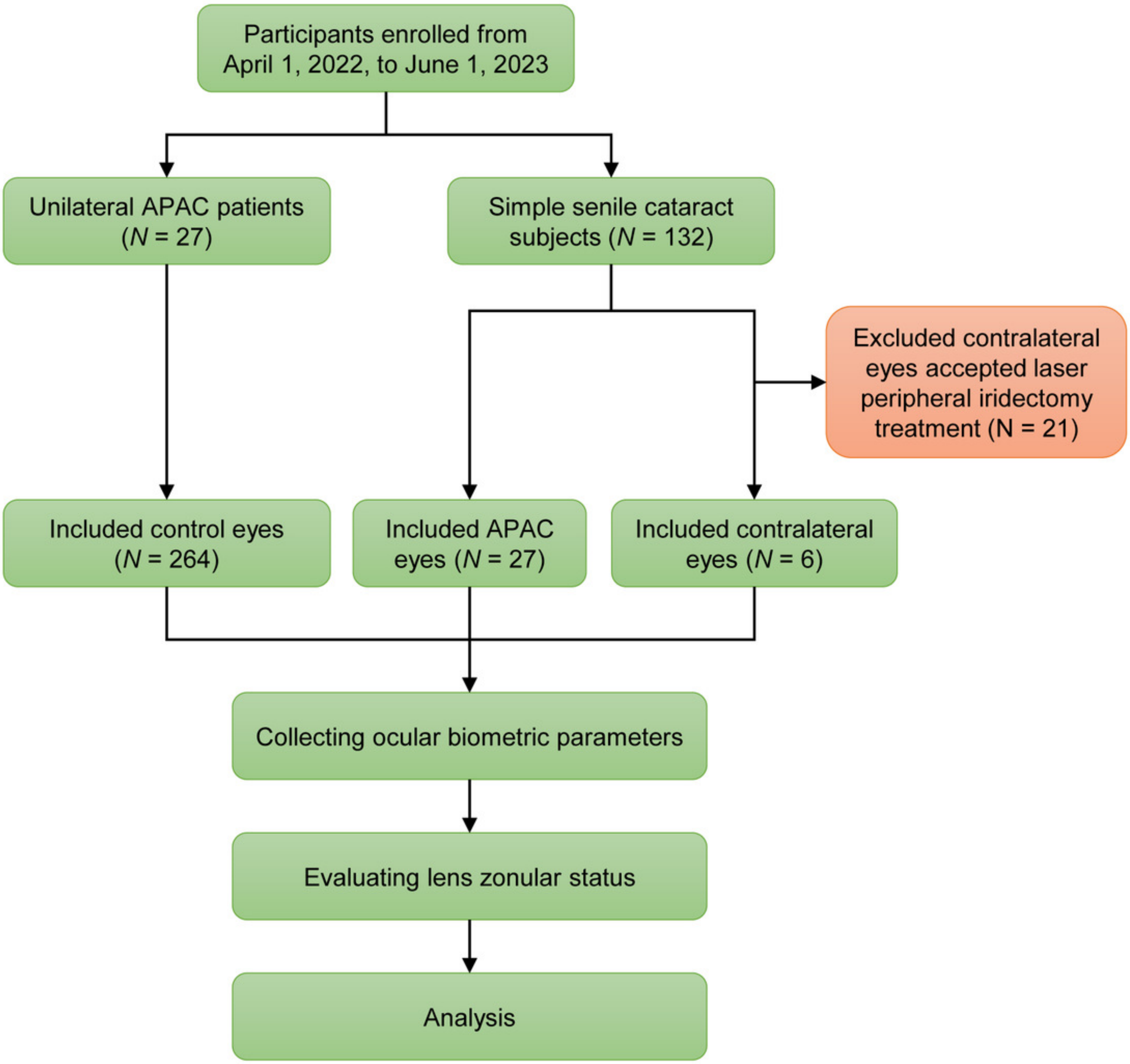

Figure 2

Diagrams of intraoperative signs of occult zonulopathy.

(**a**) Wrinkling of anterior lens capsules while making continuous curvilinear capsulorhexis; (**b**) A distorted anterior lens capsules opening and floppy capsular bag after cortical removal; (**c**) A distorted anterior lens capsules opening, floppy capsular bag and visualization of the capsular equator after cortical removal.

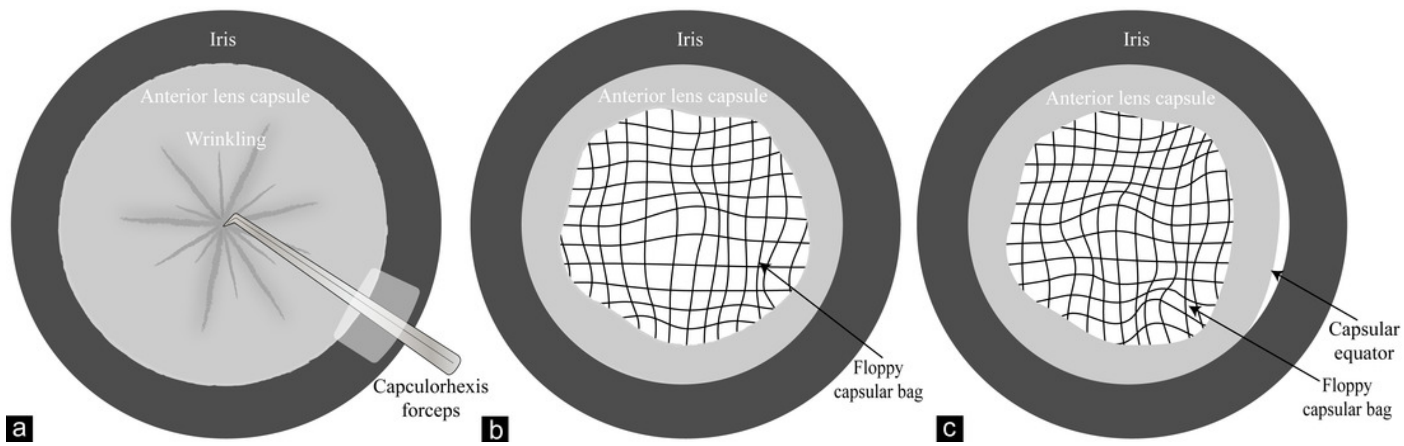

Figure 3

Distribution of angle alpha and angle kappa in control, APAC, and the contralateral eyes.

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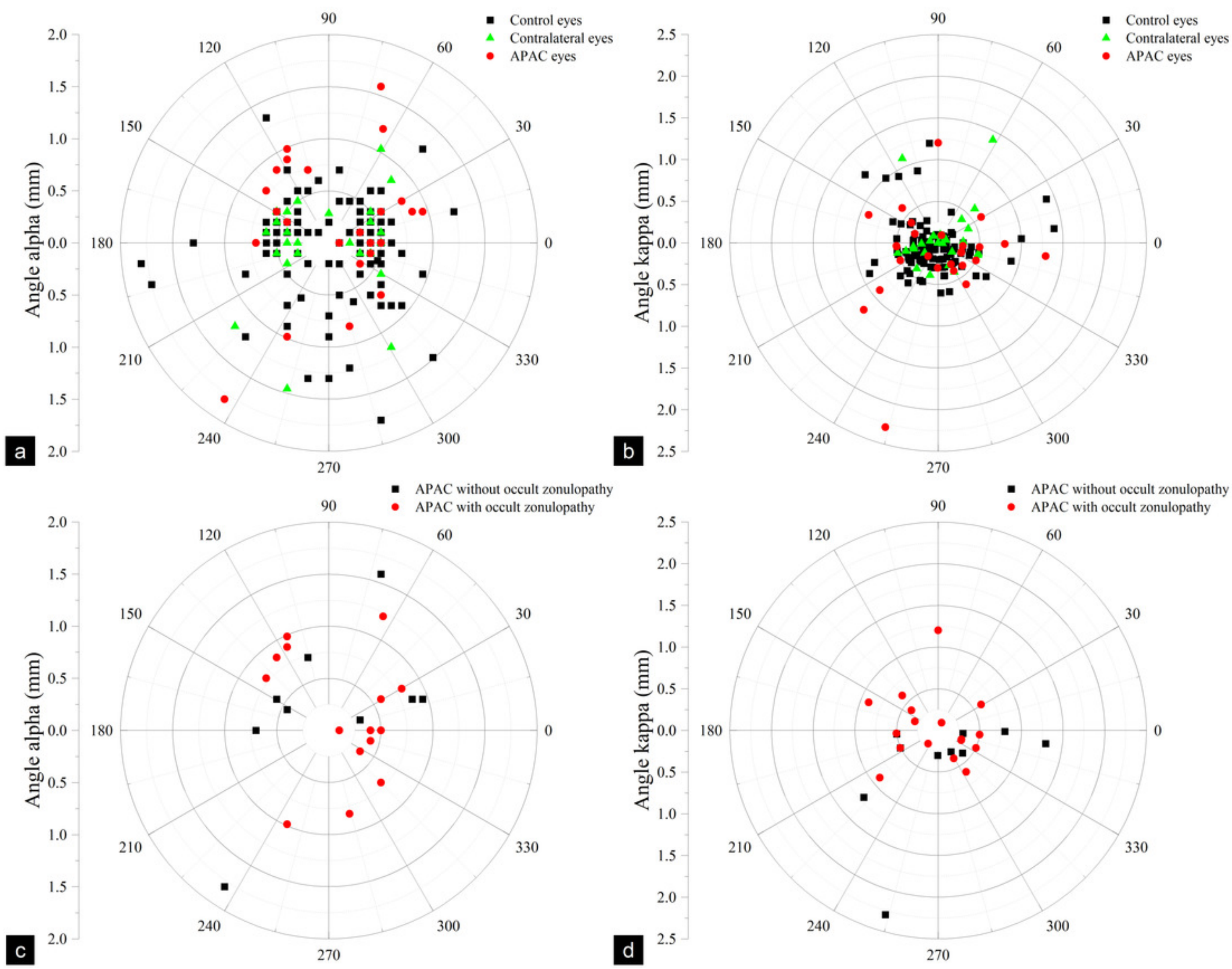
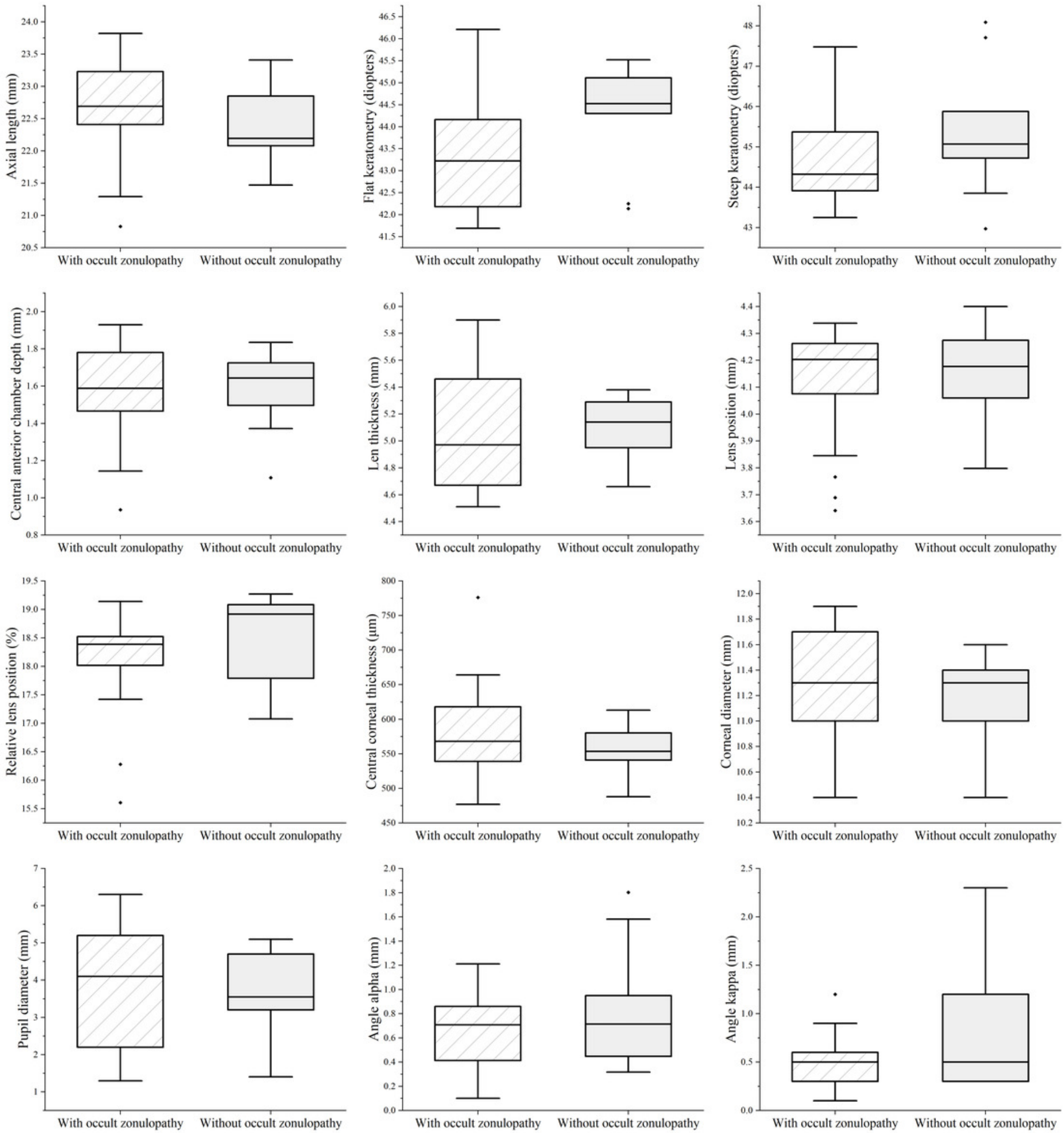


Figure 4

The difference in biometric parameters between APAC eyes with and without occult zonulopathy.

APAC eyes with occult zonulopathy showed longer AL, smaller keratometry, thinner LT, and RLP closer to anterior than that of APAC eyes without occult zonulopathy despite no statistical significance (all $P > 0.05$).



Axial length (mm)
Flat keratometry (diopters)
Steep keratometry (diopters)
Central anterior chamber depth (mm)
Len thickness (mm)
Lens position (mm)
Relative lens position (%)
Central corneal thickness (μm)
Corneal diameter (mm)
Pupil diameter (mm)
Angle alpha (mm)
Angle kappa (mm)
With occult zonulopathy
Without occult zonulopathy

Figure 5

Pupillary block and anteriorly placed lens showed in ultrasound bio-microscope measurement (UBM).

The iris closely contacts the anterior surface of the lens, rising forward with a great iris curve. A shallow anterior chamber depth is present with a lens closing to the anterior.