• Clinical Research •

Ultrasound biomicroscopy analysis of age-related trends in lens stability in cortical cataracts

Jia-Jun Chen, Ling Wang, Sha-Sha Xue, Zhi-Ying Yu, Yun-Xiao Wang, Feng-Lei Wang

Department of Ophthalmology, the Affiliated Hospital of Qingdao University, Qingdao 266003, Shandong Province, China

Correspondence to: Feng-Lei Wang. 16, Jiangsu Road, Shinan District, Qingdao 266003, Shandong Province, China. wflaiyy@126.com

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Abstract

● **AIM:** To investigate age-related differences in the iris-lens angle (ILA) among patients with age-related cortical cataracts and elucidate the impact of age on lens stability.

● **METHODS:** A prospective observational study was conducted on patients with age-related cortical cataracts scheduled for phacoemulsification surgery. Preoperative ultrasound biomicroscopy (UBM) images were collected and analyzed. Initially, patients were stratified into two age groups: <60y and ≥60y, with no significant intergroup differences in sex or eye laterality. For further analysis, participants were subdivided into three age strata: <60y, 60-75y, and >75y. The ILA was measured in four quadrants (superior, inferior, nasal, and temporal). Intergroup differences in ILA were compared, and correlations between age and ILA parameters were analyzed using statistical methods.

● **RESULTS:** The sample data were categorized into three groups according to age, <60y (113 patients; 55.8% female), 60–75y (245 patients; 61.0% female), and >75y (70 patients; 50.2% female). The superior quadrant ILA increased progressively with age stratification (P=0.02), and the maximum ILA difference (ΔILA) was significantly higher in patients over 75y (P<0.01). Simple linear regression analysis demonstrated a positive correlation between age and ILA in the superior (Y=7.487+0.096X, R=0.191, P<0.001) and temporal (Y=10.254+0.052X, R=0.104, P=0.032) quadrants. Additionally, the mean ILA across all quadrants (ILA_{mean}) and ΔILA were positively correlated with age (ILA_{mean}: Y=9.721+0.055X, R=0.138, P=0.004; ΔILA: Y=3.267+0.044X, R=0.006, P<0.05).

● **CONCLUSION:** In patients with age-related cortical cataracts, ILA increases with age, particularly in the superior and temporal quadrants, suggesting that advanced age is associated with greater lens deviation and decreased lens stability. UBM imaging can effectively evaluate the status of the zonule and lens stability, providing crucial evidence for personalized surgical planning based on patients' age.

● **KEYWORDS:** iris-lens angle; age-related cortical cataract; lens stability; ultrasound biomicroscopy; phacoemulsification; surgical planning

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INTRODUCTION

The lens is a part of the human eye, located behind the iris, and its periphery is held in place by the suspensory ligament that attaches to the ciliary body. As one of the important refractive media, the lens is in the form of a transparent biconvex lens that helps to focus light onto the retina. A cataract is characterized by opacity or loss of transparency of the lens and is the leading cause of vision impairment worldwide[1], with approximately 78 million cases worldwide. The main feature of cataracts is the loss of transparency of the lens, which causes visual impairment. Most cataracts are age-related, but the pathogenesis of cataracts is quite complex, and any factor that affects the intraocular environment, such as physical damage, chemical damage, inflammation, medications, and systemic metabolic disorders, can affect the structure of the lens, thus causing it to become opaque[2-3].

Cortical age-related cataract is the most common type of age-related cataract. A typical cortical cataract can be divided into four phases: incipient stage, intumescent stage, mature stage, and hypermature stage. The Lens Opacities Classification System III (LOCS III), based on slit-lamp and retroillumination analysis, is one of the most renowned cataract grading systems today[4-5].

Surgery remains the primary treatment for all types of cataracts[6]. Although the complications of cataract surgery have been reduced by standardized ultrasound emulsification therapy, and the use of new techniques and advanced instruments, complications persist[1]. The suspensory ligament plays an important role in maintaining the stability and centrality of the lens, and abnormalities of the suspensory ligament can increase the complexity of cataract surgery, decrease the success rate of the procedure, and increase the risk of intraoperative and postoperative complications[7-8]. Does postoperative tilt of the intraocular lens (IOL) position affect the safety of cataract surgery and postoperative visual recovery? This has caught the attention of ophthalmologists[9]. Therefore, timely preoperative detection of abnormalities in the position of the suspensory ligament and the lens is important to determine the treatment plan and thus improve the safety of surgery. Currently, there is a lack of effective methods to assess the function of the suspensory ligament and lens stability, and as mild lens subluxations are usually asymptomatic, it is difficult to identify this instability preoperatively with a slit-lamp examination, and ophthalmologists can easily miss it without a high degree of suspicion[8,10]. Ultrasound biomicroscopy (UBM) is a safe and effective ophthalmic examination method. Compared with slit-lamp and other optically based examinations, UBM allows clear imaging of structures behind the iris cover such as the ciliary body, suspensory ligament, and posterior capsule of the lens in the presence of refractive opacity, which can help ophthalmologists plan for surgery and predict potential intraoperative risks[11]. In our previous studies, we identified iris-lens angle (ILA), as a sensitive indicator of UBM, indirectly reflecting the spatial position of the lens, providing a basis for screening for lens subluxation and rupture of the suspensory ligament[12]. Aging is one of the major causes of acquiring a cataract, and previous studies have shown that the ability of the suspensory ligament to resist tension decreases with age and that the lens suspensory ligament may become loose or ruptured with age and aging[13]. We, therefore, considered the following questions: What is the pattern of change of ILA with age in the cortical age-related cataract population? What is the pattern of change in lens stability and spatial position with age? Is it possible to predict potential intraoperative risks from the information provided by the ILA so that these risks can be minimized?

This study aimed to analyze the obtained quantitative ILA data and explore the correlation between age and ILA, as well as the change of lens stability with age. Measurement of ILA in each quadrant allows assessment of lens stability and spatial position, which can guide the selection and adjustment of cataract surgical protocols to avoid unnecessary intraoperative and postoperative complications.

PARTICIPANTS AND METHODS

Ethical Approval The study was approved by the Ethics Committee of The Affiliated Hospital of Qingdao University and conducted in accordance with the principles of the Declaration of Helsinki on December 2021. Written informed consent was obtained from all subjects (ChiCTR2200056856).

Study Population This study collected preoperative UBM data from 219 patients (84 males, 135 females, 428 eyes in total) with cortical age-related cataracts admitted to the Department of Ophthalmology of the Affiliated Hospital of Qingdao University who underwent phacoemulsification surgery from December 2021 to October 2023, with a mean age of 66.05±8.92y, 217 cases in the right eye and 211 cases in the left eye (Table 1). We categorized the patients into three groups: age <60y, age 60-75y, and age >75y.

The inclusion criteria employed the Lens Opacities Classification System III to classify cortical-type age-related cataracts[1].

Exclusion criteria were history of ocular trauma or surgery; history of acute angle-closure glaucoma or other ocular diseases; ocular diseases that may cause secondary suspensory ligament pathology, including pseudoexfoliation syndrome, choroidal detachment, retinal detachment, ciliary body detachment, intraocular tumors, and Marfan syndrome; history of other diseases that result in an abnormal position of the lens; patients in poor physical condition who are unable to lie down; and patients who are unable to cooperate adequately during examinations and those with allergies to anesthetics.

The study protocol adhered to the Declaration of Helsinki and was approved by the Ethics Committee of the Affiliated Hospital of Qingdao University, China. (Approval number: QDDXFSYY-2021-0124).

Research Methods Data on age, sex, laterality of affected eye, date of symptom onset, systemic metabolic and genetic disorders, and treatment history were recorded. Each eligible participant underwent a thorough ophthalmologic examination including slit-lamp, fundus examination with a pre-lens after pupil dilation, automated refractometry (Topcon Ltd, Model KR-8900, Japan), best-corrected visual acuity (Topcon Ltd, Model CV-5000, Japan), and intraocular pressure (Goldmann applanation tonometer).

The UBM (Suowei Panoramic Biological Microscope SW-3200 L, Tianjin, China; probe frequency, 50 MHz) examination is performed by a trained ophthalmic technician. The patient was supinely placed on the examination bed under well-lit conditions, and after administering a surface anesthetic, the technician chose a suitable optic cup and placed it on the surface of the eye, filled the cup with sterilized injectable water as a coupling agent, and used a probe to scan anterior chamber and angle images of the patient at the 12, 6, 3, and 9 o'clock positions. The optimal scanned images were saved, and the ILA was measured using the system software, all examinations and measurements were performed by the same technician

Table 1 General characteristics of the patients

Parameters	Total
Number of eyes	428
OD/OS	217/211
Female/male (%)	61.7/38.3
Age (y), mean±SD	66.05±8.92

OD: Right eye; OS: Left eye; SD: Standard deviation.

to minimize error. The specific measurement method for the ILA uses the point of contact between the posterior surface of the iris and the anterior surface of the lens as the apex, and the tangent lines between the posterior surface of the iris and the anterior surface of the lens are located on either side of the apex, the angle formed by the two tangent lines was the ILA[14] (Figure 1). The average of ILAs of the four quadrants (ILA_{mean}) reflects the relative position of the iris to the lens and indirectly reflects the degree of anterior protrusion of the iris in the central region. The maximum difference in iris-lens angle (ΔILA) in the four quadrants represents the degree of tilt and stability of the lens, similar to the "see-saw" variation of lens subluxation[12].

Surgical Procedure All cataract phacoemulsification surgeries were performed by the same experienced ophthalmologist under oxybuprocaine surface anesthesia. After creating a clear main and lateral corneal incision, an ophthalmic viscosurgical device (OVD) was injected into the anterior chamber. The continuous curvilinear capsulotomy (CCC) of the anterior capsule was performed using tearing forceps by first puncturing the center of the anterior capsule and gently pulling the capsule flap with the tearing forceps to expand the tear, completing the CCC with a diameter of approximately 5.5 mm. The Goethe ultrasonic emulsifier (megaTRON S4HPS, Germany) was then used to perform nucleus emulsification of the lens and aspiration of the lens cortex. After filling the capsule with the OVD a foldable acrylic IOL can be implanted and the OVD can be thoroughly exchanged with a balanced salt solution, the balanced salt solution can be then used to achieve a watertight closure, and the surgical eye can be finally bandaged after applying tobramycin-dexamethasone ophthalmic ointment.

Statistical Analysis SPSS version 27.0 statistical software (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Results were expressed as mean±standard deviation if the parameters were normally distributed. ANOVA was used to analyze the ILA parameters between the three age groups. The age factor was analyzed by simple linear regression with the ILA, ILA_{mean}, and ΔILA. Statistical significance was set at $P<0.05$.

RESULTS

Comparative Analysis of ILA Between Three Age Groups The sample data were categorized into three groups according to age, <60y, 60-75y, and >75y (Table 2). There was no statistically significant difference between the three groups in terms of sex and eye laterality. ANOVA results showed that superior quadrant ILA increased with age strata, while ΔILA significantly elevated in patients over 75y. But there were no significant differences in ILA and ILA_{mean} in the other three quadrants (Figure 2).

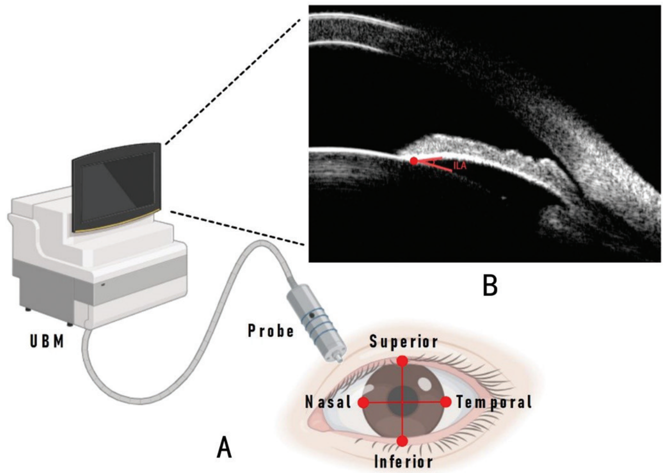

Figure 1 Standardized collection of ILA image from ocular UBM images A: Schematics of UBM probe scanning at the four-o'clock positions of the limbus; B: Magnified view of ILA measurement, where the red line denotes the tangent of the posterior iris surface and anterior lens surface, and the red dot indicates the vertex. ILA: Iris-lens angle; UBM: Ultrasound biomicroscopy.

Table 2 ILA-related data of patients with cortical age-related cataract in the three age groups

Parameters	<60y (*n*=113)	60-75y (*n*=245)	>75y (*n*=70)
Female/male (%)	55.8/44.2	61.0/39.0	50.2/49.8
OD/OS	63/50	122/123	32/38
ILA (°), mean±SD			
Superior	12.898±4.384	14.052±4.391	15.347±4.644
Inferior	13.467±3.868	13.937±4.646	13.916±5.118
Nasal	11.617±4.093	12.391±4.167	12.070±4.245
Temporal	13.439±4.465	13.771±4.570	13.743±4.394
Mean	12.842±3.342	13.546±3.597	14.019±3.515
ΔILA (°)	6.084±3.209	6.147±3.184	7.386±3.626

OD: Right eye; OS: Left eye; ILA: Iris-lens angle; ΔILA: Maximum iris-lens difference; SD: Standard deviation.

Correlation Analysis of Age with ILA and Lens Stability Simple linear regression analysis showed that the ILA_{mean} was significantly and positively correlated with age (P=0.004, R=0.138). The ΔILA was also significantly positively correlated with age (P=0.006, R=0.121). The ILA in both the superior and temporal quadrants was significantly positively correlated with age (P<0.001, R=0.191 and P=0.032, R=0.104; Figure 3). The results illustrate that iris protrusion degree in the central region and lens stability are all significantly correlated with age. However, ILA was not significantly correlated with age in the inferior and nasal quadrants.

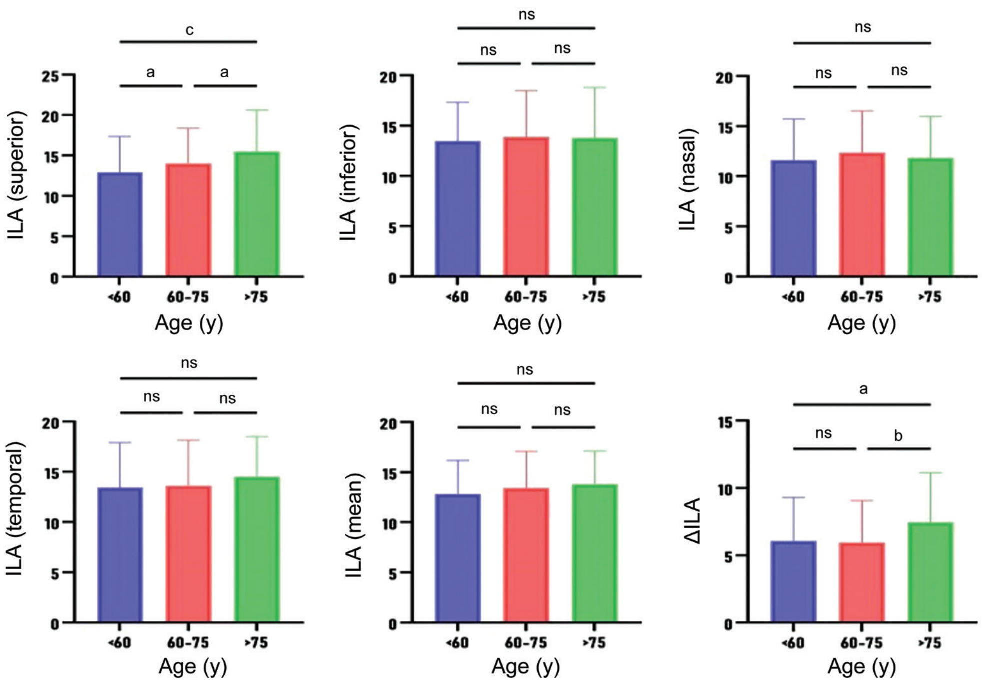

Figure 2 Comparative analysis of ILA across the three age groups $^aP<0.05$, $^bP<0.01$, $^cP<0.001$. ns: $P \geq 0.05$. ILA: Iris-lens angle.

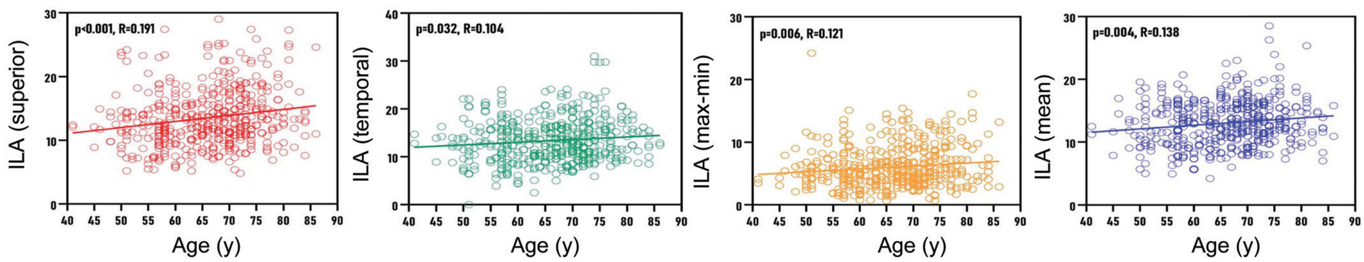

Figure 3 Simple linear regression relationships between ILA and age in cortical age-related cataract ILA: Iris-lens angle.

DISCUSSION

Age-related cataract is considered an age-related degeneration, and cortical cataract, as the most common type of age-related cataract, not only affects visual acuity. Water-absorbing swelling of the lens cortex during the expansion phase also affects the anterior chamber parameters. The ILA is the angle between the lens and the iris that is near the pupillary margin, and measuring the ILA in four quadrants using UBM can reflect the spatial position of the lens relative to the center of the iris, helping to determine whether the lens is in a stable central position. Comparing the ILA across quadrants can also indicate the direction of lens displacement[15-16]. Whether there is a correlation between ILA and age in patients with cortical age-related cataracts and whether there is an underlying pattern of change in ILA with age remain unknown. The results of this study show that ILA increases with age, the central iris becomes more protruded, the deviation of the lens becomes more severe and its stability poorer as age progresses, and the lens gradually deviates superiorly and temporally with the increase of age (Figure 4). To the best of our knowledge, this is the first study to investigate lens stability by ILA changes with age.

Anterior segment coherence optical tomography (AS-OCT) and UBM are common methods used to assess anterior chamber parameters, and most current studies on lens and anterior chamber parameters mostly use AS-OCT as the primary study tool, while UBM is less commonly used[17-19]. AS-OCT provides a rapid, noninvasive, objective, and subject-compliant method for assessing anterior segment parameters. However, AS-OCT does not show the posterior iris structures well due to the iris pigment epithelium and refractive media. The lack of concordance between UBM and AS-OCT in ILA measurements was found in our past studies, this may be due to the poorer imaging of posterior iris structures by AS-OCT[19]. UBM can show all the structures of the anterior segment of the eye including the cornea, sclera, anterior chamber, lens, suspensory ligament, ciliary body, iris, scleral prominence, and ciliary sulcus, and the advantage of UBM is that it can image the posterior structures of the iris even in the presence of refractive interstitial opacities, and because the UBM images are recorded while the patient is in the supine position, the information collected can simulate the spatial state of the lens during cataract surgery[20-21]. Therefore, we chose UBM to study and analyze the changing pattern of ILA

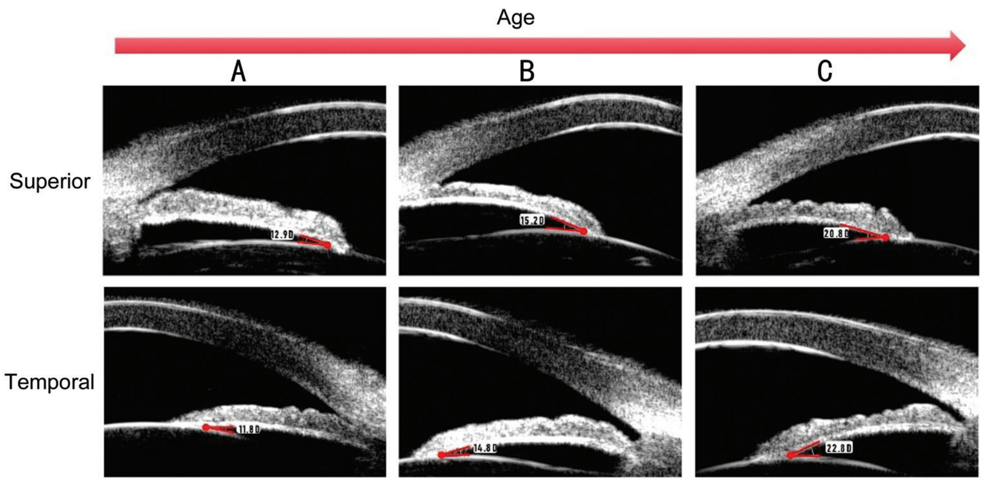

Figure 4 Advancing age, the stability of the lens deteriorates, gradually tilted superiorly and temporally A: Age <60y; B: Age 60-75y; C: Age >75y.

with age in patients with cortical senile cataract.

The suspensory ligament is a circular, fibrous structure that connects the lens to the ciliary body, and changes in both the structure and function of the suspensory ligament can affect the shape and position of the lens, increasing the complexity of cataract surgery and the risk of complications such as capsular rupture, lens dislocation, and vitreous detachment[11-22]. A single-center retrospective cohort study conducted at Moorfields Eye Hospital between January 1, 2014, and August 22, 2019, reported a 0.45% incidence of suspensory ligament abnormalities found during cataract surgery[23]. A report at Tongren Eye Hospital showed the incidence of suspensory ligament lesions in patients with age-related cataracts to be 10.9% in Chinese patients aged 45y and older, with the highest incidence occurring over the age of 80y[24]. Nishikawa and Okisaka[25] showed a reduction in the force required to rupture a sample of suspensory ligaments aged 85y and older by approximately 30%. Suspensory ligament lesions are, on one hand, due to mutations in genes encoding suspensory ligament-related proteins such as Marfan syndrome, and the suspensory ligaments become more fragile with age. Age has been identified as one of the predictors of suspensory ligament pathology, where laxity or rupture of the suspensory ligament with age causes the lens to tilt in the direction of laxity or rupture. False-negative results are possible even for experienced technicians due to a significant learning curve for UBM and the limitations of UBM's depth of detection and ability to image details of the suspensory ligament[26]. Therefore, we introduced the ILA, which is clearer and relatively easy to quantify on UBM images, and our past studies have found that the ILA can be used as a UBM-sensitive indicator to provide a basis for screening for lens subluxation and rupture of the suspensory ligament[12].

Our results show that age is the main factor influencing the change of ILA in cortical age-related cataracts. Since UBM could not measure the ILA in all quadrants of the annular distribution, we used the average of the ILA in the four quadrants to represent the overall size of the ILA, and simple linear regression analysis showed that the ILA_{mean} increases with age, which was due to the laxity of the suspensory ligaments and pupil-blocking iris becoming dilated as a result of the lens absorbing and expanding during the swelling phase of cataract. Due to the decrease in the suspensory ligaments' flexibility with age, it is prone to laxity or rupture, resulting in a decrease in the ability to maintain the normal lens shape and to regulate the amplitude of the lens, and the lens becomes closer to a spherical shape (with a greater curvature of the anterior surface) and is displaced forward. The European Glaucoma Association guidelines state that abnormalities of the suspensory ligament are part of the pathogenesis of angle-closure glaucoma (ACG), and abnormal suspensory ligaments may lead to anterior displacement of the lens and anterior displacement of the iris lens septum, resulting in closure of the anterior chamber angle[27-28]. The increase in ΔILA with age suggests that the lens is no longer in a horizontally centered position relative to the center of the iris and that the lens is tilted like a "see-saw" to the side with the larger ILA, resulting in a significant decrease in stability. Chen *et al*[29] found that in age-related cataracts, the lens was tilted approximately 5.16° to the inferotemporal side, and eccentricity to the inferotemporal side was approximately 0.22 mm. Yu *et al*[15] from our research team also found changes in ILA and lens position in patients with cortical age-related cataracts, with a tendency for ILA distribution to be nasal<inferior<temporal<superior, and for the lens to be eccentric in a superior and temporal direction. Meanwhile, this study found that ILA in both the superior and temporal quadrants showed a significant positive correlation with age. The mechanism of this regular deviation remains

unclear. The significant increase in ILA within the superior/temporal quadrants may reflect regional heterogeneity in zonular aging (*e.g.*, superior zonules are more susceptible to gravity-dependent relaxation), though histological validation is required.

Clinicians often determine suspensory ligament abnormalities prior to cataract surgery by examining the eye with a slit-lamp microscope for symptoms such as iris tremor, shallow anterior chamber, and equatorial displacement of the lens. However, these symptoms, which may be mild and not always appreciated, increase the risk of lens dislocation and vitreous prolapse if there is an insidious suspensory ligament abnormality. Lin *et al*[7] found that patients at high risk for suspensory ligament laxity had a significantly higher rate of Berger's gap detection (60.7%) than patients with no risk factors for suspensory ligament laxity (33.0%). Ultrasound emulsification performed, especially in eyes, with abnormal suspensory ligaments can disrupt the structure of the vitreous-lens interface, resulting in intraoperative fluid and particles entering the Berger gap[22]. Wang *et al*[12] found intraoperatively that when zonular rupture occurred, the lens dislocated toward the iris root in the quadrant with normal zonules, leading to a reduction in the ILA. We believe that clear ILA images can be obtained simply, objectively, and effectively by UBM to assess the status of the suspensory ligament and lens. For example, determining the ILA in each quadrant can help in choosing and creating a surgical incision on the side where the suspensory ligament is relatively intact and the lens is relatively stable, as well as reducing the risk of vitreous prolapse toward the incision by paying attention to the selection of the energy in the fragile area of the suspensory ligament and to the movement of the ultrasonic emulsification head during ultrasonic emulsification. Abnormalities in the suspensory ligament and deflections in the lens may lead to rupture of the lens' posterior capsule during intraoperative capsulotomy, and determining the lens' deflecting direction and thus identifying the center of the lens is the key to CCC, and the direction of CCC can be chosen by using a healthy suspensory ligament for countertraction or by performing a two-handed capsulotomy[30]. In the case of an abnormal suspensory ligament that results in excessive lens deviation, it is reasonable to use the capsular tension ring (CTR) more liberally to provide adequate capsular stabilization to ensure a safe cataract surgical procedure[31].

Lens instability and superior and temporal deviation become more prominent with age. Although the annual increase in ILA was minimal (0.096° per year in the superior quadrant), its cumulative effect in the ≥75 age group showed a 2.449° increase in superior ILA compared to the <60 group. ΔILA escalated to 7.386° (*vs* 6.084° in <60 group), exacerbating the inherent instability of the lens in cataract patients (based on Table 2). Hirnschall *et al*[32] reported that a preoperative lens tilt of 4.3° measured by IOL Master 700 correlated with an average postoperative IOL tilt of 6.2°, showing a strong directional correlation (r=0.71) between lens and IOL tilting. Eccentricity of multifocal IOLs exceeding 0.4 mm may compromise postoperative visual acuity, affecting surgical success and visual quality[31]. In older patients with cortical age-related cataracts, the operator needs to perform a more detailed preoperative evaluation because the lens is less stable. Since tearing the anterior capsule and performing cortical peeling and aspiration puts pressure on the suspensory ligament, intraoperative slow and precise maneuvers are more necessary to avoid excessive surgical manipulation of the superior and temporal sides to avoid complications. Meanwhile, IOL dislocation is a major complication after IOL implantation and may be related to the incompleteness of the suspensory ligament making the capsular band less supportive[33-34]. Therefore, it is extremely important to understand that this lens instability and suspensory ligament abnormality is progressive with age, which relates to the stability of the patient's postoperative IOL within the capsular band and whether there is a risk of dislocation with age.

In conclusion, this study is the first to investigate the correlation between ILA and age in patients with cortical age-related cataracts. The findings indicate that ILA, as a characteristic UBM parameter reflecting the function of the suspensory ligament and lens stability, shows that with increasing age, lens deviation becomes more severe, stability declines, and the lens gradually shifts towards the superior and temporal sides. Therefore, the pattern of change of ILA and lens position with age, combined with other diagnostic bases and signs, can provide important predictions and guidance for the selection of surgical approaches and intraoperative operations in patients of different ages. However, UBM is not perfect and may not detect subtle suspensory ligament abnormalities. This represents a limitation of this study.

This study has some limitations. First, due to clinical feasibility constraints, this study employed standard 4-quadrant scanning, which fails to fully capture the heterogeneity of the zonular fibrous ring structure. However, future work should expand to 8 or 12 quadrants to optimize the resolution for analyzing lens tilting directions. Second, it is difficult to achieve precise consistency in the measurement of the four quadrants, and small changes in the measurement position may lead to variability in the results. Third, this study did not directly grade the zonular status intraoperatively. Future research should prospectively record the correlation between intraoperative findings (lens tremor, zonular rupture grade) and ILA/ΔILA across multiple age groups. We will integrate new assisted localization methods, record the angle between the lens axis and the visual axis to supplement lens position metrics, and establish more age groups to ensure comprehensive data collection. Although this study did not track surgical outcomes, surgeons adjusted operative protocols based on ILA thresholds (ΔILA>7°, superior ILA>15°). Subsequent research will record complication rates (*e.g.*, posterior capsule rupture) in ILA-guided surgery groups' versus control groups to improve the study. Furthermore, investigations should be extended to include abnormal lens subgroups (*e.g.*, pseudoexfoliation syndrome, post-traumatic cataracts) to evaluate zonular fragility mechanisms *via* comparative ILA pattern analysis. Prospective tracking of surgical difficulty metrics (intraoperative zonular rupture rate, CTR use) will quantify ILA's predictive value for operative risk.

In conclusion, in patients with cortical age-related cataracts, the ILA is positively correlated with age, increasing as patients get older. With advancing age, the iris becomes more convex centrally, and the lens exhibits greater tilting and decreased stability, progressively shifting superiorly and temporally. The age-related changes in ILA and lens position may serve as characteristic UBM indicators for the indirect preoperative assessment of zonular function and lens stability. These findings provide predictive and guiding value for selecting the surgical approach and intraoperative techniques in patients of different age groups.

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

Conflicts of Interest: Chen JJ, None; **Wang L,** None; **Xue SS,** None; **Yu ZY,** None; **Wang YX,** None; **Wang FL,** None.

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