· Clinical Research ·

Morphological changes in the iridocorneal angle and their relationship with intraocular pressure after infantile cataract surgery

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Abstract
● **AIM:** To evaluate morphological changes in the iridocorneal angle after pediatric cataract surgery.
● **METHODS:** Children who underwent primary infantile cataract surgery were included and 64 eyes from 41 children, including 18 with unilateral cataracts (18 eyes) and 23 with bilateral cataracts (46 eyes) were examined. All patients underwent two gonioscopic examinations to evaluate the iridocorneal angle, before the primary lens removal and before the secondary intraocular lens implantation. The anatomical changes in the iridocorneal angle and the relationship between intraocular pressure (IOP) and iridocorneal angle changes were also analyzed.
● **RESULTS:** The iridocorneal angle was wide in 64 eyes before and after surgery. The trabecular meshwork pigmentation, number of iris processes in every quadrant of the iridocorneal angle, and the width of the ciliary body band in the superior and inferior quadrants at the second gonioscopic examination were significantly increased compared to those at the first examination ($P<0.001$, $P<0.05$, $P<0.05$, and $P<0.05$, respectively). IOP gradually increased at 1mo after operation, and returned to the preoperative level at 3mo. However, IOP still increased significantly at 6 and 12mo.
● **CONCLUSION:** The main changes after pediatric cataract surgery include an increase in trabecular meshwork pigmentation and number of iris processes, IOP gradually increase and has positive correlation with trabecular meshwork pigmentation and anterior insertion of iris process.
● **KEYWORDS:** gonioscopic; iridocorneal angle; intraocular pressure; pediatric cataract surgery
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INTRODUCTION
Even with the development of modern microsurgical techniques and equipment, complications following pediatric cataract surgery still remain challenging[1-4]. The Infant Aphakia Treatment Study (IATS) found that common intraocular complications include visual axis opacification, glaucoma, and intraocular lens (IOL) exchange[5-6]. Glaucoma is a major sight-threatening complication of pediatric cataract surgery that can occur from months to decades after surgery[7-11]. According to the IATS, the risk of glaucoma increases from 12% one year after the operation to 24% after 5y[12]. Although several risk factors, such as age at time of cataract surgery, surgical technique used, microphthalmia, persistent fetal vasculature (PFV), and duration of follow-up, have been reported, convincing pathophysiological evidence for glaucoma remains unavailable. Some authors have proposed the collapse of the Schlemm's canal and decreased outflow of the aqueous humor in post-lensectomy patients with glaucoma[13].

Gonioscopy is the standard examination technique used to observe the iridocorneal angle structure and provide an overview of the detectable pathological changes in the eyes of children with congenital cataract. Previously[14-15], we have shown that the iridocorneal angle of children with cataracts is open, accompanied by a small amount of pigment and iris process preoperatively, and that the proinflammatory state may be maintained for a long time postoperatively. However, it remains unknown if the aphakic status can lead to structural changes in the iridocorneal angle.

Therefore, the purpose of this study was to investigate the changes in the iridocorneal angle using a gonioscope after primary infantile congenital cataract surgery, and to explore the relationship of morphological changes and intraocular pressure (IOP).

SUBJECTS AND METHODS

Ethical Approval All procedures were conducted following the tenets of the Declaration of Helsinki and were approved by the institutional ethics committee (clinical trial number: NCT03778086). Informed consent was obtained from the children's caregivers.

Subjects This was a prospective observational study, including 64 eyes of 41 children who underwent congenital cataract surgery (23-gauge lensectomy and anterior vitrectomy) at the Eye Hospital of Wenzhou Medical University, Hangzhou, China from March 2016 to January 2018, with an average age of 4.59±2.21mo. All the children were implanted with IOL in 2y, with an average age of 29.6±7.97mo, and were followed up for 1y after secondary IOL implantation.

All surgeries were performed by the same surgeon under general anesthesia.

The inclusion criteria were as follows: the patient had pediatric cataract with obvious visual opacity (>3-mm central opacity) and the surgical technique performed was lensectomy with limited anterior vitrectomy, without primary IOL implantation. The exclusion criteria were as follows: gestational age at birth <37wk, preoperative glaucoma, high risk of glaucoma (*e.g.*, a known family history of glaucoma, systemic or topical steroid use before surgery), severe PFV, chronic anterior uveitis, removal of visual axis opacification before secondary IOL implantation, previous ocular surgery, and a history of ocular trauma.

All patients underwent two indirect gonioscopic examinations (Goldmann 2-mirror lens, VOLK, USA). The first examination was performed before primary lens removal (pre-surgery group), and the second examination (post-surgery group) was performed before secondary IOL implantation.

Examinations and Measurements All patients underwent a comprehensive ophthalmological examination, including slit-lamp bio-microscopy, dilated fundus examination, A/B-scan ultrasound examination (Quantel Medical, Cournon-d'Auvergne, France), and estimation of IOP (iCare, Vantaa, Finland). Data on the axial length (AL), corneal diameter, age of surgery, and IOP were collected before each operation. IOPs were recorded at 1, 3, 6, and 12mo after the operation.

All gonioscopy examinations were performed before surgery. The iridocorneal angle was graded for each quadrant separately, according to the Shaffer and Spaeth classification system[16-17]. The iris insertion was defined as follows: 1) anterior to Schwalbe's line; 2) between Schwalbe's line and scleral spur; 3) scleral spur visible; 4) deep with ciliary body visible; 5) extremely deep with >1 mm ciliary body band (CBB). The description of iris process insertion was defined as follows: to CBB; to trabeculae; to Schwalbe's line[18]. The number of iris process was defined as follows: 0, none; 1, minimal; 2, moderate; 3, marked. Table 1 shows the numerical method for classifying the various features of the iridocorneal angle was based on our previous research month[14]. Two experienced pediatric ophthalmologist (Wang DD and Zhao YE) graded by reviewing the surgery videos and the iridocorneal angle photographs. Any disagreement was resolved through discussion by the two ophthalmologists.

Surgical Technique Primary surgery, which combined 23-gauge lensectomy and anterior vitrectomy using the CENTURION system (Alcon Laboratories, Inc., USA), was performed under general anesthesia by the same surgeon for all patients (Zhao YE). The vacuum was set at 350 mm Hg with a cut rate of 2000 per minute, as previously reported[19]. No intraoperative complications were noted. At the end of surgery, all eyes received subconjunctival injections of 0.2 mL dexamethasone. Postoperative topical treatment was as follows: levofloxacin eye drops (0.5%, Santen, Japan) four times a day for 2wk; tobramycin dexamethasone eye drops (Alcon, USA) four times a day for 4wk, with dose reduction once a week; and compound tropicamide (Santen, Japan) once a day for 4wk.

Secondary surgery for IOL implantation was considered when the children with unilateral cataract were approximately 1.5 years old and those with bilateral cataract were approximately 2 years old. The capsular bag was reopened with auxiliary instruments, ophthalmic viscosurgical devices or a 23-gauge cutting head, and then the hyperplastic cortex in the capsular bag was removed by automated irrigation/aspiration (Figure 1). The IOL was implanted in the capsular bag for 59 eyes, while the IOL was implanted in the sulcus combined with peripheral iridectomy for 5 eyes.

Statistical Analysis All data analyses were analyzed using SPSS software, version 26.0 (SPSS Inc., Chicago, Illinois, USA). Shapiro-Wilk test is used to check the normality of continuous variables. If it meets the normality, it is expressed as the mean±standard deviation, and if it does not meet the normality, it is expressed as the median interquartile range (IQR); Categorical variables are expressed as frequency and percentage. The difference between the two groups before and after operation was compared by generalized estimation

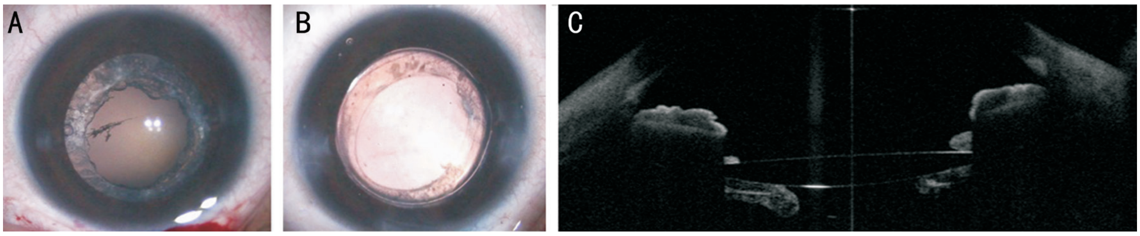

Figure 1 When the IOL was implanted, the capsular bag was reopened and the IOL was implanted in the capsular bag A: Aphakic eyes, hyperplastic cortex can be seen in the capsular bag; B: Surgical procedure, the IOL had been implanted into the capsular bag; C: High-speed swept-source optical coherence tomography, showing a well-centered IOL, and the IOL was implanted in capsular bag. IOL: Intraocular lens.

Table 1 Numerical method for classifying the iridocorneal angle before infantile cataract surgery

Feature	4	3	2	1	0
Iridocorneal angle width	Widest	Open angle	Moderately narrow	Very narrow	Closed angle
Iris insertion	Extremely deep	Deep with ciliary body visible	At the scleral spur	Between Schwalbe's line and scleral spur	Anterior to Schwalbe's line
Ciliary body band	-	Invisible	Very narrow	Normal	-
Pigmentation of trabecular meshwork	Intense	Moderate	Mild	Minimal	None
No. of iris processes					
To ciliary body band	-	Marked	Moderate	Minimal	None
To trabeculae	-	Marked	Moderate	Minimal	None
To Schwalbe's line	-	Marked	Moderate	Minimal	None

equation (GEE), and the relationship between IOP and iris angle was analyzed; Categorical variables were compared between preoperative and postoperative groups by generalized linear mixed model (GLMM). $P<0.05$ was considered statistically significant.

RESULTS

Sixty-four eyes from 41 children (19 boys and 22 girls), including 18 with unilateral cataracts (18 eyes) and 23 with bilateral cataracts (46 eyes), were included in the analysis. Table 2 presents the demographic data of the patients.

Table 2 Demographic characteristics of children subjected to infantile cataract surgery

Parameters	Before surgery	After surgery
Age, mo	4.59±2.21	29.6±7.97
Axial length (mm)	18.72±1.03	21.4±1.48
Intraocular pressure (mm Hg)	11.89±2.04	13.31±2.63
Horizontal corneal diameter (mm)	9.61±0.61	10.2±0.67

Changes in the Iridocorneal Angle Table 3 shows the comparison of the changes in the iridocorneal angle between the pre-surgery and post-surgery groups. All 64 eyes had a wide and open iridocorneal angle before and after surgery. A visible CBB was observed in 60 eyes before surgery and in 61 eyes after surgery, with a significant increase in both the superior and inferior quadrant of CBB ($P<0.05$ for both) at the second examination compared to that at the first examination. Further, at the second examination, the trabecular meshwork pigments (Figure 2) and the number of iris processes (Figure 3) in every quadrant of the iridocorneal angle were significantly increased relative to those at the first examination ($P<0.05$ for both). However, there was no significant difference in the iridocorneal angle width, iris insertion, or iris process insertion between the two groups. Moreover, there was no significant difference in the iridocorneal angle structure in the two groups between the two examinations.

Description of Other Clinical Characteristics In the post-surgery examination, peripheral anterior mini-synechia (PAS) was observed in four eyes by gonioscopy examination. Synechia were also observed in the nasal or temporal clear corneal incisions (8-10 or 2-4 o'clock), and goniosynechialysis was performed during the procedure for the secondary IOL implantation (Figure 4). One eye was observed to have multiple (more than one at different locations) PAS. Thus, peripheral iridectomy combined with goniosynechialysis was performed during the secondary IOL implantation surgery. Small cortical debris in the iridocorneal angle were observed in three eyes.

Changes in the Intraocular Pressure After Surgery

After the primary surgery The mean preoperative IOP was 11.89±2.04 mm Hg (range 6-16 mm Hg). At 1mo after surgery, IOP showed a statistically significant increase relative to that observed before surgery (13.51±2.20 *vs* 11.89±2.04 mm Hg, $P<0.001$), and the highest IOP was 24 mm Hg. The IOP decreased to a level close to the preoperative level at 3mo postoperatively (at 3mo, 12.34±1.90 mm Hg *vs* preoperative, 11.89±2.04 mm Hg, $P=0.183$), and it gradually increased in the following months. The mean IOP at 6 and 12mo was significantly higher than that before the operation (12.62±1.70 and 13.48±2.63 mm Hg, respectively, $P<0.05$).

Table 3 Comparison of the iridocorneal angle between the pre-surgery and post-surgery groups for infantile cataract *n* (%)

Parameters	Pre-surgery	Post-surgery	*P*
CBB			
Superior			<0.05
1	38 (59.4)	52 (81.3)	
2	22 (34.4)	9 (14.1)	
3	4 (6.3)	3 (4.7)	
Inferior			<0.05
1	41 (64.1)	53 (82.8)	
2	20 (31.3)	8 (12.5)	
3	3 (4.7)	3 (4.7)	
Nasal			0.584
1	46 (71.9)	49 (76.6)	
2	17 (26.6)	9 (14.1)	
3	1 (1.6)	6 (9.4)	
Temporal			0.020
1	44 (68.8)	54 (84.4)	
2	19 (29.7)	8 (12.5)	
3	1 (1.6)	2 (3.1)	
IAW			
Superior			0.99
3	2 (3.1)	2 (3.1)	
4	62 (96.9)	62 (96.9)	
Inferior			0.562
3	2 (3.1)	1 (1.6)	
4	62 (96.9)	63 (98.4)	
Nasal			0.276
0	0	1 (1.6)	
1	0	1 (1.6)	
3	1 (1.6)	2 (3.1)	
4	63 (98.4)	60 (93.8)	
Temporal			0.306
2	0	1 (1.6)	
3	0	1 (1.6)	
4	64 (100)	62 (96.9)	
TM pigmentation			<0.001
0	23 (35.9)	0	
1	27 (42.2)	0	
2	14 (21.9)	9 (14.1)	
3	0	29 (45.3)	
4	0	26 (40.6)	
No. of IP			<0.05
0	14 (21.9)	0	
1	27 (42.2)	7 (10.9)	
2	12 (18.8)	31 (48.4)	
3	11 (17.2)	26 (40.6)	
Iris insertion			0.289
B	0	1 (1.6)	
C	2 (3.1)	0	
D	20 (31.3)	18 (28.1)	
E	42 (65.6)	45 (70.3)	

CBB: Ciliary body band; IAW: Iridocorneal angle width; TM: Trabecular meshwork; IP: Iris processes.

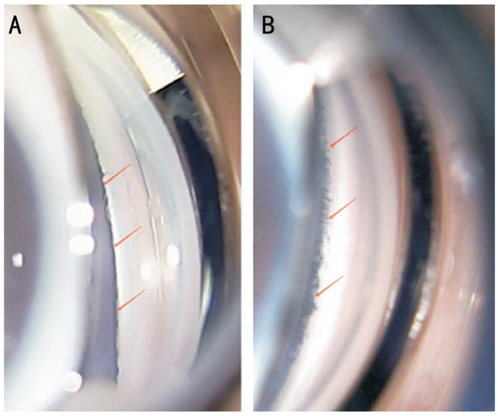

Figure 2 Increase in the number of trabecular meshwork pigments after primary surgery for infantile cataract A: Before surgery; B: After surgery. Red arrow: Angle position.

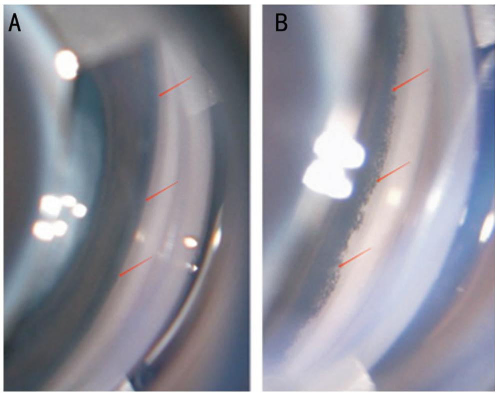

Figure 3 Increase in the number of iris processes after primary surgery for infantile cataract A: Before surgery; B: After surgery. Red arrow: Angle position.

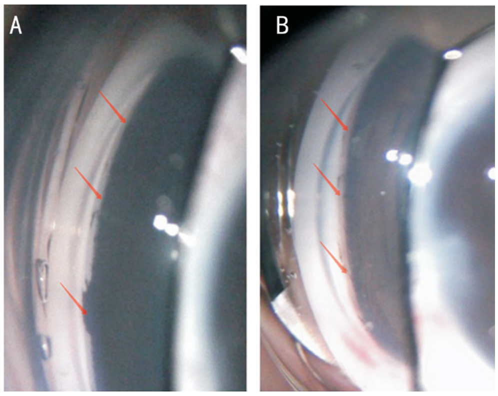

Figure 4 Gonioscopy findings after primary surgery for infantile cataract A: A small peripheral anterior mini-synechia can be observed in the nasal clear corneal incisions; B: Goniosynechialysis is performed during the secondary intraocular lens implantation. Red arrow: Angle position.

After secondary surgery for IOL implantation The change trend of IOP after two operations is similar. IOP increased gradually at 1mo after IOL implantation (preoperative, 13.31±2.63 mm Hg *vs* at 1mo 15.51±4.89 mm Hg, $P<0.0001$), and returned to the preoperative level at 3mo (at 3mo, 13.18±3.90 mm Hg *vs* preoperative, 13.31±2.63 mm Hg, $P=0.95$), and increased gradually at 6mo and 12mo (14.70±2.75 mm Hg and 15.96±3.26 mm Hg, respectively, $P<0.05$).

Univariant Linear Regression for the Correlation Between Iridocorneal Angle Morphological Changes and IOP Before Secondary Surgery The increase in trabecular meshwork pigmentation and anterior insertion of iris process were positively correlated with the elevated IOP after primary surgery (R^2=0.1005, P=0.0265 and R^2=0.1052, P=0.0230, respectively; Figure 5).

DISCUSSION

In this study, we performed gonioscopy as a routine examination to observe the changes in the iridocorneal angle in infantile cataracts. To control the influence of surgical procedures on the results obtained, all patients underwent standardized surgery performed by the same surgeon. The main outcomes of this study were that the trabecular meshwork pigments and the number of iris processes increased significantly in every quadrant of the iridocorneal angle after the primary operation, along with an increase in the width of CBB in the superior and inferior quadrants.

We found that all 64 eyes had a wide and open iridocorneal angle before and after surgery, visible CBB was observed in 60 eyes before and 61 eyes after surgery, and there was no significant difference in the iridocorneal angle width in every quadrant after surgery. A multicenter randomized controlled trial showed that glaucoma was mainly of the open-angle kind (19/20 cases, 95%) after congenital cataract, when patients were 1-6 months old at the time of the surgery[12]. Asrani and Wilensky[20] evaluated 64 eyes from 48 cases treated for glaucoma after congenital cataract surgery and found that 51 eyes (79.7%) were diagnosed with open angle glaucoma. Kirwan *et al*[8] retrospectively reviewed cases of congenital cataract surgery and found that the angles were open in the cases in which gonioscopy was performed. The results from these previous studies are consistent with those from our prospective study.

Moreover, we found that the CBB width was wider in the vertical meridian (in the superior and inferior quadrant) postoperatively. Most previous studies have reported that the anterior chamber angle and anterior chamber depth increased after routine cataract surgery in adults[21-22]. Petermeier *et al*[23] evaluated 50 pseudophakic eyes in adults and found that the vertical angle-to-angle diameter (AAD) was significantly larger than the horizontal diameter when measured with a very high frequency ultrasound. Baikoff *et al*[24] found that in the 89 adult phakic eyes studied, 74% of the eyes had a vertical AAD at least 100 μm larger than the horizontal diameter as evaluated using the anterior segment ocular coherence tomography system. Our results are consistent with the results of these studies performed in adults.

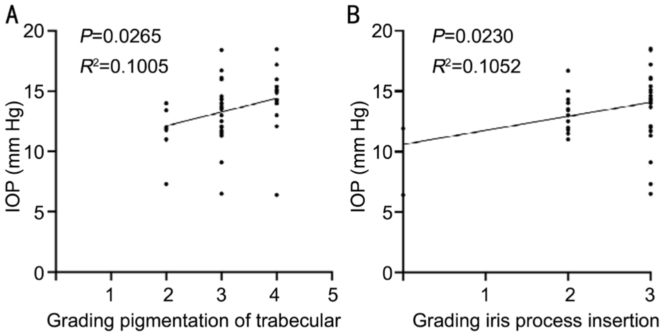

Figure 5 Univariant linear regression analysis for the correlation between iridocorneal angle morphological changes and the intraocular pressure (IOP) after primary surgery for infantile cataract surgery The increase in trabecular meshwork pigmentation and anterior insertion of the iris process are positively correlated with the elevated IOP after primary surgery (R^2=0.1005, P=0.0265 and R^2=0.1052, P=0.0230, respectively).

We hypothesized that the anterior chamber of infants was oval, which was similar to that of adults. Cataract removal may be the reason for releasing all centripetal forces, which led to an increase in the vertical meridian of the AAD relative to the horizontal meridian. Additionally, young infants with fragile eyeballs may experience mild leakage after surgery due to crying, which may lead to anterior iris synechia around incisions, particularly around the two side paracentesis positions, resulting in a narrower horizontal CBB. Therefore, it is very important to suture the incisions and completely avoid incision leakage in the case of pediatric surgery.

Another important finding in this study was that the trabecular meshwork pigmentation was obviously increased after surgery, which was consistent with the findings of many cases of postoperative glaucoma. Phelps and Arafat[7] examined and treated 18 patients who developed open angle glaucoma after an operation for congenital cataract and noted that gonioscopy revealed a heavily pigmented uveal meshwork and an anteriorly inserted iris root. Walton[25] observed that many patients who had abnormal pigment deposition may also have micro PAS. Asrani and Wilensky[20] reported that the only abnormal finding in patients with open angle glaucoma after congenital cataract surgery was increased pigmentation of the trabecular meshwork. Therefore, we suspect that one of the causes of secondary glaucoma is closely related to trabecular pigmentation caused by surgery in children with congenital cataract.

In addition, we found that the number of iris processes increased significantly after surgery. Kimura and Levene[18] reported that more iris processes and more trabecular pigmentation were found in primary open angle glaucoma in patients over the age of 40y. They believed that a congenital angle anomaly was an important factor in the pathogenesis of the elevated IOP. Similar results were also found in our study. We found that the insertion of the iris process became denser after the primary operation, and the marker pigment attached to the iris process forming a "pseudo-membrane." We speculate that the "pseudo-membrane" may subsequently develop a "pseudoangle", which is an angle lined by a spot of peripheral anterior synechiae, but seemingly open under the gonioscope. Perry *et al*[26] presented histopathologic findings showing that these anatomical derangements and pseudomembranous were the causes of goniosurgery failure in the newborn glaucoma treatment. Their results supported our postulation that the iridocorneal angle of the paired normal eye of children with unilateral cataract remained unchanged with the extension of follow-up time. This finding explained that the iridocorneal angle change was closely related to the surgery. Similarly, Haargaard *et al*[1] found that none of the children with pediatric cataract who had never undergone surgery had subsequent development of glaucoma. Therefore, we are convinced that the surgery changed the morphology of the iridocorneal angle.

Our study indicated that an increase in the number of trabecular meshwork pigments and iris processes was associated with a proinflammatory state. This has been demonstrated in our previous study, which showed a significant increase in proinflammatory cytokine levels in the aqueous humor after congenital cataract surgery[15]. Some tiny crystalline cortex debris were found in the iridocorneal angle, which came from the hyperplastic cortex. It can not only reduce the outflow facility of the iridocorneal angle but also lead to a microinflammatory state.

Our results showed that IOP gradually increased at 1mo after surgery, both primary and secondary surgery. Some previous studies have reported IOP elevation during the early postoperative period in children and adolescents[6,27]. Researchers have suspected that normal trabecular meshwork cells are likely to be infected by the presence of lens epithelial cells, followed by changes in their structural features as well as protein and gene expressions[28]. However, in the present study, we speculated that it might be due to the corticosteroid-induced mechanisms, which were related to the use of steroid eye drops after surgery, such as dexamethasone, because the IOP decreased gradually after the administration of steroid eye drops was tapered or stopped, and at 3mo post-operatively, the IOP decreased to the preoperative level. Steroid eye drops can reduce the intraocular inflammation, thereby reducing the risks of synechiae formation and angle closure. Therefore, we preferred to use high-efficiency steroid eye drops in the early stage after congenital cataract surgery. With the reduction of inflammation, steroid eye-drop administration should be stopped in time or replaced by that with less potency to prevent the early postoperative IOP increase.

Further, we found that the increase in trabecular meshwork pigmentation and anterior insertion of the iris process were positively correlated with IOP elevation. With the extension of the follow-up duration, the IOP of 6 and 12mo after surgery increased significantly (14.70±2.75 and 15.96±3.26 mm Hg, respectively). Although, there were no glaucoma cases were found in our study, based on our gonioscopy examinations findings, we suggest that more attention should be paid to monitoring the IOP in the future.

This study has several limitations. First, our study previously excluded eyes with severe PFV, which were reported as a great risk of secondary glaucoma[6,29-30]. Second, this study did not include the long-term follow-up results concerning changes in the IOP after secondary IOL implantation. Thus, a low incidence of glaucoma is expected. However, based on the strict criteria used in this study, this is an ideal method to compare the effects of surgery on the iridocorneal angle and due to the difficulty in infantile gonioscopy, this study lacks age-matched normal children as a comparative group. Finally, the subjective numerical method used in this study is also one of the limitations.

In conclusion, this prospective study revealed the changes in the iridocorneal angle after cataract surgery in infants, including an increase in the trabecular meshwork pigmentation and the number of iris processes. Furthermore, the increase in trabecular meshwork pigmentation and anterior insertion of iris process were positively correlated with the elevated IOP after surgery.

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Conflicts of Interest: Wang DD, None; **Li ZL,** None; **Zhang B,** None; **Lu ZY,** None; **Guan WC,** None; **Zhao YE,** None.

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