

Comparison of Delayed-Onset Glaucoma and Early-Onset Glaucoma after Infantile Cataract Surgery

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Purpose: To investigate the causes and characteristics of glaucoma in children following cataract surgery.

Methods: Twenty-four patients (37 eyes) with uncomplicated congenital cataracts who developed glaucoma after cataract surgery were studied retrospectively. Variables included cataract morphology, surgical techniques, post-operative complications, time to the onset of glaucoma, gonioscopic findings, presence of microcornea and the histopathologic characteristics of the filtration angle (in one case).

Results: There was a bimodal onset of glaucoma after cataract surgery. Early-onset glaucoma occurred at a mean age of 6 months in 15 eyes and delayed-onset glaucoma at a mean age of 12 years in 22 eyes. Early-onset glaucoma was significantly ($p=0.018$) more likely to be due to angle closure than delayed-onset glaucoma. With delayed-onset glaucoma, the filtration angle was open in 86% of eyes and significantly ($p=0.006$) more eyes in the delayed-onset group had microcornea. Medical treatment was sufficient to control intraocular pressure in the delayed-onset group while the early-onset group required surgical treatment ($P<0.001$).

Conclusions: The onset of glaucoma after cataract surgery during infancy follows a bimodal pattern that is correlated with the configuration of the filtration angle. The early-onset glaucoma group had high incidence of angle closure requiring surgical treatment, while in the delayed-onset group non-surgical treatment was sufficient to control intraocular pressure. Prophylactic iridectomy in eyes at risk for pupillary block is recommended. Eyes with delayed-onset glaucoma have open filtration angles yet also have findings of incomplete development of filtration structures. Microcornea is a risk factor for delayed-onset glaucoma. *Korean Journal of Ophthalmology 20(1):41-46, 2006*

Key Words: Angle closure glaucoma, Congenital cataract surgery, Delayed-onset glaucoma, Early-onset glaucoma, Open angle glaucoma

Glaucoma is one of the most serious complications following cataract surgery in children.¹⁻¹³ Pupillary block with subsequent closure of the filtration angle has been identified as one of the causes.^{14,15} Although pupillary block occurs less often with the use of contemporary surgical techniques and instruments, glaucoma continues to be a frequent complication after cataract surgery.^{4,5,7,8,11} The other form of glaucoma that has been recognized has an open angle configuration. The definite cause for the increased intraocular

pressure in open-angle glaucoma in aphakic children remains unclear.

The purpose of this study is to investigate the causes and characteristics of glaucoma after cataract surgery in young children with the goal of identifying changes in care to reduce complications that threaten vision.

Materials and Methods

This study was conducted at University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA, and was approved by the Institutional review board. The participants and their parents gave consent. We reviewed the clinical records over 25 years of all children in our academic pediatric ophthalmology practice that developed glaucoma following cataract surgery between 1982 and 2000. All cataracts were identified before one year of age and removed before 5 years of age. All operations were performed by ophthalmic surgeon A.W.B. Patients were excluded if they

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had: (1) a history of increased intraocular pressure (IOP) before cataract surgery, (2) signs of congenital glaucoma, (3) conditions other than cataract that might predispose the development of glaucoma such as rubella or persistent hyperplastic primary vitreous (PHPV), (4) syndrome-associated cataracts or (5) cataracts related to ocular trauma.

A diagnosis of glaucoma was established by having at least two of the following criteria: (1) repeated IOP measurements over 21 mmHg, (2) cupping of the optic nerve consistent with glaucoma and (3) visual field loss. The following data were recorded: cataract morphology, age at cataract surgery, corneal diameter, central corneal thickness, laterality of glaucoma, surgical techniques used to remove cataract, number and type of secondary procedures, primary or secondary insertion of an intraocular lens (IOL), visual fields, age at glaucoma diagnosis, and histopathologic findings of one eye that was enucleated. The patient with the enucleated eye was a 15-year-old female patient with uncontrollable elevation of intraocular pressure resulting in a painful, blind eye that severely interfered with her life. Corneal diameter was measured with calipers in the operating room during cataract surgery or in the outpatient clinic upon admission for surgery. Central corneal thickness was measured at the same time as corneal diameter. Types and effectiveness of glaucoma therapy were evaluated. Chi square and Mann-Whitney U tests were used for statistical analysis.

Results

Twenty-four patients (37 eyes) were identified with glaucoma after cataract surgery. Patient characteristics are summarized in Tables 1 and 2. All 24 patients were Caucasian (non-Hispanic). Eleven patients had unilateral cataract surgery and unilateral glaucoma and 13 had bilateral cataract surgery and bilateral glaucoma. Follow-up after glaucoma onset ranged from 1 to 23.7 years.

The onset of glaucoma after cataract surgery followed a bimodal pattern (Fig. 1). Fifteen eyes had an early onset of glaucoma (1 week to 13 months after cataract surgery), while

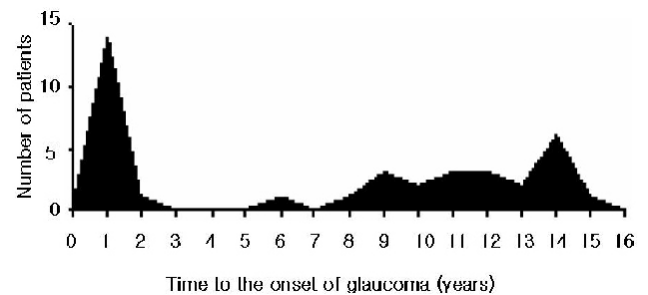


Fig. 1. Time (years) to the onset of glaucoma following removal of cataracts diagnosed before one year of age and removed before five years of age.

Table 1. Patients and characteristics of early-onset and delayed-onset glaucoma

Patients characteristics	Early-Onset Group	Delayed-Onset Group	Total
Number of patients	11	15	24*
Number of eyes	15	22	37*
Gender Male / Female	4 / 7	6 / 9	10 / 14*
Unilateral / bilateral	7 / 4	8 / 7	11 / 13*
Age (range) at glaucoma onset [†]	0.5 (0.08-1.1)	12 (6-15)	10 (0.08-15)
Interval (range) between cataract surgery and glaucoma onset [†]	0.16 (0.02-1.08)	11.75 (5.8-14.75)	8 (0.02-14.75)
Total (range) follow-up [†]	15 (4-24)	16 (3-25)	16 (3.00-25)
Follow-up (range) after glaucoma onset [†]	14.50 (3.25-23.75)	4.25 (1-15)	8 (1-23.75)

*: Note that two patients with bilateral aphakia developed early-onset glaucoma due to pupillary block in one eye and delayed-onset open angle glaucoma in the other eye, [†]: Median value in years.

Table 2. Characteristics of early-onset and delayed-onset glaucoma

Characteristics	Early-Onset Group (n=15)	Delayed-Onset Group (n=22)	p value
Microcornea	1	11	0.006
Cataract type N / C / L / AP / PP / ?*	5 / 1 / 1 / 2 / 0 / 6	7 / 6 / 5 / 2 / 1 / 1	0.509
Median age at cataract surgery (months) (range)	3 (0.25-11)	3.75 (0.25-60)	0.143
Surgical technique used			
Aspiration / asp+pc+ant vit [†]	9 / 6	11 / 11	
IOL [‡] implantation	2	4	0.532
Pupillary block	8	3	0.009
Angle closure >270	7	3	0.018

*N: Nuclear, C: Cortical, L: Lamellar, AP: Anterior polar, PP: Posterior polar, ?: unknown, [†]Aspiration / asp+pc+ant vit: aspiration alone / aspiration plus posterior capsulectomy plus anterior vitrectomy, [‡]IOL: intraocular lens.

22 eyes had delayed-onset glaucoma (70 to 177 months after cataract surgery). Two patients with bilateral aphakia developed early-onset glaucoma due to pupillary block in the first eye and delayed-onset open angle glaucoma in the fellow eye. Out of 11 patients in the early-onset group, 5 patients had unilateral cataract surgery, 4 patients had bilateral cataract surgery, and 2 patients with bilateral aphakia developed early-onset glaucoma in one eye and delayed-onset glaucoma in the other eye. Out of 15 patients in the delayed-onset group, 6 patients had unilateral cataract surgery, 7 patients had bilateral cataract surgery, and 2 patients with bilateral aphakia developed delayed-onset glaucoma following early-onset glaucoma in the other eye. Early-onset glaucoma typically had an abrupt onset. Presenting symptoms and signs included pain, photophobia, lacrimation, pupillary block, angle closure, rapid myopic shift in the refractive error and corneal edema. Delayed-onset glaucoma (in 18 of 22 eyes) had an insidious, painless onset with an increased IOP that was discovered on routine examination. Age at cataract surgery and type of glaucoma onset were not significantly related ($p=0.08$).

Corneal diameters were classified as either microcornea or normal-size for the child's age by comparing them to Wallace and Plager's¹⁶ table of age-adjusted normal corneal diameters in children. Twelve of 37 (32 %) eyes were found to have microcornea, 1 in the early-onset group and 11 in the delayed-onset group. Microcornea was highly associated with delayed-onset open-angle glaucoma ($p=0.006$, Chi-square).

Lens morphology data were available for 30 eyes. Nuclear cataracts were the most common, occurring in 12 eyes that were equally distributed in the early-onset (33%) and delayed-onset (32%) groups. The remaining cataracts were cortical, lamellar, anterior polar or posterior polar. There was no significant difference in cataract type between eyes that developed early-onset and those that developed delayed-onset glaucoma ($p=0.509$, Chi-square).

Cataracts were surgically removed by aspiration of the lens material in 20 eyes (9 in the early-onset group and 11 in the delayed-onset group) and aspiration combined with posterior

capsulectomy and anterior vitrectomy in 17 eyes (6 in the early-onset group and 11 in the delayed-onset group). Patients who had simple aspiration of the lens material more often required secondary procedures (19 of the 20 eyes) to treat posterior capsule opacification, retained lens material, or pupillary block than patients who also had primary posterior capsulectomy and anterior vitrectomy (3 of the 17 eyes) ($p<0.001$, Chi-square). A peripheral iridectomy or iridotomy was performed in only 5 eyes during cataract surgery (2 in eyes in early-onset group and 3 in the delayed-onset group). Pupillary block did not occur in any of them. However, in eyes that did not have a peripheral iridectomy, pupillary block was a frequent reason for early-onset glaucoma (8/13) compared to those with delayed-onset of glaucoma (3/19) ($p=0.009$, Chi-square).

Thirty-three of 37 eyes underwent at least one gonioscopic examination and the filtration angle was closed in at least

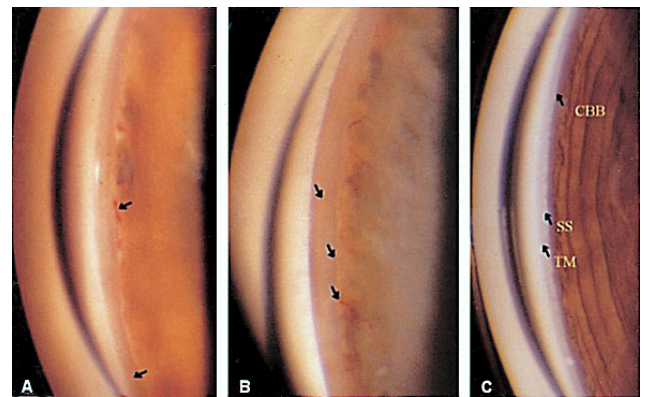


Fig. 2. (A and B) Gonioscopic appearance of two eyes with microcornea and delayed-onset aphakic glaucoma. Note the high iris insertion, lack of angle recess, lack of iris surface undulation, visible iris vessels, and pigmented membranous tissue covering the angle (black arrows in A and B). The scleral spur (SS) is indiscernible. (C) Gonioscopic appearance of an age-matched normal eye with congenital nuclear cataract and microcornea. Note the normal appearance of the iris, ciliary body band (CBB), SS, and trabecular meshwork (TM).

Table 3. Effective treatment of early-onset and delayed-onset glaucoma after cataract surgery

Effective Treatment	Number of Eyes		
	Early-onset group (n=15)	Delayed-onset group (n=22)	Total (n=37)
Topical medication only	2	16	18 ($p<0.001$)
Surgery required	13	6	19 ($p<0.001$)
Goniotomy	5	1	6
Trabeculectomy	9	2	11
Trabeculectomy with MMC*	2	4	6
Cyclocryotherapy	8	0	8
Seton implantation	1	2	3
Peripheral iridectomy	5	0	5
Nd:YAG† laser iridotomy	0	1	1

*MMC: mitomycin C, † Nd : YAG: neodymium-yttrium-aluminum-garnet.

three quadrants at the time of glaucoma diagnosis in 10 eyes (7 in the early-onset group and 3 in the delayed-onset group, $p=0.018$, Chi-square). The most consistent gonioscopic findings in the remaining 23 eyes were localized peripheral anterior synechiae (PAS) over a few clock hours, flat iris insertion, poorly developed angle recess, a sheet of translucent tissue overlying the meshwork and increased pigmentation over the trabecular meshwork, narrow or invisible ciliary band, an indistinct scleral spur, and increased vasculature, sometimes bridging the angle (Fig. 2).

Satisfactory reduction in IOP was achieved with one or two topical medications in 2 eyes in the early-onset group and 16 eyes in the delayed-onset group ($p<0.001$, Chi-square). Surgery was required to manage glaucoma in only 27% (6/22) of eyes in the delayed-onset group but in 87% (13/15) in the early-onset group ($p=0.001$, Chi-square). Surgical procedures used to control glaucoma in the two groups are summarized in Table 3. Peripheral iridectomy was performed in 5 eyes in the early-onset group, but only 1 eye had a favorable response to this procedure; the others required two or more glaucoma procedures to control the IOP.

Figure 3 shows an angle in the eye of a patient with delayed-onset glaucoma; the meshwork is compact and hypercellular, the iris stroma and neovascular tissue encroaches on the partially developed angle recess and the lumen of Schlemm's canal cannot be clearly identified.

Discussion

To learn more about the factors specific to the development of glaucoma after cataract surgery, we studied a select group of children who had cataract surgery, excluding eyes with cataracts and associated conditions that might predispose the development of glaucoma.

The bimodal onset of glaucoma after cataract surgery in

this study (Fig. 1) reaffirms the observations of Mills and Robb,⁷ who also showed a bimodal pattern of onset of glaucoma following cataract surgery in children. They noted that glaucoma with an angle-closure mechanism frequently occurs within the first few months after surgery and open-angle glaucoma has a later onset (average 7.4 years). In contrast, Chen et al¹¹ did not observe a bimodal pattern of onset of glaucoma and filtration angles were open in 94 % of their patients. In our study group, 54% of eyes with early-onset glaucoma and 15% of the eyes with delayed-onset glaucoma had angle closure.

Simon et al⁵ reported that open angle glaucoma occurs after a latent period of 5.5 years following cataract surgery in children. Asrani and Wilensky⁹ reported an average interval between cataract surgery and the onset of open angle glaucoma of 12.2 years. In this study, with a mean follow-up period of 15.3 years, open-angle glaucoma developed between 6 and 14 years after cataract surgery. The time to the onset of open angle glaucoma was longer when patients were followed for a longer period. Children who have undergone cataract surgery have a continuing risk of developing glaucoma throughout their lives.^{2,5,8,9,11,13,17,18}

Cataract surgery within the first year of life has been identified as a risk factor for glaucoma.^{3,7,10,11,12} This was also obvious in our aphakic glaucoma series; 92% of cataracts were removed before 1 year and 27% were removed before 1 month of age. Rabiah¹³ found that the incidence of glaucoma was 37 % if the cataract surgery was performed before 9 months, 14% if the surgery was performed between 9 months and 2 years of age, and only 9% if performed between 2 to 3 years of age. Vishwanath et al¹² found that after bilateral lensectomy within the first month of life, the 5 year risk of developing glaucoma in at least one eye was 50% but it decreased to 14.9% if the surgery is performed later in the first year. In this study, however, there was no statistically significant relationship between age at the time

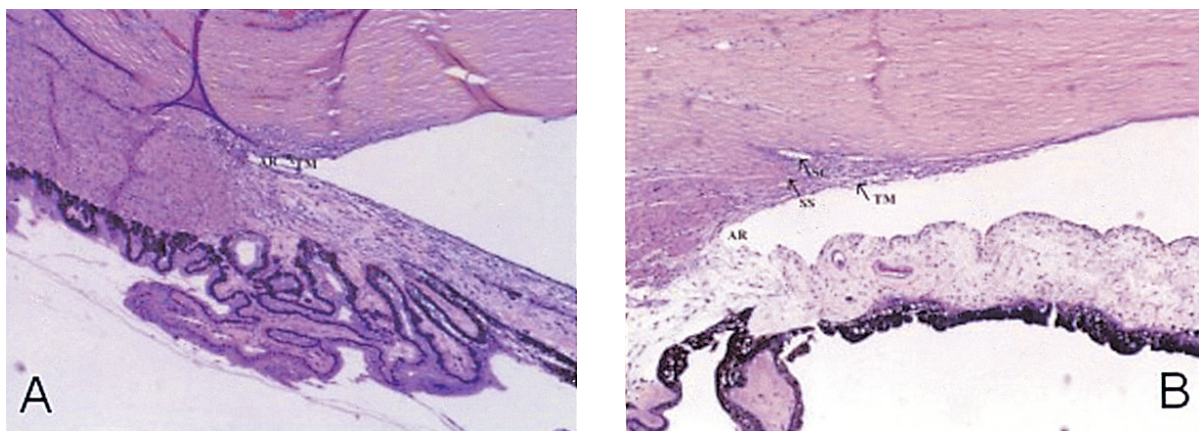


Fig. 3. (A) Histopathologic view of an angle with delayed-onset aphakic glaucoma. There is no identifiable Schlemm's canal (SC), the scleral spur (SS) is indistinct, and the trabecular meshwork (TM) is compact. The angle recess (AR) is poorly developed (H&E, magnification, $\times 12$). (B) An age-matched normal filtration angle of a 15-year-old female who received enucleation due to retinoblastoma (H&E, magnification, $\times 12$).

of cataract surgery and the type of glaucoma onset. More cases are needed to more fully study this correlation.

The timing of cataract surgery in infants may need to be reassessed. Prompt removal of congenital cataracts is considered to be important to achieve good visual and functional results^{19,20} although early surgery increases the risk for glaucoma. Vishwanath et al¹² have suggested delaying surgery until the infant is 4 weeks old in bilateral cases, and we concur on the basis of these findings. Mori et al²¹ reported 58 eyes in 41 patients with congenital cataracts that were not surgically removed. During a mean follow-up of 19 years, only 2 eyes developed glaucoma. In both cases, glaucoma was of the angle closure type related to PHPV. There are three reports of patients with bilateral congenital cataracts, but only one of the eyes was operated on.^{2,5,7} In these patients, glaucoma developed only in the surgically treated eyes. Thus, glaucoma in children with cataracts seems clearly to be related to cataract surgery.

Early-onset glaucoma is strongly associated with the surgical procedure used to remove the cataract. In this study, pupil block with secondary angle closure was the principal cause of early-onset glaucoma. Mills and Robb⁷ made similar observations. Residual lens material contributes to the development of glaucoma by forming Elschnig pearls that mechanically block the pupil and induce inflammatory adhesions in the angle and at the pupil edge which can cause pupillary block and angle closure.^{2,8,14,15} In this study, residual proliferating lens material needed to be removed later in 8 eyes. The conversion from assisted aspiration to outcome-enhanced aspiration combined with posterior capsulectomy and anterior vitrectomy has enabled the surgeon to remove the lens cortex and capsule more effectively. This change has reduced, but not eliminated, the prevalence of pupillary block and subsequent angle closure. In eyes that have poor pupil dilatation or when technical problems occur that preclude complete removal of the cortex, we recommend performing an iridectomy.

We found that sulcus-fixation of the IOL is a risk factor for the development of pupillary block, which has already been observed.^{7,22,23} In 3 of the 6 eyes in which the IOL was fixed in the sulcus, pseudophakic pupillary block developed. We recommend placement of the IOL within the capsular bag whenever possible. If this positioning cannot be accomplished, we recommend performing a peripheral iridectomy.

Microcornea is one of the risk factors for glaucoma that cannot be altered. An association between microcornea and development of glaucoma has been reported.^{7,9,10,12,13,16} Parks et al⁶ found a 33% incidence of glaucoma in eyes operated on that had a corneal diameter less than 10 mm. The prevalence of microcornea among aphakic glaucoma patients is as high as 88.5%⁶ to 94%.¹⁶ In our population, age adjusted microcornea was present in only 7% of eyes with early-onset glaucoma, but in 50% of eyes with delayed-onset glaucoma. Smaller eyes and eyes with reduced corneal diameter have a predisposition for angle closure. However,

no eye with microcornea developed angle-closure glaucoma in our population; all had open angle glaucoma. Microcornea may account for the abnormally thick corneas seen in 11 eyes in this study. The increased thickness may cause the measured IOP to seem higher than it actually is. Although many of the eyes in our study with glaucoma had a thick cornea, we felt that the changes observed in the optic nerve cup, visual field changes, and occasional spikes in IOP over 40 mmHg meant that these eyes had glaucoma but not ocular hypertension.

Mori et al¹² suggested that the aphakic state of the eye that follows the operation may be responsible for glaucoma. The volume of the lens and its dynamic role in accommodation are more prominent in younger eyes. Surgical removal of the lens early in life can alter normal development of the filtration angle. Morphologic studies of developing eyes of children have shown that the angle recess of the iridocorneal angle is expected to move toward the periphery, exposing the scleral spur and the ciliary body band.^{24,25} This study, Walton,⁸ and Keech et al⁴ show that there is altered development of the filtration angle. Eyes with delayed-onset open-angle glaucoma had an open angle, but there was anterior insertion of the iris together with the lack of development of the angle recess and filtration structures compared to adults. In the enucleated eye, we observed anterior displacement of iris tissue with incomplete development of the angle recess (Fig. 3). The trabecular meshwork was compact and thickened. These findings, and the changes observed on gonioscopy, suggest that there is a relative arrest in the normal development of the filtration angle and the trabecular meshwork in the eyes of aphakic children.

Alterations of the accommodation mechanism related to the loss of lens may also have a role in the functioning of the filtration angle. During accommodation, the longitudinal fibers of the ciliary muscle, which insert on the scleral spur, contract. This expands Schlemm's canal and opens the interstices of the trabecular meshwork, which increases aqueous outflow.²⁶⁻³⁰ Parasympathomimetic drugs stimulate the ciliary muscle, putting traction on the trabecular sheets which causes them to separate. These agents stimulate accommodation and are effective in lowering the IOP in aphakic eyes.

In conclusion, early-onset glaucoma after cataract surgery in children is usually of the angle-closure type secondary to pupillary block. Preventable risk factors for early-onset glaucoma include early cataract surgery, not performing an iridectomy when there is retained lens material after cataract extraction, a pupil that dilates poorly, a shallow anterior chamber, and sulcus fixation of an IOL. Delayed-onset glaucoma generally occurs years after surgery and is usually of the open angle type. Because of the late onset of this type of glaucoma, it is probably not directly linked to the surgery itself. Eyes with delayed-onset glaucoma have filtration angles that appear to be open yet also have findings consistent with incomplete development of filtration

structures. Cataract surgery done at an early age and microcornea are risk factors for delayed-onset glaucoma.

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