Original Investigation

Glaucoma-Related Adverse Events in the First 5 Years After Unilateral Cataract Removal in the Infant Aphakia Treatment Study

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IMPORTANCE Glaucoma-related adverse events constitute major sight-threatening complications of cataract removal in infancy, yet their relationship to aphakia vs primary intraocular lens (IOL) implantation remains unsettled.

OBJECTIVE To identify and characterize cases of glaucoma and glaucoma-related adverse events (glaucoma + glaucoma suspect) among children in the Infant Aphakia Treatment Study by the age of 5 years.

DESIGN, SETTING, AND PARTICIPANTS A multicenter randomized clinical trial of 114 infants with unilateral congenital cataract in referral centers who were between ages 1 and 6 months at surgery. Mean follow-up was 4.8 years. This secondary analysis was conducted from December 23, 2004, to November 13, 2013.

INTERVENTIONS Participants were randomized at cataract surgery to either primary IOL or no IOL implantation (contact lens). Standardized definitions of glaucoma and glaucoma suspect were created for the Infant Aphakia Treatment Study and applied for surveillance and diagnosis.

MAIN OUTCOMES AND MEASURES Development of glaucoma and glaucoma + glaucoma suspect in operated on eyes for children up to age 5 years, plus intraocular pressure, visual acuity, and axial length at age 5 years.

RESULTS Product limit estimates of the risk for glaucoma and glaucoma + glaucoma suspect at 4.8 years after surgery were 17% (95% CI, 11%-25%) and 31% (95% CI, 24%-41%), respectively. The contact lens and IOL groups were not significantly different for either outcome: glaucoma (hazard ratio [HR], 0.8; 95% CI, 0.3-2.0; $P = .62$) and glaucoma + glaucoma suspect (HR, 1.3; 95% CI, 0.6-2.5; $P = .58$). Younger (vs older) age at surgery conferred an increased risk for glaucoma (26% vs 9%, respectively) at 4.8 years after surgery (HR, 3.2; 95% CI, 1.2-8.3), and smaller (vs larger) corneal diameter showed an increased risk for glaucoma + glaucoma suspect (HR, 2.5; 95% CI, 1.3-5.0). Age and corneal diameter were significantly positively correlated. Glaucoma was predominantly open angle (19 of 20 cases, 95%), most eyes received medication (19 of 20, 95%), and 8 of 20 eyes (40%) underwent surgery.

CONCLUSIONS AND RELEVANCE These results suggest that glaucoma-related adverse events are common and increase between ages 1 and 5 years in infants after unilateral cataract removal at 1 to 6 months of age; primary IOL placement does not mitigate their risk but surgery at a younger age increases the risk. Longer follow-up of these children may further characterize risk factors, long-term outcomes, potential differences between eyes having primary IOL vs aphakia, and optimal timing of unilateral congenital cataract removal.

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Glaucoma is a well-documented and serious complication after childhood cataract removal, with reported frequency and risk factors for glaucoma and glaucoma suspect varying by study population, definition, and follow-up time in a variety of retrospective studies.[1-12] The Infant Aphakia Treatment Study (IATS)—a multicenter randomized clinical trial sponsored by the National Eye Institute—compares outcomes of surgery for unilateral cataract with primary intraocular lens (IOL) implantation to surgery without IOL implantation in infants between 1 and 6 months of age.[13-17]

Definitive knowledge of the relationship between primary IOL placement at the time of congenital cataract removal and glaucoma risk remains to be ascertained. While some studies have reported decreased glaucoma frequency among eyes with primary IOL implantation after cataract removal in the first year of life,[18-20] others have noted a similar frequency[1,10-12,21] but all lacked randomization regarding primary IOL placement.

In this article, we report 5-year results of the development of glaucoma-related adverse events in IATS participants.

At a Glance

- To identify and characterize cases of glaucoma + glaucoma suspect among children in the Infant Aphakia Treatment Study by age 5 years.
- The risk for glaucoma at 4.8 years after cataract removal was 17% (95% CI, 11%-25%).
- The risk for glaucoma + glaucoma suspect at 4.8 years after cataract removal was 31% (95% CI, 24%-41%).
- Younger age at surgery conferred an increased risk for glaucoma (hazard ratio, 3.2; 95% CI, 1.2-8.3).
- Smaller corneal diameter increased the risk for glaucoma + glaucoma suspect (hazard ratio, 2.5; 95% CI, 1.3–5.0).
- Glaucoma was predominantly open angle (19 of 20 cases, 95%), most eyes received medication (95%), and 8 of 20 (40%) underwent glaucoma surgery.

Methods

The IATS design, surgical technique, follow-up schedule, patching and optical correction regimens, evaluation methods, and patient characteristics at baseline have been previously reported in detail (eAppendix in the Supplement).[14] The definitions for *glaucoma*, *glaucoma suspect*, and *glaucoma-related adverse events* (*glaucoma + glaucoma suspect*) were established and rigorously applied, as previously reported (**Table 1**).[13]

The IATS was not originally designed to capture detailed information about the diagnosis, treatment, and course of glaucoma. However, medical record information was obtained from sites to enable the medical monitor to (1) verify application of standard definitions for glaucoma and glaucoma suspect and (2) confirm that appropriate care was provided to study participants. Available information on intraocular pressure (IOP), optic nerve head (cup-disc ratios recorded by the clinician), medications, and glaucoma surgery was gathered from these records. Statistical considerations are provided in the eAppendix in the Supplement.

For this study conducted from December 23, 2004, to November 13, 2013, institutional review board approval was obtained from each of the participating centers and written informed consent was obtained from the parents/guardians of each enrolled child.

Results

Development of Glaucoma

The IATS randomized 114 infants (57 each to the contact lens [CL] and IOL groups); 113 completed clinical examination at age 5 years (mean, 5.0 years; range, 4.7-5.4), with mean postsurgical follow-up of 4.8 years (range, 4.4-5.3 years), and 1 participant (IOL group) was lost to follow-up at 18 months.

By the 5-year follow-up, 20 eyes (18%) had developed glaucoma, and 16 additional eyes were glaucoma suspects (glaucoma + glaucoma suspect, 36 eyes total [32%]). The CL group had 9 eyes (16%) with glaucoma and 11 (19%) were glaucoma suspects (glaucoma + glaucoma suspect, 20 eyes total [35%]). The IOL group had 11 eyes (19%) with glaucoma and 5 (9%) were glaucoma suspects (glaucoma + glaucoma suspect, 16 eyes total [28%]).

In Kaplan-Meier analysis, for all study eyes combined, the risk for glaucoma after cataract removal increased from 9% (95% CI, 5%-16%) at 1 year to 17% (95% CI, 11%-25%) at 4.8 years (**Figure 1**A; eTable 1 in the Supplement); the risk for glaucoma + glaucoma suspect diagnosis after cataract removal increased from 12% (95% CI, 7%-20%) at 1 year to 31% (95% CI, 24%-41%) at 4.8 years (Figure 1B; eTable 1 in the Supplement).

Kaplan-Meier curves for developing glaucoma after cataract removal were not significantly different between the CL and IOL treatment groups (hazard ratio [HR], 0.8; 95% CI, 0.3-2.0; $P = .62$; **Figure 2**A; eTable 1 in the Supplement), with the risk rising in the CL and IOL groups from 5% (95% CI, 2%-15%) and 12% (95% CI, 6%-24%), respectively, at 1 year to 14% (95% CI, 7%-26%) and 19% (95% CI, 11%-32%), respectively, at 4.8 years. Kaplan-Meier curves for developing glaucoma + glaucoma suspect diagnosis after cataract removal were also not significantly different between the treatment groups (HR, 1.3; 95% CI, 0.6-2.5; $P = .58$; Figure 2B; eTable 1 in the Supplement), with the risk rising in the CL and IOL groups from 9% (95% CI, 4%-20%) and 16% (95% CI, 9%-28%), respectively, at 1 year to 34% (95% CI, 23%-48%) and 28% (95% CI, 18%-42%), respectively, at 4.8 years.

Cases of Glaucoma and Glaucoma Suspect Since the 1-Year Follow-up

Glaucoma was diagnosed in 10 eyes between the 1-year postoperative visit and at age 5 years (6 CL and 4 IOL). Six eyes that were glaucoma suspects at 1 year converted to glaucoma by the visit at age 5 years. Thirteen eyes became glaucoma suspects during the same time interval (10 CL and 3 IOL).

Table 1. Definitions of *Glaucoma*, *Glaucoma Suspect*, and *Glaucoma-Related Adverse Event*

Term	Definition
Glaucoma	A study eye was diagnosed as having glaucoma if the IOP was >21 mm Hg with ≥1 of the following anatomical changes: (1) corneal enlargement, (2) asymmetrical progressive myopic shift coupled with enlargement of the corneal diameter and/or axial length, (3) increased optic nerve cupping defined as an increase of ≥0.2 in the cup-to-disc ratio, or (4) a surgical procedure was performed for IOP control.
Glaucoma suspect	A study eye was designated as a glaucoma suspect if there was either: (1) recording of 2 consecutive IOP measurements >21 mm Hg on different dates after topical corticosteroids had been discontinued without any of the anatomical changes listed above for glaucoma or (2) glaucoma medication was used to control IOP without any of the anatomical changes listed above.
Glaucoma-related adverse event	Glaucoma and glaucoma suspect together (glaucoma + glaucoma suspect).[a]

Abbreviation: IOP, intraocular pressure.

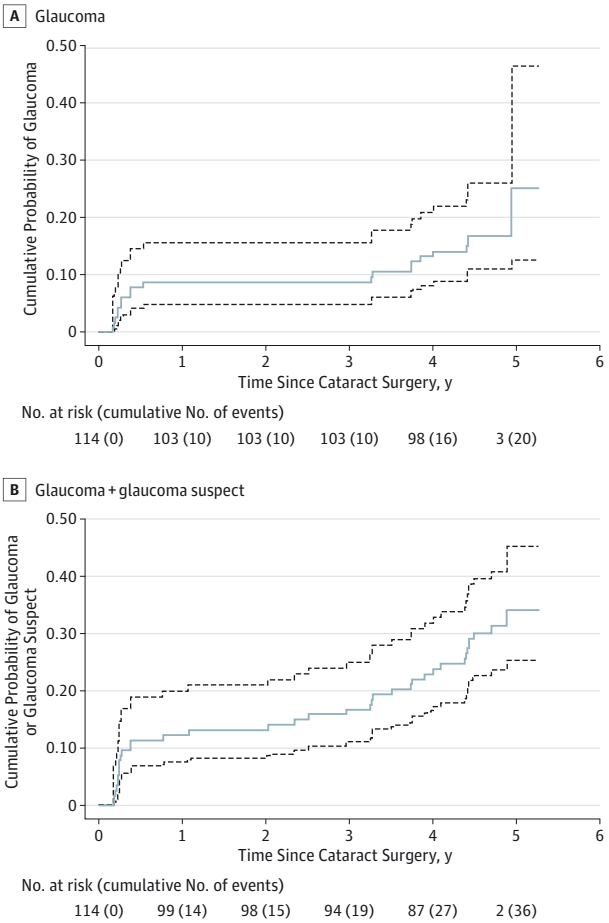
[a] In the statistical analyses, for an eye originally diagnosed as a glaucoma suspect that developed glaucoma, that eye was considered in the glaucoma group when analyzing the glaucoma outcome and in the glaucoma suspect group when analyzing the glaucoma-related adverse event outcome. For all other analyses, the eye was considered in the glaucoma group. Throughout the text, *eye* is synonymous with *child* because no fellow eye (without cataract) has developed glaucoma or glaucoma suspect in this study to date.

Influence of Baseline Characteristics of Enrolled Children/Study Eyes

Bivariate analyses evaluated selected baseline characteristics relative to the development of glaucoma and glaucoma + glaucoma suspect (**Table 2**). Children in the younger age strata at cataract surgery were at higher risk for developing glaucoma than older children by 4.8 years postoperatively (26% vs 9%, respectively; $P = .01$) and glaucoma + glaucoma suspect (45% vs 21%, respectively; $P = .006$). Eyes with smaller corneal diameter (≤10 mm) at cataract removal were also at higher risk for glaucoma + glaucoma suspect (but not of glaucoma) than those having larger corneas by 4.8 years postoperatively (50% vs 20%, respectively; $P = .001$). Neither persistent fetal vasculature (PFV) diagnosis nor IOP at surgery was associated with risk for either glaucoma or glaucoma + glaucoma suspect diagnoses by 4.8 years.

Multivariate analysis for glaucoma considered factors including age strata, CL vs IOL group, PFV, corneal diameter, and IOP at surgery: age strata was associated with glaucoma (HR [younger vs older], 3.2; 95% CI, 1.2-8.3; $P = .02$); no association was identified with any of the other factors after accounting for age. In the multivariate analysis for glaucoma + glaucoma suspect diagnoses, corneal diameter was associated with glaucoma + glaucoma suspect (HR [≤10 mm vs >10 mm], 2.9; 95% CI, 1.5-5.7; $P = .002$); no association was identified with any of the other factors after accounting for corneal diameter. Not surprisingly, there was a moderately high positive correlation between age and corneal diameter ($r = 0.65$, $P < .001$); hence, when one of these variables was in the model, an association with outcome was not identified for the other variable. Similar results were found for the bivariate and multivariate analyses with age at surgery, IOP, and corneal diameter in continuous form and are reported in eTable 2 in the Supplement.

Figure 1. Kaplan-Meier Curves Showing the Cumulative Probability of Glaucoma and Glaucoma + Glaucoma Suspect Against Time After Cataract Surgery



One additional child in the contact lens group had glaucoma diagnosed at 4.9 years, which increased the cumulative probability to 43% (95% CI, 12%-91%). The dashed lines represent 95% CIs.

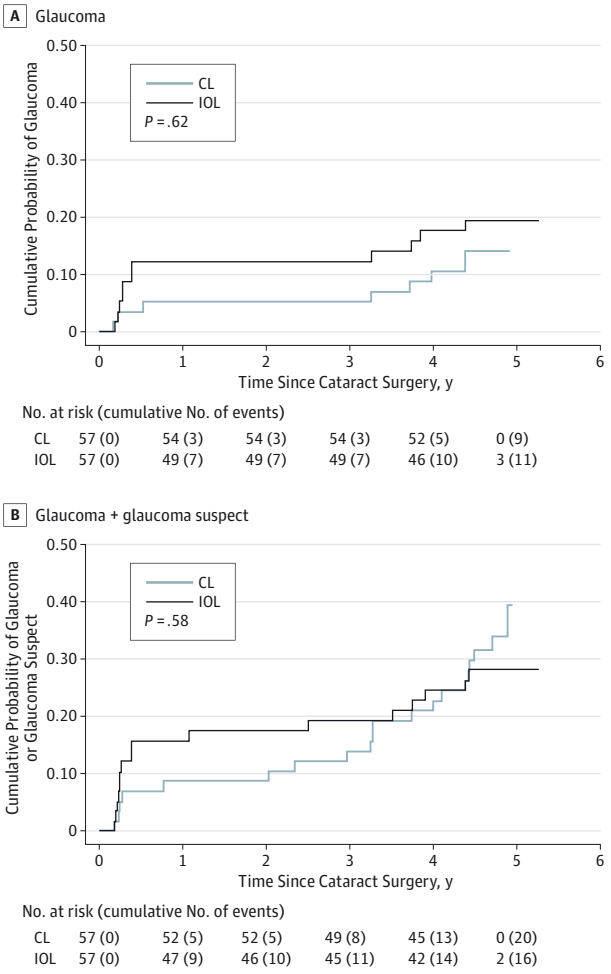
Glaucoma Characteristics, Treatment, and Outcomes

Although detailed gonioscopic information was not collected as part of the IATS, 19 of 20 eyes with glaucoma were assumed to be open angle, while 1 eye had iris bombe and angle closure. All 16 eyes with glaucoma suspect diagnosis were assumed to have open angles.

Diagnostic Criteria for Diagnosis

Among the 20 eyes diagnosed as having glaucoma, 13 (65%) showed IOP greater than 21 mm Hg with anatomic changes: corneal enlargement (3 eyes, with 2 having myopic shift), increased optic nerve cupping (8 eyes, with 1 having myopic shift), and myopic shift only (2 eyes). Seven eyes (35%) were diagnosed either by requiring glaucoma surgery (n = 4), or by 2 or more other diagnostic criteria (n = 3). Among the 16 eyes diagnosed as glaucoma suspect, 10 eyes (63%) met criteria by elevated IOP (>21 mm Hg), while 6 eyes (38%) were treated with glaucoma medications, without strictly meeting IOP diagnostic criteria.

Figure 2. Kaplan-Meier Curves Showing the Cumulative Probability of Glaucoma and Glaucoma + Glaucoma Suspect Against Time After Cataract Surgery According to the Treatment Assignment



CL indicates contact lens; IOL, intraocular lens.

The mean (SD) maximum IOP recorded was elevated in eyes with glaucoma and with glaucoma suspect diagnoses (32.1 [9.0] vs 28.9 [4.9] mm Hg, respectively) compared with eyes having neither diagnosis (18.8 [2.9] mm Hg; $P < .001$ for both comparisons). The mean (SD) maximum IOP recorded was similar for eyes with glaucoma in the CL (n = 9) vs IOL groups (n = 11): 34.7 (6.6) vs 30.0 (10.5) mm Hg, respectively ($P = .26$). The mean (SD) maximum recorded IOP in eyes diagnosed as glaucoma suspects was similar in the CL and IOL groups (27.9 [3.0] vs 30.9 [7.8] mm Hg, respectively; $P = .44$).

The optic nerve head cup-disc (CD) ratio was recorded subjectively by investigators without imaging. While the maximum recorded CD ratio varied widely, the mean (SD) CD ratio was larger in eyes diagnosed as having glaucoma (0.45 [0.22]; n = 19) vs glaucoma suspect (0.19 [0.10]; n = 15) ($P < .001$), with no significant difference between the CL and IOL groups within each respective diagnostic group.

Glaucoma Treatment

Glaucoma medications were prescribed for 19 of 20 eyes (95%) with glaucoma and 12 of 16 eyes (75%) diagnosed as glaucoma suspects; 8 of 20 eyes (40%) with glaucoma had glaucoma surgery by the visit at age 5 years (eTable 3 in the Supplement). The eye with angle closure (CL group) had limited anterior vitrectomy, pupillary membrane removal, and surgical peripheral iridectomy; despite glaucoma control postoperatively, the eye subsequently experienced retinal detachment and, ultimately, phthisis. Glaucoma surgical procedures were performed in 7 of 19 eyes (37%) with open-angle glaucoma: 5 of 11 (45.5%) in the IOL group and 2 of 9 (22.2%) in the CL group ($P = .37$). Surgical procedures included trabeculotomy, Baerveldt glaucoma drainage implant, and endoscopic diode laser (eTable 3 in the Supplement).

Of the 10 additional glaucoma cases diagnosed between the 1-year postoperative visit and the follow-up at age 5, only 1 additional eye (10%) has had glaucoma surgery. Of the 7 eyes requiring glaucoma surgery for open-angle glaucoma, 5 occurred within the first year following cataract removal. At the 5-year follow-up, these 7 eyes had mean (SD) IOP of 18.3 (3.9) mm Hg, with 4 taking glaucoma medication.

Glaucoma and Ocular Parameters at the Follow-up at Age 5 Years

The IOP at approximately age 5 years was available for 112 patients. Mean (SD) IOP was similar in eyes diagnosed as either having glaucoma (n = 19) or glaucoma suspect (n = 16; 20.2 [6.5] mm Hg vs 21.6 [4.5] mm Hg, respectively) and different from the eyes with neither diagnosis (n = 77; 16.8 [3.9] mm Hg) ($P < .01$ for both comparisons). The mean (SD) axial length at the age 5 follow-up visit was significantly longer in eyes with glaucoma (n = 13; 23.3 [2.0] mm) than those diagnosed as neither having glaucoma nor glaucoma suspect (n = 72; 21.4 [1.6] mm; $P = .001$); eyes diagnosed as glaucoma suspects (n = 12) had mean (SD) axial length of 22.0 (2.2) mm, not different from the means of either of the other 2 groups.

Glaucoma and Visual Acuity

Median visual acuity at age 4.5 years was 20/283 in eyes with glaucoma (n = 20), 20/141 in eyes with glaucoma suspect (n = 16), and 20/100 in eyes with neither diagnosis (n = 76); these 3 groups were not statistically different ($P = .13$). Results according to visual acuity categories are provided in eTable 4 in the Supplement.

Discussion

Glaucoma developed in the operated on eyes of 20 of 113 infants (18%) with unilateral cataract enrolled in the IATS by age 5 years; an additional 16 eyes were glaucoma suspects, for a total of 36 operated on eyes (32%) with glaucoma + glaucoma suspect diagnosis. The risk for developing glaucoma increased in both the CL and IOL groups between 1 and 4.8 years after cataract surgery (from 5% to 14% and from 12% to 19%, respectively), as did the risk for glaucoma + glaucoma suspect diagnosis (from 9% to 34% and from 16% to 28%, respectively). Of the 13 additional cases of glaucoma suspect diag-

Table 2. Baseline Characteristics of Children in the Infant Aphakia Treatment Study vs Development of Glaucoma and Glaucoma+Glaucoma Suspect

Baseline Characteristic	Patients, No.	Events, No. (%)	Probability, % (95% CI)[a]		*P* Value[b]	Hazard Ratio (95% CI)[c]
			By 1 y	By 4.8 y		
Glaucoma						
Age strata, d						
28-48	50	14 (28)	16 (8-29)	26 (16-41)	.01	3.2 (1.2-8.3)
49-210	64	6 (9)	3 (1-12)	9 (4-20)		
PFV						
No	90	13 (14)	7 (3-14)	13 (8-22)	.08	2.2 (0.9-5.5)
Yes	24	7 (29)	17 (7-39)	29 (15-52)		
Corneal diameter, mm[d]						
≤10	45	11 (24)	13 (6-27)	22 (13-38)	.13	1.9 (0.8-4.7)
>10	69	9 (13)	6 (2-15)	13 (7-24)		
IOP, mm Hg						
<12[e]	57	12 (21)	12 (6-24)	19 (11-32)	.28	0.6 (0.3-1.5)
≥12	57	8 (14)	5 (2-15)	14 (7-26)		
Glaucoma + Glaucoma Suspect						
Age strata, d						
28-48	50	23 (46)	18 (10-32)	45 (32-60)	.006	2.5 (1.3-5.0)
49-210	64	13 (20)	8 (3-18)	21 (13-34)		
PFV						
No	90	26 (29)	10 (5-18)	28 (20-39)	.24	1.5 (0.7-3.2)
Yes	24	10 (42)	21 (9-43)	43 (26-65)		
Corneal diameter, mm[d]						
≤10	45	22 (49)	20 (11-35)	50 (36-65)	.001	2.9 (1.5-5.7)
>10	69	14 (20)	7 (3-17)	20 (12-32)		
IOP, mm Hg						
<12[e]	57	15 (26)	16 (9-28)	27 (17-41)	.30	1.4 (0.7-2.8)
≥12	57	21 (37)	9 (4-20)	35 (24-49)		

Abbreviations: IOP, intraocular pressure (at time of cataract removal); PFV, persistent fetal vasculature (diagnosed at the time of cataract removal).

[a] The product limit estimate (95% CI) of the cumulative probability of the adverse event.

[b] The *P* value for the log-rank test comparing the Kaplan-Meier curves of the 2 categories of each characteristic.

[c] The hazard ratio estimated from a proportional hazards regression model, with the characteristic as the only factor in the model. The relative categories are age (28-48 days vs 49-210 days), PFV (yes vs no), corneal diameter (≤10 mm vs >10 mm), and IOP (≥12 mm Hg vs <12 mm Hg).

[d] Measured using calipers during examination under anesthesia prior to randomization.

[e] The median for IOP at baseline among all 114 patients was 11.75 mm Hg.

nosed between the 1 year postoperative and age 5 visits, 10 were in the CL group; these differences by treatment group were not statistically significant. Additionally, we noted a relative lull in the diagnosis of glaucoma + glaucoma suspect diagnoses between 1 and 3 years postcataract removal. However, the IATS protocol only required IOP assessment at examination at 1 year old under anesthesia and the visits at ages 4, 4.5, or 5, so surveillance bias was possible.

While most retrospective studies of glaucoma following cataract removal in infancy have lacked uniform diagnostic criteria for that complication, the 17% chance of glaucoma by 4.8 years after surgery in the IATS is consistent with other studies,[5,6] including a meta-analysis reporting glaucoma in 80 of 470 eyes (17%) after cataract surgery at a median age of 3 months, with median onset 4.3 years postsurgery.[19] Despite varying definitions of *glaucoma* used in published studies, it is clear that a significant percentage of children undergoing congenital cataract surgery develop glaucoma (or at least elevated IOP), usually with open angles, and the onset of glaucoma frequently occurs years after cataract surgery.[1,2,6,7,22]

Numerous mechanisms for the development of glaucoma after cataract removal in infancy have been postulated.[2,6,7,9-11,18,22-25] Because the IATS was not designed to investigate the mechanism of glaucoma-related adverse events, we could not differentiate among various proposed mechanisms of open-angle glaucoma but confirmed that modern surgical techniques do not eliminate this complication.[2,14]

There is controversy surrounding the possible protective effect of primary IOL implantation (vs aphakia) against glaucoma after cataract removal in infancy, with published reports both supporting[18,19] and failing to demonstrate this protective effect.[10,11] Trivedi et al[10] noted that all glaucoma cases occurred in eyes having cataract surgery in the first 4.5 months of life, with similar rates in aphakic vs pseudophakic eyes (19% vs 24%, respectively). Mataftsi and colleagues[19] noted a protective effect of primary IOL vs aphakia in their large meta-

analysis (HR, 0.1; P = .02); however, eyes were not randomized to primary IOL vs aphakia, and a consistent definition of glaucoma was not applied. The IATS—by virtue of its randomization and prospective design—lacks the potential bias of prior nonrandomized studies.[14] Neither glaucoma nor glaucoma + glaucoma suspect diagnoses were statistically different between pseudophakic and aphakic eyes at the 1-year follow-up.[13] We report an increase in both glaucoma and glaucoma suspect cases by the visit at age 5 in the IATS but no statistically significant difference in either complication by treatment group (IOL vs CL). Continued follow-up will be critical to more definitively answer the question of the possible protective effect of primary IOL placement, especially because reported onset of glaucoma occurs at a mean 4 to 5 years after cataract removal.[6,7,19,23]

Standard definitions of *glaucoma* and *glaucoma suspect* were developed and uniformly applied for surveillance and diagnosis of eyes within the IATS, with the former requiring not only elevated IOP, but also associated structural changes in the infant eye or need for glaucoma surgery.[13] Many prior studies have defined *glaucoma* solely by elevated IOP or by the physician's decision to start treatment,[19] without including secondary structural change among the diagnostic criteria.[2,6,7,23] The importance of a uniformly accepted definition of *glaucoma* as well as *glaucoma suspect* will facilitate future research and comparison among different published works.[26] The definitions of *glaucoma* and *glaucoma suspect* developed for the IATS[13] were adopted by the World Glaucoma Association consensus group.[26]

Among various risk factors previously evaluated for the development of glaucoma following cataract surgery in children, young age at surgery has been frequently identified.[10,27-29] Younger patient age at surgery (28-48 vs 49-210 days old) was also noted as a risk factor for the development of a glaucoma-related adverse event in the IATS at 1 year,[13] despite deferring cataract surgery until at least age 4 weeks based on previous studies suggesting increased glaucoma risk if surgery is performed in the first 4 weeks of life.[27,30] At the visit at age 5 years, children in the younger age strata (28-48 vs >48 days old) at cataract surgery were again noted to be at higher risk for developing glaucoma and glaucoma-related adverse events.

Multivariate analysis (considering age at surgery, corneal diameter, presence of PFV, and IOP at surgery) showed that only younger age at surgery increased the risk for developing glaucoma (by 3.2 times); only smaller corneal diameter at surgery (≤10 mm vs >10 mm) increased the risk for developing glaucoma + glaucoma suspect (by 2.9 times). This was not unexpected because young age at surgery and smaller corneal diameter were highly correlated. Because eyes with severe PFV were excluded from the IATS, it is not surprising that this feature was not noted to confer additional risk for glaucoma + glaucoma suspect diagnosis by 5 years. Evaluation of the relationship between visual acuity at 4.5 years of age and age at surgery in the IATS (28-48 vs 49-210 days at surgery) revealed median visual acuity was significantly better for eyes operated on younger vs older (0.50 vs 1.10 logMAR [Snellen equivalent, 20/63 vs 20/250]; P = .046).[31] Therefore, the desire to achieve maximum visual acuity must be counterbalanced against an increased risk for glaucoma or glaucoma suspect diagnosis in an infant with a unilateral congenital cataract.

As expected, based on the definitions of *glaucoma* and *glaucoma suspect* in the IATS, eyes with these diagnoses had higher maximum recorded IOP than those without them by the visit at age 5 years. The optic nerves showed a larger CD ratio in eyes with glaucoma than those with glaucoma suspect or without either diagnosis; the axial length was longer in eyes with glaucoma than in eyes with glaucoma suspect or without a glaucoma-related adverse event, consistent with the IOP-related structural changes required to diagnose glaucoma in the IATS.

Glaucoma following removal of a childhood cataract may require surgical treatment or remain medically controlled for some time, depending on its severity. Hence, surgical treatment was performed in 57% of 170 eyes with aphakic glaucoma in the large retrospective series by Chen et al,[23] while Bhola et al[32] noted surgical intervention in only 15 of 55 eyes (27%). At 1 year, 60% of eyes with glaucoma in the IATS received surgical intervention.[13] By the 5-year visit, glaucoma medications had been used in 19 of 20 eyes (95%) diagnosed as having glaucoma and 12 of 16 (75%) diagnosed as glaucoma suspects. Surgery had been performed in 8 eyes, 1 for angle-closure glaucoma (with initial control but later retinal detachment and phthisis). Five of 7 eyes with open-angle glaucoma requiring surgery by 5 years old had that surgery in the first year after cataract removal, and they have remained controlled (eTable 3 in the Supplement). Surgery performed in the 7 eyes with open-angle glaucoma included trabeculotomy, glaucoma drainage implantation, and endoscopic diode cyclophotocoagulation, reflecting lack of uniform initial surgery chosen by different surgeons for this type of glaucoma.[26]

Visual acuity in children who develop glaucoma following congenital cataract surgery may be limited by glaucomatous optic nerve damage, amblyopia, pupillary membranes, corneal decompensation, or complications from glaucoma surgery. At the 5-year visit, the visual acuity differences between those eyes with vs without glaucoma did not reach statistical significance, perhaps owing to the small sample size of each group; reduced visual acuity may nonetheless develop in the glaucoma group with longer follow-up.

Limitations of this study included the relatively small sample size of the entire cohort (reducing power to adequately assess some factors), intermediate follow-up of 4.8 years following cataract surgery, and lack of study-related treatment protocols for glaucoma-related adverse events. In addition, we could not evaluate IOL position as a risk factor for glaucoma-related adverse events because most eyes had in-the-bag IOLs.[33] We also could not separate out the influence of additional intraocular surgery because glaucoma-related adverse events likely affected timing of nonurgent additional surgical procedures. This study's strengths included its prospective design with randomization to primary IOL implantation vs aphakia, as well as standardized definitions of *glaucoma* and *glaucoma suspect*.

Conclusions

Planned follow-up data at age 10 years for all IATS participants should provide additional important information about risk factors for the development of glaucoma and the effect of glaucoma on visual outcomes in patients with unilateral cataract. They may also help better delineate potential differences in glaucoma severity and treatment success between eyes in the IOL and CL study groups.

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