

Glaucoma-Related Adverse Events at 10 Years in the Infant Aphakia Treatment Study

A Secondary Analysis of a Randomized Clinical Trial

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[+ Supplemental content](#)

IMPORTANCE Glaucoma-related adverse events constitute serious complications of cataract removal in infancy, yet long-term data on incidence and visual outcome remain lacking.

OBJECTIVE To identify and characterize incident cases of glaucoma and glaucoma-related adverse events (glaucoma + glaucoma suspect) among children in the Infant Aphakia Treatment Study (IATS) by the age of 10.5 years and to determine whether these diagnoses are associated with optic nerve head (ONH) and peripapillary retinal nerve fiber layer (RNFL) assessment.

DESIGN, SETTING, AND PARTICIPANTS Analysis of a multicenter randomized clinical trial of 114 infants with unilateral congenital cataract who were aged 1 to 6 months at surgery. Data on long-term glaucoma-related status and outcomes were collected when children were 10.5 years old (July 14, 2015, to July 12, 2019) and analyzed from March 30, 2019, to August 6, 2019.

INTERVENTIONS Participants were randomized at cataract surgery to either primary intraocular lens (IOL), or aphakia (contact lens [CL]). Standardized definitions of glaucoma and glaucoma suspect were created for IATS and applied for surveillance and diagnosis.

MAIN OUTCOMES AND MEASURES Development of glaucoma and glaucoma + glaucoma suspect in operated-on eyes up to age 10.5 years, plus intraocular pressure, axial length, RNFL (by optical coherence tomography), and ONH photographs.

RESULTS In Kaplan-Meier analysis, for all study eyes combined (n = 114), risk of glaucoma after cataract removal rose from 9% (95% CI, 5%-16%) at 1 year, to 17% (95% CI, 11%-25%) at 5 years, to 22% (95% CI, 16%-31%) at 10 years. The risk of glaucoma plus glaucoma suspect diagnosis after cataract removal rose from 12% (95% CI, 7%-20%) at 1 year, to 31% (95% CI, 24%-41%) at 5 years, to 40% (95% CI, 32%-50%) at 10 years. Risk of glaucoma and glaucoma plus glaucoma suspect diagnosis at 10 years was not significantly different between treatment groups. Eyes with glaucoma (compared with eyes with glaucoma suspect or neither) had longer axial length but relatively preserved RNFL and similar ONH appearance and visual acuity at age 10 years.

CONCLUSIONS AND RELEVANCE Risk of glaucoma-related adverse events continues to increase with longer follow-up of children following unilateral cataract removal in infancy and is not associated with primary IOL implantation. Development of glaucoma (or glaucoma suspect) after removal of unilateral congenital cataract was not associated with worse visual acuity outcomes at 10 years.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: [NCT00212134](#)

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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 retrospective¹⁻¹² and several prospective studies.¹³⁻¹⁸ The Infant Aphakia Treatment Study (IATS), a multicenter, randomized, controlled clinical trial sponsored by the National Eye Institute, compared outcomes of surgery for unilateral cataract with or without primary intraocular lens (IOL) implantation in infants between ages 1 and 6 months.¹⁷⁻²³

The effect of primary IOL implantation at cataract surgery in very young children has been difficult to evaluate, owing largely to the paucity of randomized trials. Five-year results of IATS¹⁸ found similar rates of glaucoma-related adverse events with and without primary IOL implantation, as did a randomized trial of primary IOL vs aphakia for bilateral cataracts operated on in children younger than 2 years.¹⁴ To our knowledge, longer-term rates and outcomes of glaucoma-related adverse events following cataract surgery in infants randomized to primary IOL or aphakia are lacking.

Optic nerve head (ONH) photographs are an established means of evaluating for glaucomatous damage.²⁴ Spectral-domain optical coherence tomography (SD-OCT) has proven invaluable for evaluating and treating adults with glaucoma and can even predict among those with glaucoma suspect those eyes at higher risk for developing visual field loss.^{25,26} In children, peripapillary retinal nerve fiber layer thickness (RNFL) assessed by SD-OCT²⁷ has been shown to be effective in differentiating between normal and glaucomatous eyes.^{28,29}

In this study, we report 10-year results of the development of glaucoma-related adverse events in IATS participants, considering original treatment group (primary IOL vs contact lens [CL]) and previously identified risk factors, as well as ONH health (RNFL by SD-OCT and masked reading of ONH photographs).

Methods

The IATS design, eligibility criteria, surgical technique, follow-up schedule, patching and optical correction regimens, evaluation methods, and patient characteristics at baseline have been previously reported.¹⁹ This study was approved by each participating site's institutional review board, and written informed consent was obtained for each participating child. The definitions for glaucoma, glaucoma suspect, and glaucoma-related adverse events (glaucoma + glaucoma suspect) were established and applied, as previously reported (eTable 1 in the [Supplement](#)),^{17,18} and management was at treating physician's discretion. The originally designed IATS study concluded 5 years following cataract removal. No IATS visits occurred between ages 5 years and 10 years, other than standard of care determined by the treating physicians.

Funding and approval were obtained to recall children enrolled into IATS for a detailed follow-up examination at a mean (SD) age of 10.5 years (3 months) (hereafter referred to as the 10-year examination, meaning approximately 10 years after

Key Points

Question What is the 10-year cumulative incidence of glaucoma and glaucoma suspect after removal of unilateral cataract in infancy in the Infant Aphakic Treatment Study, and how is the retinal nerve fiber layer and optic nerve head appearance affected?

Findings In this secondary analysis of a randomized clinical trial, risk of glaucoma and glaucoma plus glaucoma suspect diagnosis at 10 years rose to 22% and 40%, respectively, with no difference between treatment groups (primary intraocular lens vs aphakia). Eyes with glaucoma (vs glaucoma suspects or neither) had relatively preserved retinal nerve fiber layer, similar optic nerve head appearance, and visual acuity.

Meaning The results of this study support the need for lifelong surveillance for glaucoma and glaucoma-related events following cataract removal in infancy.

cataract removal). Spectral-domain OCT RNFL imaging and ONH photography were performed; all ONH photographs were graded in a standardized fashion by 3 expert examiners (eAppendix; eFigures 5 and 6 in the [Supplement](#)). Information on statistical analysis can also be found in the eAppendix in the [Supplement](#). A significance level of .05 was used in statistical inference-making, except where otherwise stated, and hypothesis tests were 2-sided.

Results

Development of Glaucoma

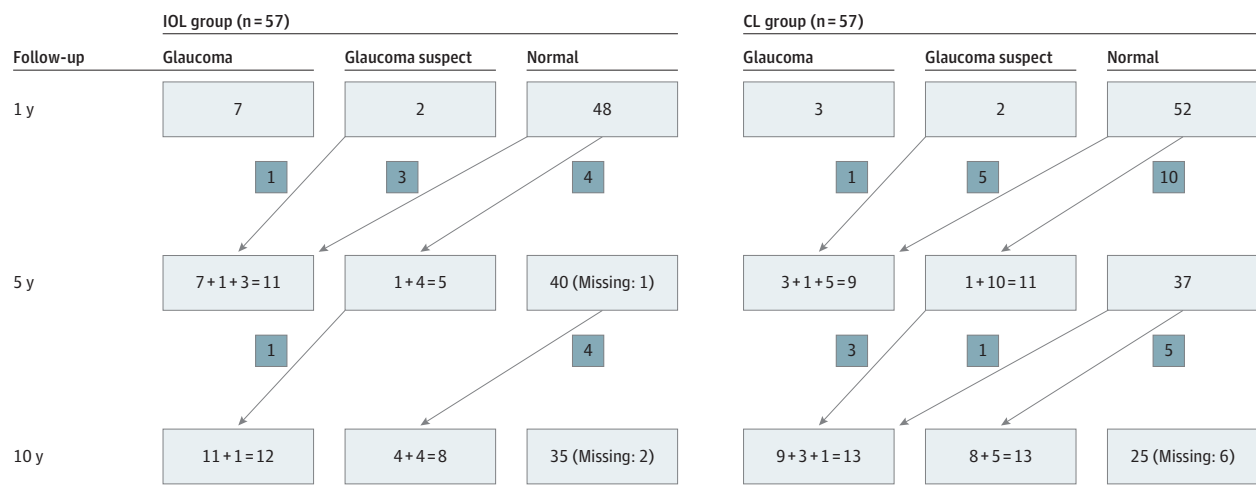
The IATS randomized 114 infants (57 each to CL and IOL); 110 (96.5%) completed clinical examination at age 10.5 years (mean [SD] age 10.6 [0.3] years; n = 55 for each group), with mean postsurgical follow-up of 10.4 years (range, 9.3-11.5); 2 participants in each group were lost to follow-up. Details of the 10.5-year testing times, CONSORT diagram for recruitment, and visual acuity results¹⁹ have been published. Glaucoma status at the 10-year examination was available for 106 participants (55 IOL and 51 CL).

By the 10-year examination, 25 eyes (23%) had developed glaucoma, and 21 eyes (20%) had glaucoma suspect (46 eyes total [43%] glaucoma + glaucoma suspect). The CL group had 13 eyes (25%) with glaucoma and 13 (25%) were glaucoma suspects. The IOL group had 12 eyes (22%) with glaucoma, and 8 (15%) were glaucoma suspect ([Figure 1](#)).

Of the 5 new glaucoma cases that were detected between the 5-year and the 10-year examinations, 4 were previously glaucoma suspect, and 1 was normal. There were 9 new glaucoma suspect cases at the 10-year follow-up ([Figure 1](#)).

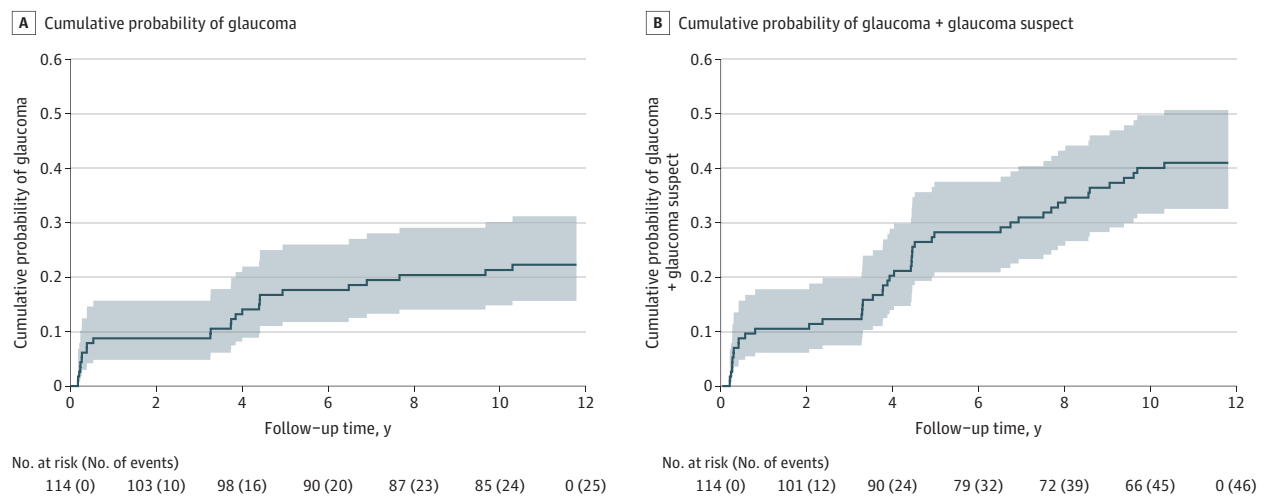
In Kaplan-Meier analysis, for all study eyes combined, risk of glaucoma after cataract removal rose from 9% (95% CI, 5%-16%) at 1 year to 17% (95% CI, 11%-25%) at 5 years to 22% (95% CI, 16%-31%) at 10 years ([Figure 2A](#)). The risk of glaucoma + glaucoma suspect diagnosis after cataract removal rose from 12% (95% CI, 7%-20%) at 1 year to 31% (95% CI, 24%-41%) at 5 years to 40% (95% CI, 32%-50%) at 10 years ([Figure 2B](#)).

Figure 1. Number of IATS Participants Diagnosed as Having Glaucoma, Glaucoma Suspect, or Normal at 1, 5, and 10 Years After Surgery in the Intraocular Lens (IOL) and Contact Lens (CL) Groups



Arrows indicate the number of participants with changes in status from 1 point to the next. Where there is more than 1 number in a box, the leftmost number is the number of participants whose status did not change from the previous point, and number that is added represents changes in status from the previous point to the current point.

Figure 2. Kaplan-Meier Curves Showing Cumulative Probability of Glaucoma (A) and Glaucoma + Glaucoma Suspect (B) vs Time (in Years) Since Cataract Surgery for 114 Study Participants



The shading denotes 95% confidence intervals for the cumulative probability. The numbers of participants at risk and the cumulative numbers of events are shown below the x-axis. The 10-year cumulative probability was 22% (95%

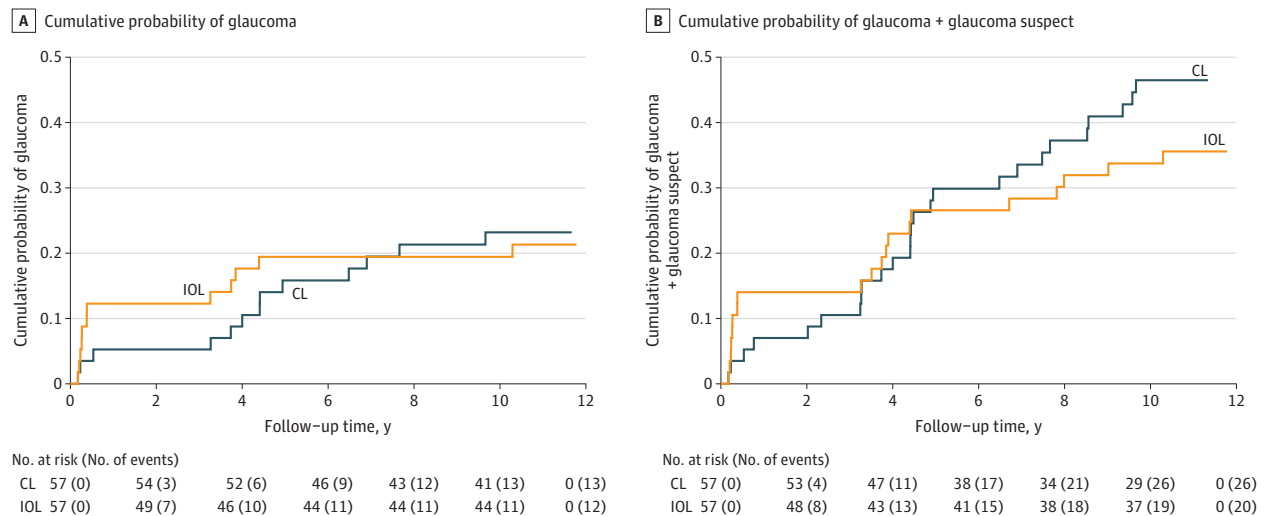
CI, 16%-31%) for glaucoma and 40% (95% CI, 32%-50%) for glaucoma + glaucoma suspect.

Kaplan-Meier curves for developing glaucoma after cataract removal were not significantly different between the CL and IOL treatment groups (Figure 3A) (hazard ratio [HR], 1.0; 95% CI, 0.5-2.3; $P = .94$), with the 10-year risk in the CL and IOL groups at 23% (95% CI, 14%-37%) and 21% (95% CI, 13%-35%), respectively. Kaplan-Meier curves for developing glaucoma + glaucoma suspect diagnosis after cataract removal were also not significantly different between the treatment groups (Figure 3B) (HR, 1.3; 95% CI, 0.7-2.4; $P = .36$), with the 10-year risk in the CL and IOL groups at 46% (95% CI, 34%-60%) and 36% (95% CI, 25%-50%), respectively.

Influence of Baseline Characteristics of Enrolled Children/Study Eyes

The associations between glaucoma at the 10-year examination and treatment group (CL vs IOL), age at surgery (age ≤ 48 days vs >48 days), persistent fetal vasculature, corneal diameter (≤ 10 mm vs >10 mm), and intraocular pressure (IOP) (≥ 12 mm Hg vs <12 mm Hg) at baseline were examined using a multivariable proportional hazards regression model. After controlling for age, the other terms were not significant. The risk of glaucoma was greater for younger age at surgery (adjusted HR, 3.2; 95% CI, 1.2-8.2) (eTable 2 in the Supplement).

Figure 3. Kaplan-Meier Curves Showing the Cumulative Probability of Glaucoma (A) and Glaucoma + Glaucoma Suspect (B) vs Time (in Years) Since Cataract Surgery for the Contact Lens (CL) and Intraocular Lens (IOL) Groups (57 Participants in Each Group)



The numbers of participants at risk and the cumulative numbers of events are shown below the x-axis. At 10.5 years, the cumulative probability of glaucoma was 23% (95% CI, 14%-37%) for the CL group and 21% (95% CI, 13%-35%) for

the IOL group. The 10-year cumulative probability of glaucoma + glaucoma suspect was 46% (95% CI, 34%-60%) for the CL group and 36% (95% CI, 25%-50%) for the IOL group.

The risk of glaucoma + glaucoma suspect was greater for smaller corneal diameter at surgery (adjusted HR, 2.0; 95% CI, 1.1-3.8) (eTable 2 in the Supplement).

Glaucoma Characteristics, Treatment, and Outcomes

Diagnostic Criteria for Diagnosis

The glaucoma and glaucoma suspect diagnoses at 10 years were PI determined via application of rigorous definitions. Among the 5 eyes newly diagnosed as having glaucoma between the 5-year and the 10-year examinations, 3 showed IOP greater than 21 mm Hg with optic nerve head changes, and 2 had glaucoma surgery. Among the 9 eyes diagnosed as glaucoma suspect between the 5-year and 10-year examinations, all reported IOP greater than 21 mm Hg and 2 were receiving glaucoma medications.

Glaucoma Treatment

At the 10-year examination, 12 of 25 (48%) eyes with glaucoma were in patients reportedly taking glaucoma medications, as were 9 eyes with glaucoma suspect diagnosis (of 18 with available information). Between the 5-year and 10-year examinations, 4 eyes had glaucoma surgery. Of 25 eyes with glaucoma by the 10-year examination, 11 eyes underwent glaucoma surgery, cumulatively; 7 (64%) required a single surgery. Glaucoma surgical procedures performed (eTable 3 in the Supplement) included trabeculotomy, glaucoma drainage implant, endocyclophotocoagulation, trabeculectomy, and peripheral iridectomy. A single eye with presumed angle-closure glaucoma (after surgical iridectomy) developed retinal detachment and ultimately phthisis bulbi prior to the 5-year examination.¹⁸

Glaucoma and Ocular Parameters at the 10-Year Follow-up

There were no significant differences in mean (SD) IOP of eyes diagnosed as having glaucoma (n = 25; 19.0 [5.9] mm Hg), glau-

coma suspect (n = 20; 19.5 [4.2] mm Hg), and with neither diagnosis (n = 60; 16.9 [3.7] mm Hg) (eFigure 1 in the Supplement). Mean (SD) axial length for eyes with glaucoma (n = 22), glaucoma suspect (n = 19), and neither diagnosis (n = 60) was 24.8 (2.4), 23.3 (1.9), and 22.8 (2.2) mm, respectively. Eyes with glaucoma were significantly longer than those with neither diagnosis (95% Tukey-Kramer-adjusted CI, 0.7-3.3 mm); mean axial lengths were similar for glaucoma vs glaucoma suspect and glaucoma suspect vs neither diagnosis (eFigure 2 in the Supplement).

Glaucoma Status and Secondary IOL

There was no association between secondary IOL placement and glaucoma status (eAppendix in the Supplement).

Glaucoma Status and Visual Acuity and Refraction

Median visual acuity at the 10-year examination in eyes with glaucoma was 0.9 logMAR (Snellen equivalent 20/160; n = 25, interquartile range [IQR], 0.1-2.9); in eyes with glaucoma suspect was 0.9 (n = 19; IQR, 0.2-1.7); and in normal eyes was also 0.9 (n = 60; IQR, 0-2.7). For the entire treated cohort at 10 years, median visual acuity was 0.55 logMAR (Snellen equivalent 20/70; n = 50; IQR, 0.2-1.5) when age at surgery was 28 to 48 days vs 1.1 logMAR (Snellen equivalent 20/250; n = 58; IQR, 0.7-1.4) for older age at surgery (P = .03). Mean refraction was similar between eyes with glaucoma, glaucoma suspect, or neither (eAppendix and eFigure 3 in the Supplement).

Optic Nerve Head Imaging

Optical coherence tomography peripapillary RNFL imaging was attempted for every patient at the 10-year examination, obtained in 97 of 110 (88.2%), and adequate for reading in 75 treated and 85 fellow eyes. Among treated eyes with readable

Table. Retinal Nerve Fiber Layer Optical Coherence Tomography Quality and Thickness Measurements vs 10-Year Glaucoma Status

RNFL (quality and thickness)	P value comparing group means ^a	Mean (SD) [range]		
		Glaucoma (n = 15)	Glaucoma suspect (n = 13)	Neither (n = 44)
Image quality, 1-40 dB	.77	28.0 (5.9) [20.0-40.0]	27.0 (6.9) [15.0-37.0]	26.7 (5.9) [14.0-37.0]
Overall, μm	.08	93.3 (18.1) [55.0-128.0]	104.2 (12.7) [87.0-126.0]	103.5 (15.4) [63.0-145.0]
Nasal, μm	.80	74.8 (18.4) [36.0-103.0]	76.4 (22.6) [45.0-113.0]	79.1 (20.4) [42.0-129.0]
Nasal inferior, μm	.06	96.3 (27.5) [56.0-153.0]	105.7 (32.3) [55.0-161.0]	121.8 (41.1) [63.0-274.0]
Nasal superior, μm	.36	100.1 (31.9) [39.0-159.0]	111.8 (29.8) [71.0-150.0]	113.2 (30.3) [56.0-195.0]
Temporal, μm	.08	75.1 (16.6) [52.0-107.0]	87.8 (15.4) [68.0-115.0]	78.7 (14.9) [55.0-118.0]
Temporal inferior, μm	.20	133.1 (33.1) [68.0-191.0]	147.5 (28.8) [66.0-192.0]	147.1 (23.5) [100.0-206.0]
Temporal superior, μm	.08	117.2 (33.4) [43.0-177.0]	136.5 (23.3) [82.0-169.0]	134.1 (24.8) [83.0-187.0]

Abbreviation: RNFL, retinal nerve fiber layer.

^a For each RNFL measurement, a 1-way fixed-effects analysis of variance *F* test was performed to compare the 3 group means.

images, there was no significant difference ($P = .08$ in overall mean RNFL for eyes with glaucoma [$n = 15$], glaucoma suspect [$n = 13$], or neither [$n = 44$]: mean [SD] 93.3 [18.1] μm ; range, 55-128; 104.2 [12.7] μm ; range, 87-126; and 103.5 [15.4] μm ; range, 63-145; respectively) (Table); quadrant and sectoral RNFL thickness were not significantly different. Paired (fellow vs treated eyes) differences in OCT RNFL thickness were examined and stratified by glaucoma, glaucoma suspect, and neither categories; no statistically significant differences were found (eTable 4 in the Supplement). There were 12 cases where the glaucomatous eye had thinner RNFL compared with the fellow eye (individual data not shown); one representative case is detailed (eFigure 4A and B in the Supplement).

Optic nerve head photographs were obtained in 104 of 110 treated eyes (95%); 94 were adequate for grading (3 of 3 graders agreed in 91 cases). Of ONH photographs graded, 82 of 94 (87%) were classified as "normal," with agreement in 3 of 3 readers for 79 of these 82 eyes (96%); 7 of 94 (7%) were classified as glaucoma suspect (3 of 3 graders agreed in all 7 cases); and 5 of 94 (5%) were classified as glaucoma (3 graders agreed on 4 eyes; 1 grader found the remaining eye imaging inadequate).

There was slight/fair agreement between the clinical diagnoses of glaucoma/glaucoma suspect/neither by IATS criteria vs the diagnosis made based on ONH reading (κ , 0.29; 95% CI, 0.12-0.46) (eTable 5 in the Supplement). While 58 of 60 eyes (97%) that were normal (neither glaucoma nor glaucoma suspect by IATS clinical criteria) had ONH photographs graded normal, only 2 of 15 eyes (13%) with clinical glaucoma suspect diagnosis had matching ONH grading (the rest being read as normal), and 4 of 19 eyes (21%) with clinical glaucoma diagnosis had matching ONH grading (with 4 of 19 suspect and 11 of 19 normal). Because ONH photographs were not available prior to the 10-year examination, information on ONH cupping reversal in eyes whose elevated IOP was successfully controlled is unavailable.

Among 20 eyes with glaucoma (by IATS criteria) and adequate ONH photographs, RNFL imaging was available for 13. There was no difference in RNFL parameters for ONH photo-

graphs graded as glaucoma vs glaucoma suspect vs neither (eTable 6 in the Supplement; representative case Figure 4A and B).

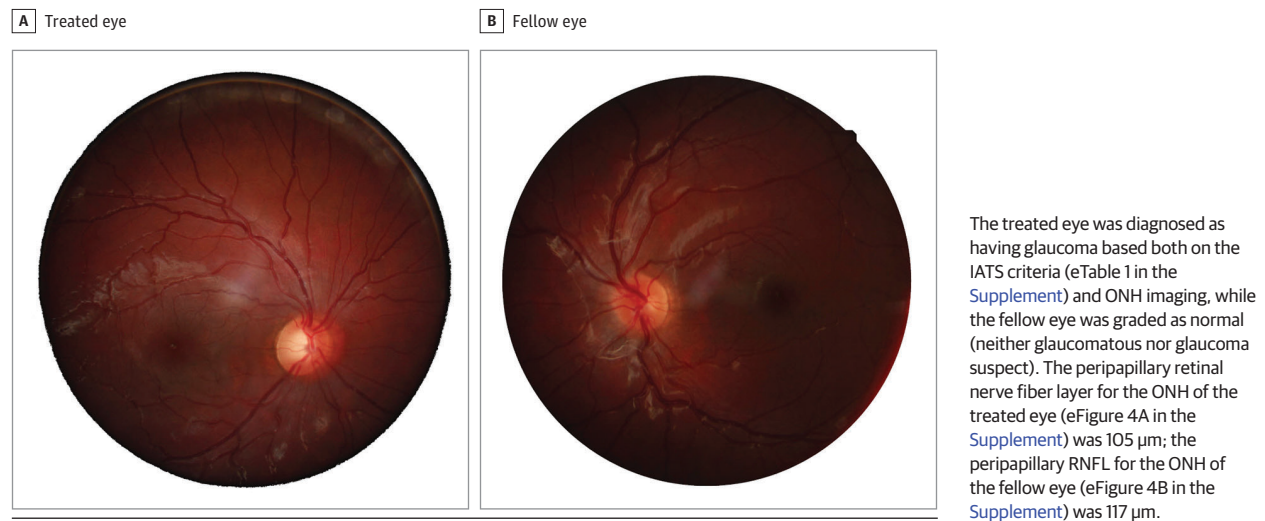
Discussion

Glaucoma developed in the operated-on eyes of 25 of 110 infants (23%) with unilateral cataract enrolled in the IATS by age 10.5 years; an additional 21 eyes were glaucoma suspects, for a total 46 operated-on eyes (40%) with glaucoma + glaucoma suspect diagnosis. The risk of developing glaucoma rose similarly in both CL and IOL groups between 5 and 10 years after cataract surgery, as did the risk of glaucoma + glaucoma suspect diagnosis. Because the IATS protocol required IOP assessment only at the 1-year examination under anesthesia and the 4-year, 4.5-year, or 5-year visits and again at the 10-year visit, the IATS protocol precludes any comment on the annualized rate of conversion to glaucoma suspect and glaucoma among treated eyes.

Five-year follow-up from the only other randomized clinical trial of primary IOL vs aphakia, in this case for bilateral congenital cataracts removed before age 2 years, using similar diagnostic criteria,¹⁴ found similar rates of glaucoma between the pseudophakic and aphakic eyes (16% vs 14%, respectively), with most having cataract surgery at younger than 6 months, and most cases occurring in the first year following surgery. We are not aware of any other prospective study with 10-year follow-up that also used uniform definitions of glaucoma and glaucoma suspect and that randomized eyes receiving primary IOL implantation vs remaining aphakic.

The question of whether primary IOL implantation affects the risk of glaucoma or glaucoma suspect development following cataract removal in infancy has been addressed by many retrospective studies^{1-12,30-34} and some prospective but nonrandomized studies,^{13,15,16} all subject to some degree of selection bias. The IATS, by virtue of its random assignment, prospective design, and excellent participant retention rate, lacks the corresponding bias of prior nonrandomized studies.¹⁹

Figure 4. Examples of Optic Nerve Head (ONH) Images for the Treated (A) and Fellow Eye (B) of the Same Infant Aphakia Treatment Study (IATS) Participants Whose ONH Optical Coherence Tomography Images Are Shown in eFigure 4A and B in the Supplement



As we reported at 1-year and 5-year follow-up times,^{17,18} we now report similar but rising rates of glaucoma and glaucoma + glaucoma suspect diagnoses in each treatment group (IOL vs CL) at 10 years following surgery. In their prospective randomized study of primary IOL placement vs aphakia (for bilateral congenital cataracts), Vasavada et al¹⁴ similarly noted no difference in glaucoma cases between groups, at 1 year or 5 years after cataract removal.

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.^{17,18} The definitions of glaucoma and glaucoma suspect developed for IATS¹⁷ were adopted by the international consensus group.³⁵

Among various risk factors previously evaluated for the development of glaucoma following cataract surgery in children, young age at surgery has been frequently identified.^{11,12,14,15,32,36} Younger patient age at surgery (ages 28-48 days vs 49-210 days) was also noted as a risk factor for the development of a glaucoma-related adverse event in the IATS at 1 year and 5 years following cataract removal^{17,18}; in multivariate analysis, it remains the strongest and only independent risk factor for glaucoma 10 years after surgery. For development of any glaucoma-related adverse event at 10 years, small corneal diameter at surgery, closely related to age at surgery,¹⁸ emerged as the only risk factor. Secondary IOL was not significantly associated with glaucoma-related adverse events in the CL group at 10 years, although numbers were small, and there may be selection bias favoring the group of eyes that did receive secondary IOL surgery.

While there was a wide range of visual acuity outcomes at 10 years in the IATS,²³ mean visual acuity was similar among eyes with glaucoma, glaucoma suspect, and neither diagnosis. As was the case at 5 years,³⁷ those children having earlier vs later surgery (28-48 vs 49-210 days) had better median acu-

ity. Therefore, the desire to achieve maximum visual acuity must be counterbalanced against an increased risk of glaucoma or glaucoma suspect diagnosis in an infant with a unilateral congenital cataract.

Eyes diagnosed with glaucoma at 10 years after cataract removal in the IATS had longer axial lengths than those with glaucoma suspect or neither diagnosis (in keeping with the requirement for anatomic changes for glaucoma diagnosis), but similar IOP, refraction, and visual acuity. Ours is the only prospective study of glaucoma-related adverse events following cataract surgery in infancy that included an attempt to evaluate the optic nerve status with OCT and masked grading of ONH photographs at the 10-year examination. Despite their age, adequate OCT imaging was not achieved in all treated or fellow eyes of participants. Perhaps reassuringly, the mean global RNFL thickness was similar among eyes with glaucoma, glaucoma suspect, and neither diagnosis, suggesting adequate glaucoma treatment to date. Pairwise comparison between treated and fellow eyes by glaucoma category did not yield meaningful differences. While there was excellent agreement among 3 masked graders of ONH photographs, most ONH photographs appeared normal even in eyes with the clinical IATS definitions of glaucoma and glaucoma suspect, again suggesting (along with similar 10-year mean IOP among glaucoma, suspect, and normal eyes) either reversal of cupping in eyes with glaucoma or adequate treatment to maintain a healthy-appearing ONH by photography. While ONH cupping reversal commonly occurs following IOP control in childhood glaucoma, glaucomatous damage to RNFL does not recover; therefore, the relatively normal RNFL in most glaucomatous eyes in IATS supports good glaucoma control.³⁸

While the IATS did not dictate clinical management of glaucoma following cataract surgery, it is interesting to note that by 10 years, glaucoma surgery had been performed in 11 of 25 eyes (48%) with glaucoma (7 requiring a single surgery by the 10-year examination). Trabeculotomy was the most com-

monly performed glaucoma surgery, followed by glaucoma drainage device implantation. One eye lost light perception (owing to retinal detachment prior to the 5-year report).¹⁸ Others have reported varying rates of glaucoma surgery for glaucoma following cataract surgery,^{14,39,40} likely influenced by patient characteristics and follow-up times. Medication use was reported in approximately 50% of eyes with glaucoma or glaucoma suspect at the 10-year examination.

Limitations

Limitations of this study include the relatively small sample size of the cohort (reducing power to adequately assess some factors), lack of study-related treatment protocols for glaucoma-related adverse events, and lack of required study follow-up between 5 and 10 years. We cannot suggest a mechanism for glaucoma-related adverse events nor make treatment recommendations. Additionally, we cannot comment about glaucoma-related adverse event risk in children older than 6 months at surgery, although a 2019 retrospective study⁴¹ addressed this issue and reported a much lower rate of glaucoma (no cases of glaucoma and 4% incidence of glaucoma suspect by 5 years).⁴¹ Similarly, while the IATS included only those with unilateral cataract, Vasavada et al¹⁴ report similar findings in a bilateral cohort with shorter follow-up.¹⁴ Finally, we can only report on the risk of developing glaucoma-related adverse events up to age 10.5 years; this risk would likely increase with longer follow-up. This study's strengths include its prospective design with randomization to primary IOL im-

plantation vs aphakia, standardized definitions of glaucoma and glaucoma suspect, long-term follow-up with excellent retention, and incorporation of anatomic features of ONH health including OCT and photography.

Conclusions

Risk of glaucoma-related adverse events continues to rise with longer follow-up of children following unilateral cataract removal in infancy and is not influenced by primary IOL implantation. Development of glaucoma (or glaucoma suspect) did not significantly affect visual acuity outcomes at 10 years after removal of unilateral congenital cataract. The RNFL and ONH photographic appearance (with good agreement among 3 expert masked graders) was relatively well preserved in eyes with glaucoma and glaucoma suspect diagnoses.

While it is clear that the risk of glaucoma and glaucoma + glaucoma suspect (with strict application of uniform definitions for both diagnoses) continues to rise over time after removal of unilateral cataract in infancy, we cannot predict, based on our data, whether some of these treated eyes will ultimately avoid developing glaucoma or glaucoma suspect. Lifelong surveillance for the development of glaucoma-related adverse events remains important, with the hope that early diagnosis and treatment may facilitate preservation of ONH health and maximal visual function.

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Contact Lens Committee: Buddy Russell, COMT; Michael Ward, MMSc.

Participating Clinical Centers (in order by the number of patients enrolled):

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Harvard University, Boston, Massachusetts: Deborah K. Vanderveen, MD; Theresa A. Mansfield, RN; Kathryn Biscaglia Miller, OD; Tamar Winter, RN, IBCLC.

University of Minnesota, Minneapolis,

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Cleveland Clinic, Cleveland, Ohio: Elias I.

Traboulsi, MD; Susan Crowe, BS, COT; Heather Hasley Cimino, OD. Case Western Reserve: Faruk Orge, MD; Megin Kwiatkowski; Beth Colon; Angela Meador, COA, MHA.

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Kimberly G. Yen, MD; Maria Castanes, MPH; Alma Sanchez, COA; Shirley York, OD; Stacy Malone, COA; Margaret Olsson; Gihan Romany, MBChB, COMT, CCRC.

Oregon Health and Science University, Portland, Oregon :

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