



Published in final edited form as:

J AAPOS. 2022 August ; 26(4): 174.e1–174.e4. doi:10.1016/j.jaapos.2022.05.003.

Long-term strabismus outcomes after unilateral infantile cataract surgery in the Infant Aphakia Treatment Study

Erick D. Bothun, MD^{a,b}, Marla J. Shainberg, CO^c, Stephen P. Christiansen, MD^{d,e}, Deborah K. Vanderveen, MD^f, Dan E. Neely, MD^g, Stacey J. Kruger, MD^h, George Cotsonis, MSⁱ, Scott R. Lambert, MD^j,

Infant Aphakic Treatment Study*

^aDepartment of Ophthalmology, Mayo Clinic, Rochester Minnesota

^bDepartment of Ophthalmology and Visual Sciences, University of Minnesota, Minneapolis, Minnesota;

^cDepartment of Ophthalmology, University of Tennessee, Memphis, Tennessee;

^dDepartment of Ophthalmology, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts;

^eDepartment of Pediatrics, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts;

^fDepartment of Ophthalmology, Harvard Medical School, Boston, Massachusetts;

^gIndiana University, Indianapolis, Indiana;

^hDepartment of Ophthalmology, Zucker School of Medicine at Northwell Health, Great Neck, New York;

ⁱDepartment of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, Georgia;

^jDepartment of Ophthalmology, Stanford University, Palo Alto, California

Abstract

PURPOSE—To characterize long-term strabismus outcomes in children in the Infant Aphakia Treatment Study (IATS).

METHODS—This study was a secondary data analysis of long-term ocular alignment characteristics of children aged 10.5 years who had previously been enrolled in a randomized clinical trial evaluating aphakic management after unilateral cataract surgery between 1 and 6 months of age.

RESULTS—In the IATS study, 96 of 109 children (88%) developed strabismus through age 10.5 years. Half of the 20 children who were orthophoric at distance through age 5 years maintained

*See eSupplement 1, available at jaapos.org.

Correspondence: Erick Bothun, MD, Mayo Clinic, Department of Ophthalmology, 200 First Street SW, Rochester, Minnesota 55905 (bothun.erick@mayo.edu).

orthophoria at distance fixation at 10.5 years. Esotropia was the most common type of strabismus prior to age 5 years (56/109 [51%]), whereas exotropia (49/109 [45%]) was the most common type of strabismus at 10.5 years (esotropia, 21%; isolated hypertropia, 17%). Strabismus surgery had been performed on 52 children (48%), with 18 of these (35%) achieving microtropia <10 . Strabismus was equally prevalent in children randomized to contact lens care compared with those randomized to primary intraocular lens implantation (45/54 [83%] vs 45/55 [82%]; $P=0.8$). Median visual acuity in the study eye was 0.56 logMAR (20/72) for children with orthotropia or microtropia <10 versus 1.30 logMAR (20/400) for strabismus 10 ($P=0.0003$).

CONCLUSIONS—Strabismus—in particular, exotropia—is common irrespective of aphakia management 10 years following infant monocular cataract surgery. The delayed emergence of exotropia with longer follow-up indicates a need for caution in managing early esotropia in these children. Children with better visual acuity at 10 years of age are more likely to have better ocular alignment.

Strabismus is a common association with infantile cataract, with reported frequencies varying by laterality, population, and follow-up time.^{1–10} Despite early reports that suggested an IOL might protect against the development of strabismus, no such effect has been identified in randomized studies.^{1,2} Prior studies with limited follow-up have shown that better visual acuity correlates with better ocular alignment and stereopsis.^{7,10} Long-term strabismus outcomes, with or without strabismus surgery, in the setting of a history of infantile cataract surgery remain to be ascertained.

The Infant Aphakia Treatment Study (IATS), a multi-center, randomized clinical trial for infants 1–6 months of age with a unilateral cataract, previously reported visual acuity, strabismus, and sensorimotor outcomes 5 years after cataract surgery.^{10–15} The National Eye Institute approved and funded further study of this cohort, including recalling children initially enrolled in IATS for a follow-up examination at a mean age (with standard deviation) of 10.5 years \pm 3 months. Long-term visual acuity and glaucoma outcomes have been recently published.^{16–18} This report documents the strabismus outcomes 10 years after infantile cataract surgery. Strabismus management was based on treating physician discretion and no study visits occurred between ages 5 and 10 years.

Materials and Methods

The original IATS design, eligibility criteria, surgical and clinical care, including patching and optical regimens, and evaluation methods have been previously reported.¹¹ This study was approved by the institutional review boards at all participating institutions and was in compliance with the US Health Insurance Portability and Accountability Act of 1996. Ocular alignment at distance and near was assessed at 10.5 years of age by an IATS-certified investigator. Strabismus was quantitated in prism diopters using the prism and alternate cover test and simultaneous prism cover test or Krismky light reflex testing when fixation was poor.

Analysis Methods

In descriptions of strabismus patterns, children with a combination of horizontal and vertical strabismus were grouped according to the horizontal deviation. Unless otherwise noted, the strabismus result is the measurement made at distance fixation. Microtropia was defined as a deviation of $<10^\circ$. The proportion of children with strabismus was compared between groups using the Fisher exact test. The median visual acuity was compared between groups of children with and without strabismus using the Wilcoxon rank-sum test. All statistical tests were two-sided. No adjustment was made for multiple testing. A P value of <0.05 was deemed statistically significant.

Results

Of the 114 children originally enrolled in IATS, 109 (96%) completed a clinical evaluation with ocular alignment testing at a mean postsurgical follow-up of 10.4 years (range, 9.3–11.5). The distance alignment measurements of the IATS cohort at 5 and 10.5 years are provided in Table 1. Of the 109 children seen at 10.5 years of age, 96 (88%) had strabismus at distance or near fixation. A distance deviation was measured in 90 children (83%), with 64 of the 72 patients with a horizontal deviation at distance (89%) having the same horizontal deviation at near. Strabismus was equally prevalent at the 10.5-year examination in children randomized to contact lens care compared to those with primary IOL (45/54 [83%] vs 45/55 [82%]; $P=0.8$).

Fifty-two children (48%) underwent strabismus surgery at investigator discretion prior to age 10. A similar proportion of children in each treatment group had strabismus surgery (CL, 26/54 [48%]; IOL 26/55 [47%]; $P=0.9$). Of the 45 children who had a history of strabismus surgery prior to age 5 years, 10 (22%) had additional surgery between 5 and 10 years of age (including 1 with two additional strabismus surgeries). Conversely, of the 65 patients without surgery by age 5, only 7 (11%) had strabismus surgery between ages 5 and 10 years (including 2 with 2 surgeries). Of the 52 children who underwent strabismus surgery, 18 (35%) achieved microtropia or orthotropia at the 10.5-year examination; of these 18 children, 6 (12% overall) were orthotropic.

Whether by surgical or nonsurgical treatment, an orthotropic or microtropic outcome was achieved in 25 children (46%) in the CL group and in 26 (47%) in the IOL group ($P=0.9$) at age 10.5 years. Exotropia was present in 49 children (45%), with a mean deviation of $18 \pm 13^\circ$ (standard deviation; range, 4° – 60°). Exotropia was seen in 25 of 57 (44%) children without and 24 of 52 (46%) children with one or more prior strabismus surgeries. Esotropia was present in 23 children (21%; mean, $9 \pm 8^\circ$ [range, 2° – 25°]), including 15 of 57 (26%) without and 8 of 52 (15%) with one or more prior strabismus surgeries.

The horizontal alignment of the 57 children without any strabismus surgery was compared between the 5 and 10.5-year examinations. Of 21 children who were orthophoric at the 5-year examination, 19 remained orthophoric ($n=10$) or developed a microtropia ($n=9$) by age 10.5 years. Two children developed strabismus $>10^\circ$, both of whom developed exotropia. Visual acuity in the treated eyes was better than 20/40 in 5 of 10 children (50%) who remained orthophoric and in 4 of 11 (36%) who developed strabismus at distance

after age 5 years ($P=0.5$). Of the 22 children with esotropia at age 5, 11 (50%) remained esotropic while 8 (36%) developed exotropia by age 10.5 years (the remaining 3 were orthotropic). Conversely, 9 of 12 children (75%) with exotropia at age 5 years continued to have exotropia 5 years later with no child developing esotropia. The prevalence of exotropia at age 10.5 years in children with prior strabismus surgery (46%) was similar to the prevalence of exotropia in patients without prior extraocular muscle surgery (44%). Eighteen children (17%) had only a vertical deviation, either hypertropia (5) or dissociated vertical deviation (13), with a mean deviation of 7 ± 6 (range, 2 –12). An additional 36 children with a primary horizontal deviation were reported to have an associated dissociated vertical deviation (21/36 [58%]) or hypertropia (15/36 [42%]).

Visual acuity at age 10.5 years was significantly associated with better distance alignment, with or without prior strabismus surgery. Median visual acuity in the operative eye was 0.56 logMAR (20/72) for children with orthotropia or microtropia (<10) and 1.30 logMAR (20/400) for children with strabismus ≥ 10 ($P=0.0003$). Of the 30 children with visual acuity of 20/40 or better, 21 (70%) had a deviation of <10 , compared with 29 of 77 (38%) with visual acuity worse than 20/40 ($P=0.003$). There was no statistically significant association, however, between visual acuity and orthotropia (median visual acuity of 0.60 logMAR in 18 children with orthotropia) vs any strabismus (median visual acuity 0.90 in 89 children with any strabismus; $P=0.1$ [Wilcoxon]).

Gross stereopsis was detected at age 10.5 years using Randot testing in 18 of 109 (16%) children; they were disproportionately likely to be orthotropic at near (8/18) rather than strabismic at near ($P=0.02$). Among children with either orthotropia or microtropia of <10 , 27% showed measurable stereopsis compared with 10% of children with strabismus of ≥ 10 ($P=0.02$). No child with strabismus at near or prior strabismus surgery achieved stereopsis better than 800 arcsec.

Discussion

With long-term follow-up in this randomized controlled trial, IATS investigators did not find a statistically significant difference in the frequency of strabismus based on aphakia management (83% children in the CL group and 82% in the IOL group). Prior to IATS, some reports suggested that IOL insertion might reduce the high incidence of strabismus identified after unilateral cataract surgery.^{1,2} Yet a consistent limitation to retrospective series was that the decision to place an IOL was at investigator discretion. Despite 10 years of rehabilitative care and the intervention of strabismus surgery, the number of IATS children with ocular misalignment, and exotropia in particular, remains substantial. This poor sensorimotor result in this cohort likely correlates with dense recalcitrant amblyopia associated with infantile cataract (44% of children had a visual acuity of 20/200 or worse in the affected eye).¹⁶

A notable observation between the 5- and 10-year outcomes involves the instability of early ocular alignment over the first decade of life. Approximately half of the children with orthotropia after the 1- and 5-year examination developed strabismus in the following 5 years. Visual acuity in the treated eyes was not predictive of the development of

strabismus in this subgroup. Additionally, at the 5-year follow-up in the IATS, esotropia outnumbered exotropia 2:1 (50% vs 27%).¹⁰ Others have reported similarly high rates of early esotropia after infantile cataract surgery (Lambert and colleagues,¹ 50%; Spanou and colleagues,³ 76.5%; Parks and Hiles,⁵ 66%). With follow-up to 10 years for IATS children, this ratio has flipped (exotropia 49% vs esotropia 21%). Given that half of the cohort underwent strabismus repair prior to age 10, one might suggest that consecutive deviations have contributed to this instability.¹⁵ However, a spontaneous exodeviation shift was identified among children who never had strabismus surgery and who were esotropic at 5 years of age, with 36% developing an exotropia by age 10.5 years. Conversely, among children who had no strabismus surgery, no child with exotropia at age 5 years developed an esotropia with further follow-up. The prevalence of exotropia at age 10.5 years in children with prior strabismus surgery was similar to the prevalence of exotropia in patients without prior extraocular muscle surgery. Potential alignment variability and the risk of a long-term exoshift in these patients might suggest that a conservative approach to treatment of esotropia in the first 5 years after cataract extraction is warranted. Although a modest number of small, isolated vertical deviations was seen in children at 10.5 years, most children with vertical misalignment had dissociated vertical deviation, typically in the setting of a comitant horizontal deviation.¹⁰

We previously reported that children without strabismus more commonly had better visual acuity and stereopsis than those with strabismus.¹⁰ At 10.5 years of age, orthotropia or a microtropia was found in 70% of children with visual acuity better than 20/40 in the operative eye compared with only 38% of children with visual acuity of 20/40 or worse in the operative eye. It remains unclear whether better alignment improves amblyopia treatment after cataract surgery, or better acuity in the treated eye protects against the development of strabismus or fosters stable alignment after strabismus surgery. Despite anecdotal reports of good stereopsis outcomes, most children do not demonstrate stereopsis despite rehabilitative care for unilateral congenital cataract.^{19–23} Hartmann et al described primarily only gross stereopsis by one or more of three tests in 25.5% of children enrolled in the IATS at age 4.5 years.¹⁴ At age 10.5 years, gross stereopsis was only detected in approximately 1 of 6 children, yet was more common when orthotropia was present.

Two principal limitations of this analysis include the relatively small sample size and the fact that strabismus management was at investigator discretion. The poor sensory results may have influenced investigators to be more conservative with strabismus reoperations after age 5 years. The reason to pursue additional surgery was not recorded, so strabismus operations may also have been performed for psychosocial reasons, and not reasons related to visual performance.

In conclusion, strabismus is common 10 years following unilateral infantile cataract surgery, irrespective of aphakic management. Better alignment was associated with better visual acuity in the affected eye. The delayed emergence of exotropia with longer follow-up should lead to caution in managing early esotropia with strabismus surgery in these children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by National Institutes of Health Grants U10 EY13272 and U10 EY013287 and in part by NIH Departmental Core Grant EY06360 and Research to Prevent Blindness, Inc, New York, New York. This study is registered with [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT00212134) (NCT00212134).

References

1. Lambert SR, Lynn M, Drews-Botsch C, et al. A comparison of grating visual acuity, strabismus, and reoperation outcomes among infants with aphakia and pseudophakia after unilateral cataract surgery during the first six months of life. *J AAPOS* 2001;5:70–75. [PubMed: 11304812]
2. Atrata R, Rehurek J, Vodickova K. Visual results after primary intraocular lens implantation or contact lens correction for aphakia in the first year of age. *Ophthalmologica* 2005;219:72–9. [PubMed: 15802930]
3. Spanou N, Alexopoulos L, Manta G, Tsamadou D, Drakos H, Paikos P. Strabismus in pediatric lens disorders. *J Pediatr Ophthalmol Strabismus* 2011;48:163–6. [PubMed: 21608524]
4. Watts P, Abdolell M, Levin AV. Complications in infants undergoing surgery for congenital cataract in the first 12 weeks of life: is early surgery better? *J AAPOS* 2003;7:81–5. [PubMed: 12736618]
5. Parks MM, Hiles DA. Management of infantile cataracts. *Am J Ophthalmol* 1967;63:10–19. [PubMed: 6018201]
6. Lee SJ, Kim W. Factors associated with strabismus after cataract extraction and primary intraocular lens implantation in congenital cataracts. *Int J Ophthalmol* 2014;7:522–7. [PubMed: 24967203]
7. Bothun ED, Cleveland J, Lynn MJ, et al. Infant Aphakic Treatment Study. One-year strabismus outcomes in the Infant Aphakia Treatment Study. *Ophthalmology* 2013;120:1227–31. [PubMed: 23419803]
8. Bothun ED, Wilson ME, Vanderveen DK, et al. Outcomes of bilateral cataracts removed in infants 1 to 7 months of age using the Toddler Aphakia and Pseudophakia Treatment Study Registry. *Ophthalmol* 2020;127:501–10.
9. Bothun ED, Wilson ME, Traboulsi EI, et al. Toddler Aphakia and Pseudophakia Study. Outcomes of unilateral cataracts in infants and toddlers age 7 to 24 months: Toddler Aphakia and Pseudophakia Study Group (TAPS). *Ophthalmology* 2019;126:1189–95. [PubMed: 30880109]
10. Bothun ED, Lynn MJ, Christiansen SP, et al. , Infant Aphakia Treatment Study. Sensorimotor outcomes by age 5 years after monocular cataract surgery in the Infant Aphakia Treatment Study (IATS). *J AAPOS* 2016;20:49–53. [PubMed: 26917072]
11. Infant Aphakia Treatment Study Group. The Infant Aphakia Treatment Study: design and clinical measures at enrollment. *Arch Ophthalmol* 2010;128:21–7. [PubMed: 20065212]
12. Infant Aphakia Treatment Study Group, Lambert SR, Lynn MJ, Hartmann EE, et al. Comparison of contact lens and intraocular lens correction of monocular aphakia during infancy: a randomized clinical trial of HOTV optotype acuity at age 4.5 years and clinical findings at age 5 years. *JAMA Ophthalmol* 2014;132:676–82. [PubMed: 24604348]
13. Plager DA, Lynn MJ, Buckley EG, Wilson ME, Lambert SR, Infant Aphakia Treatment Study Group. Complications in the first 5 years following cataract surgery in infants with and without intraocular lens implantation in the Infant Aphakia Treatment Study. *Am J Ophthalmol* 2014;158:892–8. [PubMed: 25077835]
14. Hartman EE, Stout AU, Lynn MJ, Yen KG, Kruger SJ, Lambert SR, Infant Aphakia Treatment Study. Stereopsis results at 4.5 years of age in the Infant Aphakia Treatment Study. *Am J Ophthalmol* 2015;159: 64–70. [PubMed: 25261241]
15. Bothun ED, Lynn MJ, Christiansen SP, et al. , Infant Aphakic Treatment Study. Strabismus surgery outcomes in the Infant Aphakia Treatment Study (IATS) at age 5 years. *J AAPOS* 2016;20:501–5. [PubMed: 27815186]

16. Lambert SR, Cotsonis G, DuBois L, et al. , Infant Aphakia Treatment Study Group. Long-term effect of intraocular lens verses contact lens correction on visual acuity after cataract surgery during infancy: A randomized clinical trial. *JAMA Ophthalmol* 2020;138:365–72.
17. Lambert SR, Nizam A, DuBois L, Cotsonis G, Weakley DR, Wilson ME, Infant Aphakia Treatment Study Group. The myopic shift in aphakic eyes in the Infant Aphakia Treatment Study after 10 years of follow up. *Eye Contact Lens* 2021;47:108–12. [PubMed: 32568929]
18. Freedman SF, Beck AD, Nizam A, et al. Infant Aphakia Treatment Study Group. Glaucoma-related adverse events at 10 years in the Infant Aphakia Treatment Study: a secondary analysis of a Randomized Clinical Trial. *JAMA Ophthalmol* 2021;139:165–73. [PubMed: 33331850]
19. Gregg FM, Parks MM. Stereopsis after congenital monocular cataract extraction. *Am J Ophthalmol* 1992;114:314–17. [PubMed: 1524121]
20. Birch EE, Swanson WH, Stager DR, Woody M, Everett M. Outcome after very early treatment of dense congenital unilateral cataract. *Invest Ophthalmol Vis Sci* 1993;34:3687–99. [PubMed: 8258529]
21. Brown SM, Archer S, Del Monte MA. Stereopsis and binocular vision after surgery for unilateral infantile cataract. *J AAPOS* 1999;3:109–13. [PubMed: 10221805]
22. Hosal BM, Biglan AW, Elhan AH. High levels of binocular function are achievable after removal of monocular cataracts in infants before 8 years of age. *Ophthalmology* 2000;107:1647–55. [PubMed: 10964822]
23. Fawcett SL, Wang Y, Birch EE. The critical period for susceptibility of human stereopsis. *Invest Ophthalmol Vis Sci* 2005;46:521–5. [PubMed: 15671277]

Table 1.

Ocular alignment at distance among children at age 5 and 10.5 years

Deviation	5-year exam (n = 112)		10.5-year exam (n = 109)	
	No. (%)	PD, mean \pm SD (range)	No. (%)	PD, mean \pm SD (range)
Orthotropia	19 (17)		19 (17)	
Esotropia	56 (50)	21.7 \pm 14.1 (2–70)	23 ^a (21)	9 \pm 8 (2–25)
Exotropia	30 (27)	25.8 \pm 13.7 (3–50)	49 ^b (45)	18 \pm 13 (4–60)
Isolated hyperdeviation	19 (17)	13.0 \pm 7.7 (2–20)	18 ^c (17)	7 \pm 6 (2–12)

DVD, dissociated vertical deviation; *PD*, prism diopters.

^aWith hypertropia in 3 and DVD in 6.

^bWith hypertropia in 12 and DVD in 15.

^cHypertropia in 5 and DVD in 13.