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PURPOSE To report the long-term clinical and endothelial cell count (ECC) results of lensectomy with primary anterior chamber iris claw lens implantation in the eyes of patients ≤18-year-old with ectopia lentis due to Marfan syndrome.

METHODS The medical records of Marfan patients operated on at a single institution from September 2007 to August 2020, with minimum follow-up of 2 years, were reviewed retrospectively. The following data were analyzed: sex, age at surgery, indication for surgery, the position of the lens in relation to the undilated and dilated pupil, corneal endothelial cell counts (ECC), peri- and postoperative complications, pre- and postoperative best-corrected visual acuity.

RESULTS A total of forty-two eyes of 23 patients (12 girls and 11 boys) were included. At least two or more postoperative ECCs were collected from 33 eyes (17 patients). Median age at IOL implantation was 6.1 years (range, 1.8-18). Median overall follow-up time was 6.2 years (range, 2-13.5). Median ECC follow-up time was 6.2 years (range, 2-10). Mean best-corrected visual acuity was 0.71 ± 0.38 logMAR before surgery and 0.02 ± 0.25 logMAR at final follow-up. The mean annual ECC decline was 0.71% ± 2.24. Total cell loss from first to last postoperative measurement was 150 cells ± 394 cells/mm^2 (4.81%). Pre- and first postoperative data were available for 17 eyes of 10 patients, with a mean cell loss before and directly after surgery of 269 ± 268 cells (7.94%). Surgery related complications were iris bombé due to blockage of peripheral iridectomy in 3 eyes and claw dislocation due to direct impact trauma in 3 eyes.

CONCLUSIONS In our large, pediatric study cohort, anterior chamber iris claw IOL implantation resulted in an excellent visual outcome and normal endothelial cell loss compared with normative data. Safety measures are recommended to avoid traumatic dislocation of IOLs. (J AAPOS 2024;28:103922)

Ectopia lentis is a dislocation or displacement of the natural crystalline lens due to disruption of the microfibrils of the ciliary zonules. Nontraumatic ectopia lentis can be associated with systemic disease, including Marfan syndrome, Weill Marchesani syndrome, Homocystinuria, and other hereditary causes, such as ectopia lentis et pupillae. More advanced subluxations can cause severe visual impairment due to the crystalline lens bisecting the center of the pupil and resulting in high myopia, highly variable refractive errors, high astigmatism due to tilting of the lens, or diplopia. When performing surgery on the luxated crystalline lens, the remaining lens capsule does not have adequate zonular support to be strong enough to hold a posterior chamber in-the-bag intraocular lens (IOL). The absence of capsular support poses a challenge for lens implantation. Various options for IOL implantation in the absence of capsular support have been described, all with their own potential complications and mostly with short term follow up. Options are (intra)scleral fixation of a posterior chamber IOL, either sutured, sutureless or glued, or iris fixated (iris-sutured or anterior or posterior claw IOL).[1,2]

The human cornea has approximately 6,000 endothelial cells/mm^2 of posterior corneal surface shortly after birth. This number decreases rapidly during infancy and continues to decrease.[3] A normal endothelial cell density

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(ECD) ranging from 2,407 to 2,977 cells/mm^2 in the third decade of life is found in normal human eyes in different populations.[4] Endothelial cell loss is followed by migration and spreading of neighboring endothelial cells.[5] The exact lower limit of endothelial cells necessary to keep the cornea clear is estimated to be about 500 cells/mm^2.[6]

Normal annual decline in endothelial cell density is around 0.3%-0.6% in adults; in children, the annual decline is much higher. [7] Nucci and colleagues[8] estimated an ECD decrease of 13% between ages 5 and 7 years and an additional decrease of 12% by the age of 10 years in 214 school children aged 5-14 years. Møller-Pedersen[3] studied ECD in donor eyes of patients aged 6 months to 90 years. A two-phase linear regression showed an annual cell loss of 2.9% for eyes younger and 0.3% for eyes >14 years of age. Müller and Doughty[9] found a decline of 1.3% per year in eyes of children 5 to 15 years of age. In a study on 118 children, Elbaz and colleagues[10] found an ECD decline per year of 8.2% in children <2 years and 2.7% in children aged 2-5 years.

The current study focuses on iris claw IOL implantation in the anterior chamber (AC) in pediatric patients with advanced ectopia lentis due to Marfan syndrome. These children had severe visual loss and often required services of visual aid centers for education and daily functioning. The surgical technique itself is minimally invasive, because IOL implantation is confined to the anterior chamber and offers the advantage of sutureless fixation. The main concerns associated with the procedure are its impact on corneal endothelial cell loss and potential for (traumatic) lens dislocation; here we report on corneal endothelial cell counts (ECC) in particular, because of concern that this surgery may induce higher-than-expected annual cell loss.

Subjects and Methods

The surgical outcomes in children and adolescents that underwent surgery for ectopia lentis from September 2007 to August 2020 at the Leiden University Medical Center, a tertiary referral center for children with cataract and lens subluxation, were analyzed retrospectively. Inclusion criteria were age ≤18 years at time of surgery, availability of pre- and postoperative visual acuity data, and minimum postoperative follow-up of 2 years. This study complied with the tenets of the Declaration of Helsinki and was approved by the Leiden University Medical Center Institutional Review Board. Informed consent from patients and/or parents was obtained prior to surgery.

Collected chart data included sex, age at surgery, indication for surgery, position of the lens in relation to the undilated and dilated pupil, corneal ECC, peri- and postoperative complications, and pre- and postoperative best-corrected visual acuity (BCVA), which was measured in Snellen and converted to logarithm of the minimum angle of resolution (logMAR) for analysis.[11] IOL calculation was performed at the preoperative visit or under anesthesia when cooperation was insufficient to perform accurate measurements. Corneal ECCs were obtained with the noncontact autofocus Topcon SP-2000P until 28 August 2012 and thereafter using the Topcon SP-3000P (Topcon, Tokyo, Japan). All ECCs were generated automatically and manually corrected for accurate delineation of the separate cells if necessary. The appropriate conversion factors were applied for the consecutively used Topcon devices, as has been described: conversion factor 0.835 for the SP-2000, and 1.014 for the SP-3000.[12] These conversions are needed because every individual corneal specular microscope has its own magnification and calibration settings, warranting customized software for quantitative endothelial cell analysis. Because this is a longitudinal cohort, the Topcon devices used have been replaced during this study. By using the conversion factor as an external calibration, the interchangeability concerns caused by software imprecision and erroneous calibration were addressed.[12]

Surgical Technique

All surgical procedures were performed under general anesthesia by a single surgeon (NSC). After preparation of a 5,5 mm scleral tunnel and two limbal paracenteses, the anterior lens capsule was opened with a 20-gauge vitrectome. Lens aspiration was performed with the vitrectomy instrument and irrigation cannula in the capsular bag to prevent excessive movement and further dislocation. The capsular bag was completely removed by vitrectomy in all cases to prevent contraction from circular bag remnants. For optimal fixation of the IOL to the periphery of the iris, carbachol (Miostat, Alcon, TX) was inserted to achieve miosis. The anterior chamber was filled with 1.0% sodium hyaluronate (Healon, Abbott Medical Optics [AMO], Uppsala, Sweden), the scleral tunnel was enlarged and an aphakia iris-claw IOL (Artisan Aphakia, Ophtec, Groningen, The Netherlands; Verisyse VRSA54, AMO, Santa Ana, CA) with a diameter of 8.5 mm and an optical zone of 5 mm was inserted and attached to the iris. To prevent pupillary block, a peripheral iridectomy (PI) was performed in all eyes at the 12 o'clock position with the vitrectome and was checked for patency using the red reflex. The scleral tunnel was closed with 2 crossed 10.0 nylon sutures and covered with conjunctiva. An air bubble was inserted in the anterior chamber and the wounds were checked for vitreous strands. At the end of surgery 1 mg intracameral cefuroxim (since 2008) and 1 cc subconjunctival dexamethasone 4 mg/ml was administered.

Statistical Analysis

Cross-sectional data were analyzed using descriptive statistics, where numerical variables were presented as median and range or mean with standard deviation, and categorical variables as number and percentages. Analyses were performed in Excel (Office 365). GraphPad Prism 5 for Windows (version 5.00, 2007) was used to create figures.

Results

A total of 42 eyes of 23 patients (12 girls and 11 boys), were included. Four patients underwent unilateral surgery. Median age at IOL implantation was 6.1 years (range, 1.8-18). Median follow-up time was 6.2 years (range, 2-13.5). Mean

BCVA was 0.71 ± 0.38 logMAR preoperative and 0.02 ± 0.25 logMAR at last follow-up. The overall mean vision gain was –0.7± 0.37 logMAR. Preoperatively, 30 eyes of 19 patients (both eyes in 11 patients) had a visual acuity of 6/18 decimals (0.48 logMAR) or worse, the World health Organization's definition for low vision. At last visit, only 2 patients each had 1 eye with a visual acuity <0.48 logMAR due to residual amblyopia.

Before surgery, 11 of 17 patients were supported by an institute for the visually impaired or blind and needed visual aids because even with optimal correction their visual acuity was insufficient to perform daily tasks or schoolwork. After surgery, all patients were completely self-supporting.

Complications

Shortly after surgery 3 eyes had a fibrinous reaction, resulting in iris bombé, caused by fibrin blocking the PI in 2 eyes. One other eye presented with a flat AC due to closure of the PI 2 years after surgery. One eye experienced a macula-on retinal detachment 8 months after surgery. Three eyes of 2 patients needed surgical repositioning of one of the claws after high-impact trauma to the eye while playing or fighting with siblings at 24, 51, and 69 months after surgery. None of the iris-claw haptics subluxated without a history of trauma.

Endothelial Cell Data

For 33 eyes (17 patients), we collected 2 or more postoperative ECCs. Mean preoperative BCVA of this subgroup was 0.68 ± 0.34 logMAR and 0.01 ±0.26 logMAR at last follow-up. Median age at IOL implantation was 6.2 years (range, 2.6-18). Figure 1 shows the ECC of all 33 individual eyes, with preoperative measurement if available, first measurement after surgery, and last follow-up. The median ECC follow-up time was 6.2 years (range, 2-10.3). Mean ECC was 3,127 ± 517 cells/mm^2 at the first and 2,977 ± 604 cells/mm^2 at the last postoperative visit. Mean total cell loss from first postoperative until last postoperative measurement was 150 cells ± 394 cells/mm^2 (4.81%). The mean annual ECC decline of 33 eyes with 2 or more postoperative measurements during follow-up was 0.71% ± 2.24%. To gain insight into the effect of complications on ECC loss, mean annual endothelial cell decline was calculated for eyes of patients without complications (0.38% ± 1.5 %) and with complications (1.9% ± 3.8%). More profound loss was only found in the patient with trauma to both eyes and significant delay in seeking treatment, with annual endothelial cell loss of 6.54% for the right eye and 8.25%% for the left eye. The other patient experienced no cell loss after IOL dislocation and swift lens repositioning.

Pre- and postoperative ECC data were available for 17 eyes of 10 patients. Mean ECC of these 17 eyes before surgery was 3,381 ± 217 cells/ mm^2, and 3,113 ± 385 cells/mm^2 at first count after surgery. Mean cell loss before and directly after surgery was 269 cells ± 268 cells/mm^2 (7.94%). Our patient data was plotted against the normative databases of Nucci and colleagues[8] (Figure 2), and Møller-Pederson and colleagues[3] (Figure 3).

Discussion

We report the long-term outcome of lensectomy with primary anterior chamber iris claw lens implantation in a large group of children with ectopia lentis due to Marfan syndrome. In our study cohort, anterior fixation of the IOL did not increase endothelial cell decline compared with normative values for ECC loss, even in the long term. This is important because normal ECC and a clear cornea are crucial for good future visual acuity. Furthermore, the significant gain of vision in our young patients after surgery was remarkable. Before surgery, most patients had high refractive errors and were supported by an institute for the visually impaired or blind; after surgery, all patients were completely self-supporting, had low residual refractive errors, and spontaneously affirmed significant improvement. This emphasizes the need for timely surgical intervention and optimal optical correction, either by contact or intraocular lens, when visual acuity becomes inadequate to perform daily and educational tasks.

Sminia and colleagues[13] proposed that ECC measurements be made preoperatively, once within the 0-6 months postoperative period, at 6 months, and 1 year, followed by yearly measurements. Yet capturing ECC measurements in young children can be extremely challenging because of lack of cooperation, unstable positioning, or inability to fixate the target steadily. Our study cohort included a high number of children <10 years of age. This resulted in not being able to capture a useful specular image at every visit, and is reflected in sometimes marked intrapatient variation across serial measurements, occasionally resulting in an apparent increase in ECC over time. Therefore, our results may best be regarded as cross-sectional data, because true longitudinal changes in ECC were difficult to assess.

The effectively cross-sectional nature of our data and its retrospective design are limitations of our study. Nevertheless, our data provided insight into endothelial cell loss over time. Mean endothelial cell loss of 7.9%, comparing pre- and first postoperative ECC in our study, accords with other studies that report endothelial cell loss of 5.2% to 9.2% as a result of pediatric cataract surgery.[14-17] A postoperative decline in ECC of 0.71% ± 2.24% per year in our patient group was found, after a median ECC follow-up of 6.2 years (range, 2-10.3). This is less than the decline of 1.3% that Müller and Doughty[9] found in their study of patients 5-15 years of age, and less than the normal limits of 1.1%-2.9% loss per year reported in children without a history of intraocular surgery,[3] and in accord with a recent study by Fuerst and colleagues[18] reporting an average annual

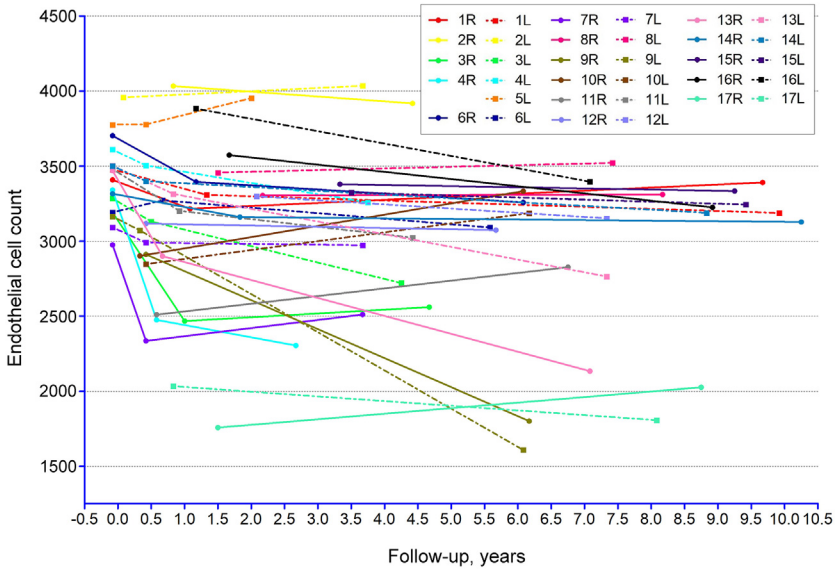

FIG 1. Preoperative, first, and last postoperative endothelial cell count per eye. Continuous lines indicate values for the right eye; dotted lines,for the left eye. Each color depicts an indivual patient. (R = right eye, L = left eye). A preoperative measurement was depticed at −0.05.

ECC decline of 1.34 % after a median of 3.59 years' follow-up in children with anterior iris-claw IOL implantation. We compared our data to two normative databases for similar age groups Figures 2-3. Nucci and colleagues[8] included children 5-14 years of age, whereas Møller-Pederson and colleagues[3] also included a younger age group and extended the range to the age of 25. The data of our youngest patients is best compared with and is predominantly within 2 standard deviations of Nucci's data. Marked deviations are seen in 2 patients. Patient number 17 only had postoperative measurements with a remarkably low cell count but remained stable over time. He experienced postoperative iris bombé caused by fibrin blocking the PI shortly postoperatively. Patient 9 is the patient with traumatic haptic luxation in both eyes who was treated after significant patient delay. For long-term follow-up, comparison with the Møller-Pederson[3] data is more useful and shows that our patients with longer follow-up have ECC within the normal range for age.

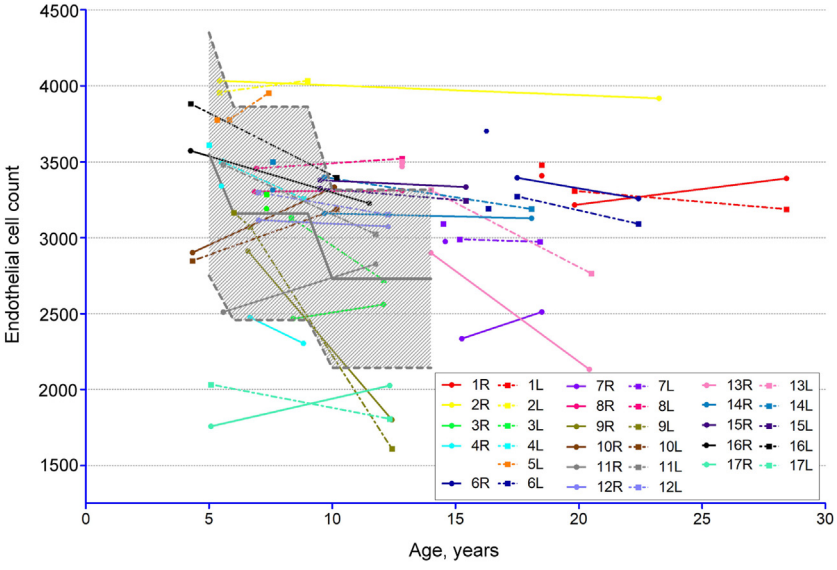

FIG 2. Individual endothelial cell density (ECD) as a function of age compared with normative data.[8] Connected dots indicate postoperative values of the right eye; connected squares, of the left eye. Single squares indicate left eye preoperative values; separate dots, right eye preoperative values. The Gray line represents the mean ECD data of Nucci and colleagues[8] in normal eyes as a function of age, and gray overlay represents values plus or minus two standard deviations from the mean.

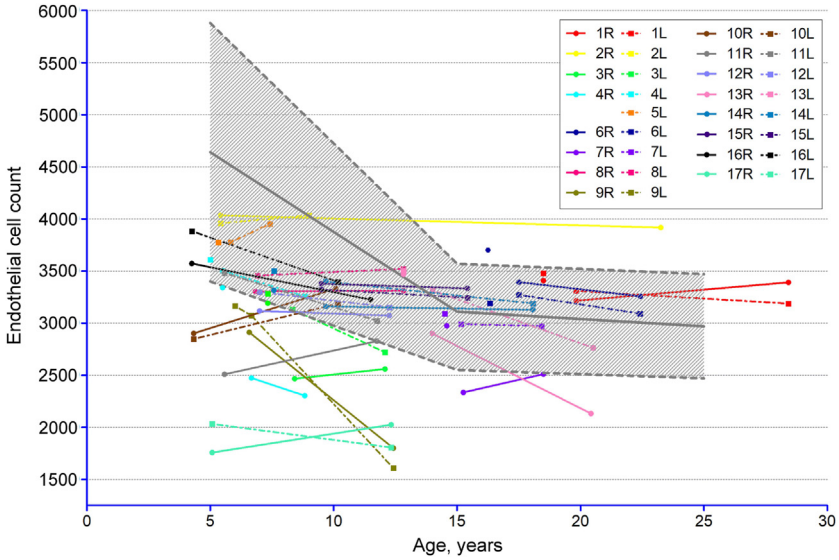

FIG 3. Individual ECD as a function of age compared with normative data of Møller-Pedersen and colleagues.[3] Connected dots indicate postoperative values of the right eye; connected squares, postoperative values of the left eye. Single squares indicate left eye preoperative values; separate dots, right eye preoperative values. The Gray line represents the mean ECD data of Møller-Pedersen and colleagues[3] in normal eyes as a function of age, and the gray overlay represents values plus or minus two standard deviations from the mean.

Cheung and colleagues[2] described a mean ECC decline ranging from 14.2% to 18.5% with follow-up from 12 to 49.2 ± 33.6 months in children with hereditary disorders and ectopia lentis who underwent Artisan IOL anterior chamber implantation. Our study adds to this study with long follow-up ECC outcomes up to 10 years of a large cohort of 42 eyes, although we noted less ECC decline.

Our results did not show large deviations from the normal ECC spectrum, even after more than 10 years' follow-up in these young patients. Nevertheless, long-term monitoring of the endothelium after anterior iris claw IOL implantation remains important, and patients and parents should be aware of possible long-term complications and preventive measures. Based on our clinical experience, we have two recommendations to prevent endothelium-compromising complications. First, in children, we recommend a PI, at least 2 mm wide at the base—large enough to prevent fibrin blockage in the immediate postoperative period or collapse/closure in the long term. Second, parents and children should be made aware of the importance of eye protection after surgery. Dislocation of the anterior fixated claw lens after direct impact trauma while playing or fighting without wearing protective spectacles is a major concern, and cases of traumatic IOL luxation, which may cause greater-than-average endothelial cell loss, have been reported.[2,18] We therefore emphasize to patients and parents the importance of wearing glasses for all activities, and although we do not recommend that these patients perform high-impact activities or contact sports, we do make a point of recommending protective glasses whenever they choose to participate in these high-risk activities. In addition, we stress the importance of ophthalmological examination immediately after eye trauma or in case of a red eye to prevent treatment delay.

In conclusion, we report good clinical results after anterior chamber iris claw IOL implantation in children with lens subluxation due to Marfan syndrome with long-term follow-up. Despite some adverse events, we found excellent visual outcome, high patient satisfaction, and a mean endothelial cell loss within normal limits after ECC follow-up of >10 years. As high endothelial cell loss may have significant effects, surveillance of the endothelium and clear instructions with prompt intervention in case of traumatic luxation is recommended. Based on our experience, we believe that iris-claw IOL implantation is a viable option for children with ectopia lentis and low visual acuity despite optimal optical correction.

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