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Descemet Stripping Endothelial Keratoplasty in Patients With a Custom Foldable Silicone Artificial Iris: Safety and Efficacy Outcomes

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Purpose: To assess outcomes of Descemet stripping endothelial keratoplasty (DSEK) in eyes with custom artificial iris (CAI) implantation.

Methods: This is a retrospective, interventional, consecutive, surgical case series of patients who underwent DSEK after CAI implantation between 2010 and 2021 at 2 referral centers. Primary safety measures were loss of corrected distance visual acuity (CDVA), increase in intraocular pressure (IOP), development or progression of glaucoma, and intraoperative and postoperative complications. Efficacy measures were graft survival at year 1 and improvement in cosmesis at postoperative month 3. In general, measures were compared between baseline and postoperative year 1 while any complication was reported for the full follow-up period.

Results: Thirty-nine eyes of 39 patients were identified. 64.1% of eyes had acquired aniridia from trauma. The mean follow-up interval was 27.7 months (range 12.2–117.4). Median CDVA improved from logMAR 1.0 to 0.7 at year 1 ($P = 0.0047$). At the final follow-up, permanent loss of CDVA occurred in 25.6% of eyes, of which 90% was due to glaucoma. The most common postoperative complication was IOP elevation (66.7% of eyes). Graft survival at postoperative year 1 was 82.0% (95% confidence interval, 66.3–91.4). Secondary graft failure occurred in 28.2% of eyes at a mean duration of 39.7 months (SD 27.9 months) after DSEK. Cosmesis improved among 87.2% of eyes at postoperative month 3.

Conclusions: DSEK is an effective procedure for addressing corneal edema in eyes with a CAI, but a majority develop elevated IOP and graft survival is shorter than in eyes without a CAI.

Key Words: artificial iris, cornea, endothelial keratoplasty, intraocular lens, triple procedure

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Congenital and acquired aniridia and aphakia lead to significantly reduced quality of life from reduction of visual acuity (VA), photophobia, glare sensitivity, and the psychosocial impact of an abnormal ocular appearance.[1,2] Congenital causes of aniridia include inherited disorders such as Axenfeld–Rieger syndrome or mutations in *PAX6* or sporadic disorders such as WAGR syndrome.[3] Acquired partial or complete aniridia typically results from blunt or penetrating trauma, surgical (iatrogenic) trauma, chronic intraocular inflammation, or several stationary and progressive disorders such as iridocorneal endothelial syndrome.[4] Both congenital and acquired causes of aniridia can be associated with dry eye, corneal epithelial irregularity, corneal scaring, corneal endothelial decompensation leading to visually debilitating corneal edema, lenticular abnormalities or aphakia, intraocular inflammation, ocular hypertension, and glaucoma.[5]

Over the past 2 decades, iris reconstruction lenses and aniridia implants have demonstrated promising visual outcomes[6–8]; however, their use has been limited by a lack of intermediate to long-term safety data, customization options, and commercial availability.[6,7] Silicone-based anterior chamber artificial iris implants have been used for purely cosmetic reasons or to correct aniridia, but these models have been associated with significant complications, and many have required explantation due to endothelial decompensation, chronic anterior uveitis, iris atrophy, premature cataract development, and glaucoma.[9–19]

The CustomFlex Artificial Iris (custom artificial iris [CAI], HumanOptics AG, Erlangen, Germany) is a silicone implant that has demonstrated safety and efficacy in 2 major case series and a subsequent US Food and Drug Administration (FDA) multicenter prospective interventional trial that resulted in FDA approval in May 2018.[20–22]

Corneal decompensation is often present in eyes requiring anterior segment reconstruction with a CAI; thus,

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penetrating keratoplasty (PK) or Descemet stripping endothelial keratoplasty (DSEK) can be used for visual rehabilitation. Staged or simultaneous artificial iris implantation and PK are feasible with significant gains in corrected distance visual acuity (CDVA).[22–24] DSEK is a reasonable option in eyes with an artificial iris without corneal stromal pathology. This study was performed to evaluate the safety and efficacy of a combination of procedures including CAI implantation, intraocular lens (IOL) implantation, and DSEK.

PATIENTS AND METHODS

This was a retrospective, interventional, nonrandomized case series with patients treated at 2 referral ophthalmology centers in the United States. The IRB of the University of California, Los Angeles (UCLA, #21–002154), and the IRB of Minnesota Eye Consultants (MEC, Salus IRB #1022) approved this study. Data collection and management were compliant with the US federal Health Insurance Portability and Accountability Act, and all research protocols adhered to the tenets of the Declaration of Helsinki. Patients provided written consent for participation in the studies, the surgical procedures, and the use of full-face photographs for academic purposes. At UCLA, patients were recruited by the senior author (K.M.M.) who performed artificial iris and IOL implantations. Either a senior corneal surgeon (A.J.A.) or K.M.M. performed the DSEK procedures. At MEC, the patients were recruited by a senior corneal surgeon (D.R.H.) who performed the artificial iris and IOL implantations and the DSEK procedures. All surgeries were performed between March 2010 and December 2021. The minimum follow-up interval was 12 months. Irises were implanted on a compassionate-use basis between March 2010 and March 2015. The FDA clinical trial ran from March 2015 to May 2019. FDA-approved devices were implanted from May 2019 onward.

Inclusion criteria for this study were as follows: 1) age 18 years or older at initial surgery; 2) the presence of a large iris defect with concomitant symptoms of photophobia, glare, decreased VA, and dissatisfaction with nonsurgical management; 3) corneal edema or bullous keratopathy from endothelial failure requiring EK; and 4) altered lens status (traumatic cataract, phakic dislocation, aphakia, IOL dislocation, and/or poor capsular bag support prohibiting in-the-bag or ciliary sulcus IOL placement). Exclusion criteria were as follows: 1) eyes with small iris defects and 2) lack of corneal endothelial disease.

Artificial Iris Sizing

For the patients in this study, each artificial iris was sized according to surgeon preference. K.M.M. implanted all devices without trephination. D.R.H. used the full 12.8-mm diameter or trephine devices to 1 mm less than the horizontal corneal white-to-white measurement obtained preoperatively.

Biometry, Tomography, and Endothelial Cell Count

Biometry measurements were obtained using Lenstar LS900 (Haag-Streit AG, Bern, Switzerland), IOLMaster 500, or IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany). Lens power calculations were performed using the Sanders-Retzlaff-Kraff/theoretical (SRK/T) or Barrett II Universal formulas. Scheimpflug tomography was performed preoperatively with a Pentacam HR or AXL Wave (Oculus GmbH, Wetzlar, Germany). Endothelial cell count (ECC) was acquired preoperatively and at follow-up visits using automated specular microscopy (CellChek, Konan Medical, Hyogo, Japan).

Surgical Technique

Surgeries were performed under combined retrobulbar block with monitored anesthesia care in most cases, although some patients required general anesthesia. The CAI implants were fiber-free for implantation into the capsular bag or fiber-containing for suturing to the sclera. For cases requiring suture fixation of the iris and/or IOL, the technique is briefly described as follows. A scleral tunnel incision was made; Hoffman pockets were created at the thickest parts of the sclera in eyes with scleral thinning[25]; if necessary, a dislocated IOL was removed from the eye facilitated by large IOL scissors and intraocular forceps; the new IOL was sutured to the posterior surface of the artificial iris using the 2 haptic–optic junctions with 9-0 or 10-0 Prolene sutures (Ethicon Inc, Bridgewater, NJ) or CV-8 GORE-TEX sutures (W.L. Gore & Associates, Newark, NJ); the artificial iris/IOL complex was then sutured with 9-0 Prolene or GORE-TEX sutures 180 degrees apart either at 2 closely spaced points inside the Hoffman pockets or assisted by 23-gauge trocars to externalize for transscleral fixation. Care was taken to bury all knots in the sclera with scleral patch grafts used to cover the sutures if this could not be achieved. For phakic eyes with adequate capsular bag support, after cataract phacoemulsification, capsular tension rings were injected into the capsular bag and a posterior chamber IOL was inserted into the capsular bag. A fiber-free CAI was injected through the main wound (cornea or scleral tunnel) and positioned within the capsular bag.

A DSEK was performed after CAI and IOL implantation. It occurred either during the same operation or later when clinically indicated. Briefly, the DSEK was performed with precut donor tissue. Air was injected into the anterior chamber to prevent contact with the CAI, with the bubble typically migrating into the posterior chamber around the implant, requiring significant additional air fill. Nearly all DSEK grafts were positioned using a suture pull-through technique with 10-0 nylon or 10-0 Prolene, which acted as a stay suture to prevent graft dislocation. One case was performed with a Busin glide (Moria SA, Antony, France), after which a stay suture was placed. The stay suture was typically cut at postoperative week 1. The anterior chamber was refilled with an air bubble to produce a tense air fill for 8 to 10 minutes, and then physiologic intraocular pressure (IOP) was restored with a large, partial air bubble left in the anterior chamber. Final centration of the artificial iris was evaluated by senior surgeons and adjusted as needed (K.M.M. at UCLA, D.R.H. at MEC).

In all cases, necessary supplemental procedures were performed, such as superficial keratectomy, subtotal vitrectomy, native iris trimming/iridectomy, glaucoma tube shunt modification, and temporary tarsorrhaphy.

Data Collection

To identify patients who meet the eligibility criteria, an exhaustive chart review at both clinical centers was performed using CPT codes and text search terms of "Descemet stripping," "DSEK," "DSAEK," and "artificial iris". Patients were matched and manually verified to have undergone both procedures by 2 of the authors (P.D.C., T.M.T.). Data collected included demographic information, medical history, preoperative state of the eye including the lens and cornea, ocular history, medications, previous ocular surgeries and details, and subjective testing as well as supplemental diagnostic testing such as specular microscopy. Data were acquired from preoperative visits and postoperative follow-up examinations on day 1, week 1, week 2, month 1, month 3, month 6, year 1, and once every 6 months thereafter if the patient kept follow-up appointments. The baseline was defined as the state of the eye at the initial evaluation for CAI implantation before any surgical intervention, and the final follow-up was defined as the state of the eye at the last examination of record at the time of data collection for this study, which ended May 15, 2023.

Safety and Efficacy Outcomes

Safety measures included loss of CDVA, changes in ECC, increases in IOP, development or progression of glaucoma as documented by formal perimetry and optical coherence tomography, intraoperative and postoperative complications, and secondary surgical interventions directly or indirectly related to the CAI and DSEK surgeries. Safety measures were compared between baseline and postoperative year 1. An increase in IOP was defined as IOP >24 mm Hg or an increase of 8 mm Hg from baseline. DSEK graft rejection was defined as the presence of white blood cells in the anterior chamber, not present at baseline; inflammatory precipitates on the donor endothelium; and/or an acute increase in corneal thickness evaluated by slitlamp biomicroscopy and handheld pachymetry (Pachmate; DGH Technology, Exton, PA).

Cosmesis was graded at postoperative month 3 following DSEK by the surgeon who implanted the CAI at each site; the Global Aesthetic Improvement grading scale was used and ranged from worse (1), no change (2), improved (3), much improved (4), to very much improved (5)[20]; the scale incorporated 1 objective measure of centration within 1 mm of the optical axis, which was required to achieve a grade of 3 (improved). Efficacy was assessed as corneal clarity at postoperative year 1 after DSEK (the primary DSEK if multiple DSEKs were performed) and improvement in CDVA at postoperative month 1, 3, 6, and 12 after primary DSEK.

Statistical Analysis

Data were stored and managed on Microsoft Excel (Microsoft Corp, Redmond, WA) and imported into STATA 17 (StataCorp, College Station, TX) for parametric and nonparametric significance testing and regression modeling. A P value <0.05 was used as a cutoff for statistical significance.

RESULTS

Eight eyes from UCLA and 31 eyes from MEC met the inclusion criteria for a total of 39 eyes of 39 patients. The mean follow-up interval was 27.7 months (SD 19.2, range 12.2–117.4 months).

TABLE 1. Patient Demographics and Baseline Clinical Characteristics (N = 39 Eyes)

Variable	Data Point
Age in yr: Mean (SD), range	55.3 (17.7), 18–86
Female, n (%)	17 (43.6)
Right eye, n (%)	20 (51.3)
Ethnicity (%)	
White	36 (92.3)
Hispanic	2 (5.1)
Black	1 (2.6)
Etiology of iris defect, n (%)	
Blunt globe trauma	13 (33.3)
Iatrogenic	12 (30.8)
Open globe injury	6 (15.4)
Congenital aniridia	3 (7.7)
Anterior dysgenesis	2 (5.1)
Iridocorneal endothelial syndrome	2 (5.1)
Iris coloboma	1 (2.6)
Condition of the iris at baseline, n (%)	
Complete aniridia	13 (33.3)
Complete mydriasis	9 (23.1)
Partial aniridia (iris loss of 75%–99%)	8 (20.5)
Partial aniridia (iris loss of 50%–74%)	8 (20.5)
Iridodialysis (iris separation of 75%–99%)	1 (2.6)
Corneal status at baseline, n (%)	
Microcystic corneal edema	33 (84.6)
Bullous keratopathy	11 (28.2)
Corneal scar	7 (17.9)
Epithelial basement membrane dystrophy	4 (10.3)
Fuchs endothelial corneal dystrophy	2 (5.1)
Band keratopathy	2 (5.1)
Limbal stem cell deficiency	1 (2.6)
Lens status, n (%)	
Aphakic	12 (30.8)
Posterior chamber IOL (dislocated)	12 (30.8)
Posterior chamber IOL (not dislocated)	5 (12.8)
Phakic with moderate cataract	5 (12.8)
Phakic with traumatic cataract	4 (10.3)
Anterior chamber IOL (malposition)	2 (5.1)
Posterior segment status at baseline, n (%)	
Postvitrectomy	9 (23.1)
Epiretinal membrane	8 (20.5)
Cystoid macular edema	2 (5.1)
Macular scar	1 (2.6)
Foveal hypoplasia	1 (2.6)
Myopic degeneration	1 (2.6)
Nonexudative age-related macular degeneration	1 (2.6)
Glaucoma pre-DSEK, n (%)	23 (59.0)
Medical management only, n (%)	13 (33.3)
Tube shunt or trabeculectomy, n (%)	10 (25.6)

Demographic and Surgical Details

Patient demographics, baseline condition of the eyes, and surgical details are provided in Table 1. The mean age at the time of CAI surgery was 55.3 years (SD 17.7), 43.6% were female, and most patients identified as White (92.3%). The most common etiologies of iris defects were blunt trauma (33.3%) and iatrogenic surgical trauma (30.8%), with near-complete or complete lack of iris tissue in 56.4% of eyes. All eyes had visually significant corneal edema from endothelial failure, and 28.2% had bullae. Most eyes had dislocated posterior chamber IOLs (30.8%) or were aphakic (30.8%). Nine eyes (23.1%) were postvitrectomy. Most eyes (59.0%) had glaucoma, and 25.6% of eyes had undergone tube shunt implantation or trabeculectomy before DSEK.

Twenty seven of the 39 eyes (69.2%) underwent concurrent CAI implantation and DSEK, all at MEC (Table 2). All eyes at UCLA and 4 eyes at MEC underwent staged DSEK after CAI implantation with a mean duration of 80.8 months (range 5.8–110.8) between CAI implantation and DSEK. No intraoperative complications occurred. The mean donor age was 49.1 years (SD 16.6), the mean donor ECC was 2849 cells/mm^2 (SD 289), and the mean DSEK graft size was 7.75 mm (range 6.0–8.5). Most CAIs (82.1%) were suture-fixated to the sclera, and most IOLs (76.9%) were fixated by suturing them to the CAI. A concurrent vitrectomy was performed in 79.5% of eyes and superficial keratectomy in 56.4% to enable adequate visualization. Concurrent Ahmed glaucoma tube shunt (New World Medical, Rancho Cucamonga, CA) implantation was performed in 5.1% of eyes by a glaucoma specialist, and none of these cases led to intraoperative decentration of the CAI or prohibited CAI centration. Trabecular meshwork bypass stents (iStent, Glaukos Corp, Laguna Hills, CA) were placed concomitantly in 5.1% of eyes.

TABLE 2. Operative Details (N = 39 Eyes)

Variable	Data Point
Staged DSEK after CAI, n (%)	12 (30.8)
Duration between CAI and DSEK in months: Mean (SD), range	80.8 (35.2), 5.8–110.8
Concurrent DSEK and CAI, n (%)	27 (69.2)
DSEK size in mm: mean (range)	7.75 (6.0–8.5)
DSEK insertion (%)	
Suture pull through with retention	38 (97.4)
Busin glide with retention	1 (2.6)
Donor age in yr: Mean (SD), range	49.1 (16.6), 18–77
Donor graft ECC in cells/mm^2: Mean (SD)	2849 (289)
IOL used, n (%)	
Alcon CZ70BD (1-piece PMMA) sutured to CAI	23 (59.0)
J&J Tecnis (1-piece acrylic) in the bag	6 (15.4)
B&L P366UV (1-piece PMMA) sutured to CAI	5 (12.8)
Alcon CR70BU (1-piece PMMA) sutured to CAI	2 (5.1)
Staar AQ2010V (3-piece silicone) in the bag	1 (2.6)
J&J Sensar AR40M (3-piece acrylic) in the bag	1 (2.6)
Alcon SN60WF (1-piece acrylic) in the bag	1 (2.6)
CAI implantation, n (%)	
Sutured to the sclera	32 (82.1)
Injected into the bag	7 (17.9)
Concurrent procedures with DSEK, n (%)	
Subtotal vitrectomy	31 (79.5)
Superficial keratectomy	22 (56.4)
IOL exchange	10 (25.6)
Removal of remaining iris tissue	10 (25.6)
Cataract extraction	9 (23.1)
Placement of a trabecular meshwork bypass stent	2 (5.1)
Ahmed glaucoma implant	2 (5.1)
Removal of unsafe cosmetic artificial iris	1 (2.6)

B&L, Bausch & Lomb; J&J, Johnson & Johnson; PMMA, polymethyl methacrylate.

Safety Outcomes

Safety data are summarized in Table 3. The median preoperative CDVA was 1.0 logMAR (range 0.3–2.3), which improved to median 0.7 (range 0.0–3.0) at year 1 (Fig. 1A, $P = 0.0047$). The proportions of eyes with improvements in CDVA were 51.3%, 66.7%, 61.5%, and 64.1% at postoperative months 1, 3, 6, and 12, respectively. The proportion of patients with CDVA Snellen 20/40 or better was significantly higher at year 1 and final follow-up than at baseline ($P = 0.015$). In eyes that achieved better than 20/200 CDVA at postoperative month 1, the incidence rate of losing vision worse than CDVA 20/200 was 0.0078 per person-month (95% confidence interval [CI], 0.0035–0.017; Fig. 1B). Permanent vision loss occurred in 25.6% of eyes while moderate (1–2 Snellen lines) and severe (>2 Snellen lines) vision loss occurred in 17.9% and 7.7% of eyes, respectively. Glaucoma progression accounted for permanent vision loss in 90.0% of affected eyes and all 3 eyes with severe vision loss.

Postoperative Complications

Table 3 summarizes postoperative complications. The most common postoperative complication was secondary IOP elevation, occurring in 26 eyes (66.7%); despite this, the mean IOP at year 1 of 17.1 mm Hg was not increased from the baseline IOP of 17.7 mm Hg ($P = 0.637$). Glaucoma progression was documented in 11 eyes (28.2%), and 6 eyes (15.4%) required operative management. Of those with glaucoma tube shunts, 5.1% required revision after DSEK. Transient corneal edema responding to medical therapy and DSEK graft detachment requiring rebubbling occurred in 14 eyes (35.9%) and 8 eyes (20.5%), respectively. Graft detachment was not significantly different between staged procedures (4 of 12, 33.3%) and concurrent procedures (4 of 27, 14.8%) ($P = 0.196$). Infectious keratitis occurred in 4 eyes (10.3%) (2 bacterial, 2 herpetic keratitis) occurring on average 272.5 days after DSEK and unrelated to the donor grafts. All cases were treated with resolution within 2 to 5 months without severe complications, although a case of recurrent herpetic keratitis that led to a secondary graft rejection required long-term medical management, but did not result in graft failure. Chronic anterior uveitis occurred in 4 eyes (10.3%), requiring prolonged treatment with topical corticosteroids; none of these 4 eyes had a history of anterior uveitis, and all had their CAIs sutured. Hyphemas developed in 2

TABLE 3. Safety and Efficacy of DSEK in Eyes With CustomFlex Artificial Irises (N = 39 Eyes)

Variable	Data Point	Significance Testing
Length of follow-up in months: Mean (SD), range	27.7 (19.2), 12.2–117.4	—
Baseline CDVA in logMAR:	1.3 (0.75), 0.3–2.3	$P = 0.0047$ (Wilcoxon matched pairs signed-rank test, difference baseline and postoperative year 1)
Mean (SD), range	1.0 (0.5–2.0)	
Median (IQR)		
Postoperative year 1 CDVA in logMAR:	0.92 (0.80), 0–3.0	
Mean (SD), range	0.7 (0.3, 1.18)	
Median (IQR)		
Improvement in CDVA at month 1, n (%)	20 (51.3)	—
Improvement in CDVA at month 3, n (%)	26 (66.7)	—
Improvement in CDVA at month 6, n (%)	24 (61.5)	—
Improvement in CDVA at year 1, n (%)	25 (64.1)	—
Permanent moderate vision loss (1–2 Snellen lines), n (%)*	7 (18.0)	—
Glaucoma progression	6 (15.4)	—
Macular hole progression	1 (2.6)	—
Permanent severe vision loss (>2 Snellen lines), n (%)*	3 (7.7)	—
Glaucoma progression	3 (7.7)	—
Baseline IOP: Mean (SD), range	17.7 (5.4), 8–27	$P = 0.637$ (two-sided t test, difference baseline and postoperative year 1)
Postoperative year 1 IOP: Mean (SD), range	17.1 (7.7), 5–46	
Donor ECC in cells/mm^2: Mean (SD)	2849 (289)	$P < 0.001$ (two-sided t test, difference donor and postoperative year 1)
Postoperative year 1 ECC in cells/mm^2: Mean (SD)	2113 (473)	
Approximated ECC loss per year (percentage): Mean (SD)	−13.5% (11.6)	—
Baseline CCT in μm: Mean (SD)	757 (179)	—
Postoperative year 1 CCT in μm: Mean (SD)	695 (106)	
Postoperative complications, n (%)		—
Secondary IOP elevation	26 (66.7)	—
Secondary glaucoma (new diagnosis)	3 (7.7)	—
Glaucoma progression not requiring surgery	5 (12.8)	—
Glaucoma progression requiring tube shunt or CPC for patients already with shunts	6 (15.4)	—
Glaucoma drainage implant problems requiring revision	2 (5.1)	—
Corneal edema	14 (35.9)	—
Cystoid macular edema	12 (30.8)	—
DSEK graft partial detachment requiring rebubbling	8 (20.5)	—
Infectious keratitis (etiologies listed below)	4 (10.3)	—
Herpes simplex virus	2 (5.1)	—
Staphylococcus aureus	1 (2.6)	—
Staphylococcus epidermidis	1 (2.6)	—
Chronic anterior uveitis	4 (10.3)	—
Hyphema	2 (5.1)	—
Hypotony	2 (5.1)	—
Endothelial rejection, n (%)	8 (20.5)	—
Time from DSEK in months: Mean (SD)	12.6 (11.5)	—
Secondary graft failure, n (%)	11 (28.2)	—
Time from DSEK in months: Mean (SD)	39.7 (27.9)	—
Cornea clear at postoperative year 1, n (%)	32 (82.0, 95% CI, 66.3–91.4)	
Improved cosmesis at postoperative month 3, n (%)	34 (87.2)	—

*This does not include temporary causes of vision loss, such as secondary graft rejection or SGF, which were treatable and reversible.
CPC, cyclophotocoagulation.

eyes (5.1%); 1 eye eventually required repeat DSEK for endothelial blood staining. Postoperative cystoid macular edema (CME) developed in 12 eyes (30.8%) and was medically treated with topical nonsteroidal anti-inflammatory agents and topical corticosteroids. Two of the 12 eyes had a history of CME; thus, there were 10 eyes that developed CME de novo (25.6%).

Endothelial rejection occurred in 8 eyes (20.5%) at a mean duration of 12.6 months (SD 11.5) after primary DSEK. Secondary graft failure (SGF) occurred in 11 eyes (28.2%) at

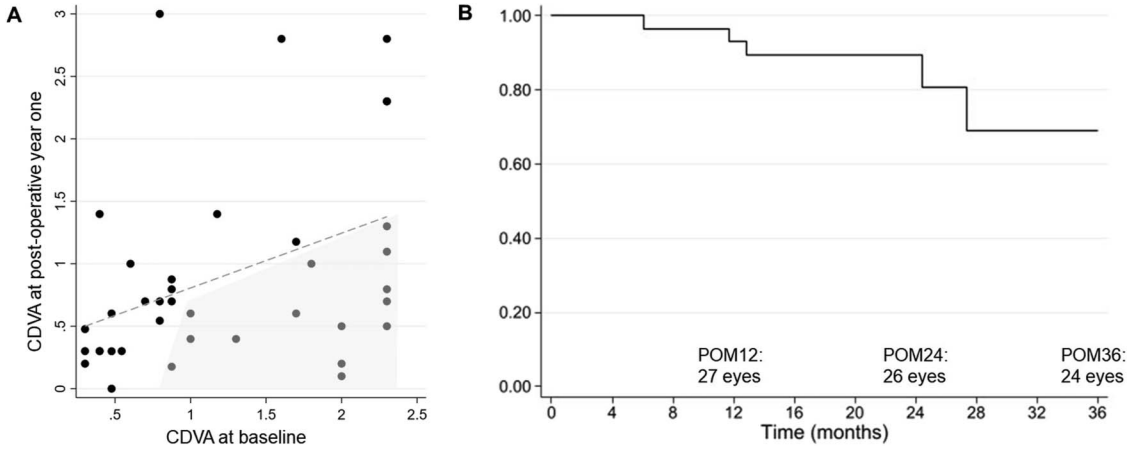

FIGURE 1. VA after DSEK (N = 39 eyes). A, Visual outcomes assessed between baseline and postoperative year 1. Scale in logMAR. Correlation coefficient: 0.41, $P = 0.0047$. Shaded area: eyes with highest margin of visual improvement. B, Kaplan–Meier curve for the 29 eyes that obtained VA of 20/200 or better at postoperative month 1 demonstrating the percentage that retained 20/200 up to 36 months after surgery. Incidence rate: 0.0078 per person-month (95% CI, 0.0035–0.017).

a mean duration of 39.7 months (SD 27.9) after primary DSEK, including 5 of the 8 eyes (62.5%) that developed endothelial rejection. Among 34 of 39 eyes for which data were available, the percentage of ECC loss was approximately 13.5% per year (SD 11.6), using the donor postpreparation ECC as the baseline. The decrease in mean ECC from baseline (donor graft) to postoperative year 1 was significant ($P < 0.001$). The postoperative year 1 central corneal thickness (CCT) was slightly lower than baseline with mean 695 versus 757 μm ($P = 0.121$). Ten of 11 cases of SGF were treated with at least 1 repeat DSEK while 1 is under observation.

Efficacy Outcomes

The primary outcome measure was DSEK graft survival at postoperative year 1 (graft clarity), and the rate in our

TABLE 4. Factors Associated With Graft Survival at Postoperative Year 1 After DSEK in Eyes With CustomFlex Artificial Irises (N = 39 Eyes)

	Univariate Logistic Regression, Odds Ratio (95% CI, *P*)	Multivariate Logistic Regression, Odds Ratio (95% CI, *P*)
Age of patient	0.95 (0.89–1.01), 0.102	0.99 (0.98–0.1.00075), 0.083
Female sex	0.51 (0.098–2.68), 0.429	0.89 (0.72–1.12), 0.340
Baseline CDVA	0.26 (0.069–0.95), 0.042	0.86 (0.74–1.0031), 0.055
Etiology: any trauma	1.51 (0.29–7.87), 0.624	—
Etiology: open globe trauma	1.38 (0.14–13.75), 0.781	—
Cornea baseline status with bullous keratopathy	1.26 (0.94–1.69), 0.115	—
Lens baseline status with posterior chamber IOL dislocation or subluxation	0.34 (0.064–1.82), 0.207	—
Lens baseline status with aphakia	1.13 (0.19–6.89), 0.889	—
Glaucoma at baseline	0.30 (0.065–0.084), 0.014	0.79 (0.62–0.99), 0.042
Baseline CCT	1.0038 (0.99–1.010), 0.253	—
ECC loss per year	0.42 (0.29–6.25), 0.698	—
Vitrectomized at baseline	1.14 (0.19–6.89), 0.889	—
Age of DSEK graft donor	0.99 (0.95–1.050), 0.970	—
ECC of DSEK graft	0.99 (0.99–1.0020), 0.524	—
Concurrent DSEK and CAI	0.88 (0.14–5.34), 0.889	—
Complication: any	0.76 (0.13–4.59), 0.768	—
Complication: IOP elevation	0.28 (0.030–2.59), 0.261	—
Complication: glaucoma progression requiring tube shunt or CPC	0.21 (0.14–2.56), 0.224	—
Complication: endothelial rejection	0.58 (0.089–3.72), 0.563	—
Complication: secondary graft failure	0.98 (0.16–5.98), 0.981	—

CPC, cyclophotocoagulation.

series was 82.0% (95% CI, 66.3–91.4). In the multivariate logistic regression model, only glaucoma at baseline was associated with lower odds of graft clarity at postoperative year 1 ($P = 0.042$, Table 4). A lower baseline CDVA (higher logMAR value) was significantly associated with lower odds of graft clarity in the univariate regression only. Concurrent CAI and DSEK and trauma as the etiology of aniridia were not associated with a decreased odds of graft clarity at postoperative year 1 and was borderline associated with a lower rate of any complications (odds ratio 0.11, 95% CI, 0.01–1.008, $P = 0.051$). At postoperative month 3, 87.2% of eyes had good CAI centration (<1 mm decentration from the optical axis) and achieved a cosmesis grade of improved or higher.

Non-Traumatic Etiology of Aniridia

Analyzing by non–trauma-related etiologies (n = 8 eyes [20.5% of all eyes]: congenital aniridia, anterior segment dysgenesis, ICE syndrome) versus trauma-related etiologies (n = 31 eyes), the mean change in CDVA from baseline compared with postoperative year 1 after DSEK was worse for non-trauma etiologies (logMAR +0.481) versus logMAR −0.553 for traumatic etiologies ($P = 0.001$). Glaucoma progression as a postoperative complication was much more likely in the non-trauma group (odds ratio 14.5, 95% CI, 1.97–35.64, $P = 0.009$). Endothelial rejection occurred in 19.4% of trauma eyes and 25% of non-trauma eyes ($P = 0.725$). SGF occurred in 25.8% of trauma eyes at a mean duration of 41.3 months (SD 31.7) and 37.5% of non-trauma eyes at a mean duration of 35.4 months (SD 18.5; $P = 0.515$). Graft clarity at postoperative year 1 after DSEK was not significantly worse in the non-trauma etiologies (odds ratio 0.24, 95% CI, 0.042–1.46, $P = 0.113$).

DISCUSSION

We report, in the largest cohort to date, the outcomes of DSEK in eyes with CAI implants with short to intermediate-term follow-up. At the time of working on this report, there were only 2 other reports related to this study. The senior surgeons of this study previously described DSEK outcomes after Ophtec 311 artificial iris IOL implantation, with 75% survival at 1 year and 25% survival at the 2-year mark.[26] Ang and Tan[27] recently reported success with DMEK in 5 eyes performed between 1 and 5 months after CAI implantation; all 5 eyes had clear corneas at the final follow-up between 8 and 12 months postoperatively. The VA in the cohort recruited by Ang and Tan was limited in one eye by an epiretinal membrane with persistent CME and in another eye by glaucoma progression. The frequent presence of comorbid, visually limiting disorders in these eyes results in the limited utility of CDVA as an outcome measure; thus, the FDA trial for approval of the CAI device met its end point for improvement in visual function primarily through reduction in photophobia and glare symptoms.[20]

Our study's primary efficacy end point was graft clarity at 1 year. The 82.0% graft survival at 1 year that we report is significantly lower than a pooled average of 98.7% (95% CI, 98.3–99.0) among 889 eyes from 13 previously published series ($P < 0.001$, see Supplement Table, Supplemental Digital Content 1, http://links.lww.com/ICO/B660).[28] No eyes in these reports had an implanted artificial iris, and only 1.3% of the 889 eyes in the published series could be considered complex (ie, secondary IOLs, aphakia, severely traumatized, abnormal anterior segment anatomy).

Severe vision loss (>2 Snellen lines) was our primary safety end point. This occurred in 7.7% of eyes, and all were due to progression of glaucomatous optic neuropathy. This did not occur in any eye in the main FDA CAI approval trial,[20] although the percentage is similar to the 7.1% of eyes that developed severe vision loss following CAI and PK reported by 2 of this study's senior authors.[23] Still, there was a statistically significant and clinically meaningful improvement in CDVA at postoperative year 1 and at the final visit. Moderate vision loss (1–2 Snellen lines) was primarily due to progression of glaucoma. Secondary IOP elevation and secondary glaucoma were the most frequent complications in our study. Several postulated mechanisms for secondary glaucoma include corticosteroid response and surgically induced inflammation in eyes with an already compromised trabecular meshwork. In the American Academy of Ophthalmology's seminal DSEK report, corticosteroid response was highlighted as a common post-DSEK complication.[28] While our rate of secondary glaucoma de novo was low at 7.7%, a total of 28.2% of eyes had documented glaucoma progression with 15.4% of eyes requiring operative intervention. This proportion is significantly higher than the average of 3% among routine DSEK.[28] Most of these eyes already had a compromised trabecular meshwork, and the majority had glaucoma at baseline; thus, IOP elevations in the postoperative period were to be expected, as was a common occurrence in the CAI FDA approval trial (23.2% of all eyes in the FDA trial vs. 66.7% in our series).[20] Eyes with non-traumatic etiologies of aniridia fared worse from a glaucoma progression standpoint and loss of CDVA at postoperative year 1. Although the primary outcome of graft survival was not significantly different, these eyes have a significantly different postoperative course and require closer monitoring and significant counseling if CAI implantation and DSEK are offered.

Compared with a series reporting outcomes of DSEK for more routine or purely endothelial disease indications, our study had a higher rate of endothelial rejection at 20.5% versus a pooled rate of 4.3% (95% CI, 2.1–6.6) among 1582 eyes (see Supplement Table, Supplemental Digital Content 1, http://links.lww.com/ICO/B660).[28] Most eyes with endothelial rejection in our cohort progressed to SGF. This is expected in these eyes with known risk factors of SGF, such as prior glaucoma surgery or severe anterior segment abnormalities.[29–33] The 13.5% mean annual ECC loss that we report in this series is on the lower end of the spectrum in prior reported series of routine DSEK,[28,34] but is significantly higher than the 7.2% mean annual ECC loss in the FDA CAI trial.[20] In addition to these risk factors, eyes that are candidates for CAI implantation may be predisposed to graft rejection as healthy iris tissue has a role in immune privilege, and its removal disrupts the natural blood–aqueous barrier;

this leads to far more inflammatory proteins and cytokines in the aqueous humor, which have been associated with corneal graft rejection.[35–37]

Other common complications in our study included CME, graft detachment, infectious keratitis, and chronic anterior uveitis. The CME incidence of 25.6% in our series is significantly higher than 2.9% reported in the CAI FDA trial (CAI without DSEK)[20] while CME after DSEK without CAI has been reported at 12.7% in the largest consecutive series to date.[38] In addition, CME in the setting of scleral suture fixation of an IOL is a well-recognized complication, even in eyes without a history of CME, and the incidence in these eyes without DSEK or CAI is 16.7%.[39,40] An adequate subtotal anterior vitrectomy, which was performed in 80% of eyes in our cohort, likely prevented more cases of CME. Graft detachment was anticipated given the movement of the air bubble placed intraoperatively to the posterior segment given the lack of a complete lens–iris diaphragm in these eyes. Given the risk of the DSEK graft following the air into the posterior chamber in the event of detachment, we recommend the placement of a retention suture in all cases.

While the concurrent CAI and DSEK surgical approach was noninferior to a staged approach in our study, the staged approach with CAI before DSEK has 3 major advantages: 1) It allows resolution of intraoperative bleeding from iris manipulation and iridectomy, 2) it allows resolution and optimal control of inflammation, and 3) it enables better control of secondary IOP elevation after CAI implantation. A staged approach should enable more stability with air bubble pressurization as well, yet in our study, this did not significantly reduce the risk of postoperative minor graft detachment. All of these factors can negatively affect DSEK graft survival and should be considered if staging is a possibility. In our cohort, if patients' eyes did not have endothelial decompensation at the time of CAI evaluation, then DSEK was not performed concurrently.

This study is limited by the heterogeneity of the eyes that were included, although this is likely unavoidable given the fact that CAI implantation remains relatively uncommon and the indications for implantation are quite varied. It is hoped that a sizeable number of eyes and consistent surgical and medical practices among 3 senior surgeons with vast experience in CAI implantation and DSEK surgery mitigate some of the patient-related variations.

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