Safety and Efficacy of Sequential Intracorneal Ring Segment Implantation and Cross-linking in Pediatric Keratoconus

YOUSSEF ABDELMASSIH, SYLVAIN EL-KHOURY, ALI DIRANI, RAFIC ANTONIOS, ALI FADLALLAH, CAROLE G. CHERFAN, ELIAS CHELALA, AND ELIAS F. JARADE

• PURPOSE: To evaluate the safety and visual outcome of intracorneal ring segment (ICRS) implantation followed by cross-linking in pediatric keratoconus patients.
• DESIGN: Retrospective interventional case series.
• METHODS: This retrospective study included pediatric patients (aged ≤14 years) with keratoconus and poor corrected distance visual acuity (CDVA) that underwent ICRS implantation and cross-linking (CXL). ICRS were inserted under topical anesthesia after creating a corneal tunnel with a femtosecond laser. Cross-linking was performed 1 month subsequently. Records were reviewed and data collected preoperatively and at 6 months, 1 year, 2 years, and 4 years postoperatively.
• RESULTS: Twelve patients (17 eyes; 10 male, 2 female) aged 9–14 years (mean age 12.3 years) received ICRS implantation followed by CXL. Follow-up times ranged from 6 months to 4 years after surgery. At the 6-month follow-up all eyes were evaluated; at the 1-year, 2-year, and 4-year follow-up 11, 10, and 7 eyes were evaluated, respectively. At the 6-month follow-up, mean CDVA in comparison to preoperative levels improved significantly ($P = .001$) from 0.30 ± 0.19 logMAR to 0.12 ± 0.1 logMAR; mean uncorrected distance visual acuity (UDVA) also improved significantly from 0.90 ± 0.50 logMAR to 0.43 ± 0.31 logMAR. A significant decrease in both keratometry readings and spherical equivalent (from −4.0 to −1.56 diopters) was also noted after ICRS insertion. At the 1-year, 2-year, and 4-year follow-up refractive values remained relatively stable in comparison to the 6-month follow-up, except for a minor but significant improvement in cylinder and, at 4 years, in UDVA. All patients tolerated the surgery well and no intraoperative or postoperative complications were reported, except for 1 ring segment that had to be removed after 2 years owing to vascularization and corneal thinning.
• CONCLUSION: ICRS implantation is a safe and effective procedure for visual rehabilitation in children with keratoconus and poor CDVA. (Am J Ophthalmol 2017;178:51–57. © 2017 Elsevier Inc. All rights reserved.)

AJO.com Supplemental Material available at AJO.com.

Accepted for publication Mar 13, 2017.

From the Faculty of Medicine, Saint Joseph University, Beirut, Lebanon (Y.A., S.E.-K., A.D., A.F., E.C.); Beirut Eye Specialist Hospital, Beirut, Lebanon (Y.A., S.E.-K., A.D., A.F., C.G.C., E.F.J.); Faculty of Medicine, American University of Beirut, Beirut, Lebanon (R.A.); and Mediclinic Dubai Mall, Dubai, United Arab Emirates (E.F.J.).

Inquiries to Elias F. Jarade, Beirut Eye Specialist Hospital, Al-Mathaf Square, Beirut, Lebanon; e-mail: ejarade@yahoo.com

KERATOCONUS IS A PROGRESSIVE, NONINFLAMMATORY thinning disorder of the cornea that is most frequently diagnosed after the age of adolescence. Patients usually present for a deteriorated visual acuity secondary to irregular astigmatism.[1,2] In some cases, however, corneal ectasia may even begin in childhood.[3] At these ages, it is often underdiagnosed. Compared to adults, keratoconus in children progresses faster and is usually more severe at diagnosis.[4,5] Hence, especially in young patients a prompt management to contain the progression of the disease and to enhance visual performance is crucial for the outcome. This treatment necessity often presents a challenge to the corneal surgeon, as the established methods available for keratoconus treatment and vision rehabilitation in adults are less effective when they are applied to children. Treatment options for keratoconus in adults include spectacles, contact lenses, intracorneal ring segment (ICRS) and implantable collamer lens (ICL) implantation, corneal collagen cross-linking (CXL), penetrating keratoplasty (PKP), and deep anterior lamellar keratoplasty (DALK).[4,5] In children, conservative measures, such as spectacles or contact lenses, are not well tolerated, are difficult to fit, and are often not enough to obtain satisfactory visual acuities. Furthermore, they do not stop the progression of the disease. In children, CXL provides disease stabilization and, sometimes, improvement in visual acuity and in spherical aberrations.[6–8] PKP, however, is challenging at this age and is associated with a higher risk of graft failure than in adults.[9–11] As an alternative to PKP, DALK can be performed in advanced cases of pediatric keratoconus. It exhibits a lower risk of graft rejection, but likewise bears a substantial risk for postoperative complications, such as interface vascularization, ulcers, and infections.[5]

Considering the reversibility, the adjustability, and the efficacy in improving corrected distance visual acuity (CDVA) in adults,[12–14] ICRS implantation seems to be a viable option for the treatment of keratoconus in children. Nonetheless, until the present, few authors

0002-9394/$36.00
http://dx.doi.org/10.1016/j.ajo.2017.03.016

have reported on the outcome of ICRS implantation in children (≤16 years old).[15,16]

Following a report that was presented by our study group on the incidence of pediatric keratoconus and a suggested treatment algorithm that includes ICRS implantation in cases of poor CDVA or high anisometropia,[3] the aim of this paper is to retrospectively evaluate the long-term safety and efficacy of ICRS implantation followed by CXL for keratoconus patients ≤14 years of age including a larger set of patients.

METHODS

THIS RETROSPECTIVE INTERVENTIONAL CASE SERIES included 17 eyes of 12 children (10 male, 2 female) with keratoconus who underwent ICRS implantation followed by CXL. All surgeries were performed by the same surgeon (E.F.J.) at the Beirut Eye Specialist Hospital in Beirut, Lebanon, between May 2006 and December 2015. This study was approved by the Institutional Review Board and complied with the Declaration of Helsinki. The risks, benefits, and treatment alternatives were thoroughly explained to the patient's parents preoperatively and written informed consent was obtained. We included all children who had previously undergone an ICRS implantation followed by CXL and who were aged ≤14 years at the time of the intervention. None of the children had central corneal scarring, previous keratitis, peripheral marginal degeneration, previous corneal or intraocular surgeries, or any autoimmune or connective tissue disease.

Preoperative and postoperative examinations comprised a complete ophthalmic evaluation including assessment of uncorrected distance visual acuity (UDVA), CDVA, manifest and cycloplegic refractions, anterior and posterior segment evaluation with dilated fundus examination, and keratometry measured either by Pentacam (Oculus Optikgerate GmbH, Wetzlar, Germany), Tomey TMS-4a (Tomey Corp, Nagoya, Japan), or Galilei Dual Scheimpflug analyzer (Ziemer, Port, Switzerland). A total corneal pachymetric map was determined using either an optical (Pentacam) or an ultrasound pachymeter.

All patients were examined on the first postoperative day and 1 week, 1 month, and 6 months after surgery. Thereon, patients were advised to abide by regular ophthalmologic examinations every 6 months.

Data were collected and statistically analyzed (SPSS version 22.0; SPSS Inc, Chicago, Illinois, USA) at baseline and at the 6-month, 1-year, 2-year, and 4-year follow-up. Keratoconus was graded with stages I to IV according to the Amsler-Krumeich classification. Descriptive statistics were reported as mean ± standard deviation for continuous variables and as percentage for categorical variables. A Wilcoxon rank-sum test was used to compare the different continuous parameters. P value $< .05$ was considered to be statistically significant. At each follow-up, only patients that had reached this follow-up were included in the statistical analysis.

Indication for surgery was according to "Jarade's nomogram" for the treatment and visual rehabilitation in pediatric keratoconus, which is the personal treatment nomogram of the present surgeon (E.J.). ICRS implantation was indicated in case of poor CDVA or in case of significant anisometropia. The early results of some of the cases included in this paper have already been published in a sub-chapter of the above-mentioned publication.[3] The present paper, however, includes a larger patient cohort and long-term outcomes.

• **SURGICAL TECHNIQUE:** Before the ICRS insertion, 2 drops of topical anesthetic (oxybuprocaine 0.4%; Bausch & Lomb Inc, Rochester, New York, USA) were instilled into the eye. A 360-degree tunnel was created at the mid-peripheral cornea and with a mean of 70% of depth of the thinnest area; the minimum corneal tissue depth under the ring was assumed to be at least 100 μm. According to the topo-guided nomogram for ICRS insertion in keratoconus,[17] the incision site was chosen in order to allow the insertion of the thickest ring segments underneath the steepest area of the cornea. The number of implanted rings (1 or 2) and ring thickness largely depended on the refractive errors to be treated. In the case of a decentered cone and a low CDVA, only 1 ring was implanted and placed under the steep area of the cornea in order to regulate the surface of the corneal and herewith improve CDVA. Two rings were implanted in central cones with high keratometric readings in order to decrease spherical equivalent (SE) and to improve UDVA. The thickest ring was inserted below the steepest area of the cornea in order to maximize the effect. If the cone was pellucid in shape, located at the periphery, and larger than 180 degrees, a 210-degree Keraring segment (Mediphacos, Belo Horizonte, Brazil) was used. If it was nipple-shaped, INTACS segments (Addition Technology Inc, Des Plaines, Illinois, USA) were used.[17] All patients were operated under topical anesthesia and with the help of the Intralase FS60 (AMO Inc, Santa Ana, California, USA) femtosecond laser to create the ring pockets.

Peripheral pachymetry was used in all cases to ensure a sufficient corneal thickness and a ring segment placement at an appropriate depth. Either INTACS segments with a thickness ranging from 0.15 mm to 0.45 mm or Keraring segments with a thickness ranging from 0.25 mm to 0.35 mm and a size of 210 degrees were inserted. After inserting the ring segments, the tunnel was irrigated with a gentamycin–saline solution (concentration of 8 mg/cc), and the incision was sutured with 10-0 nylon. Topical tobramycin 0.3%-dexamethasone sodium phosphate 0.1% (Tobradex; Alcon Laboratories Inc, Fort Worth, Texas, USA) were instilled into the eye 4 times daily for 10 days.

Standard epithelium-off CXL was performed 1 month after ICRS insertion and according to Wollensak and

TABLE 1. Preoperative Characteristics of Pediatric Keratoconus Eyes

KC Stage[a]	Eyes	Sphere	Cylinder	SE	UDVA	CDVA	K_{flat}	K_{steep}	K_{max}
I	3	−2.33	2.92	−0.88	0.27	0.09	42.67	46.67	50.13
II	10	−5.85	4.30	−3.70	1.11	0.33	45.17	49.02	53.79
III	1	−8.50	1.50	−7.75	1.30	0.30	43.00	45.72	50.50
IV	3	−8.42	3.08	−6.88	0.70	0.39	57.57	66.00	79.40

CDVA = corrected distance visual acuity (in logMAR); K = keratometric readings; KC = keratoconus; SE = spherical equivalent (in diopters); UDVA = uncorrected distance visual acuity (in logMAR).

[a]All 17 eyes were categorized according to keratoconus stage (Amsler-Krumeich classification) and analyzed for visual, refractive, and topographic parameters.

associates.[18] After application of topical anesthesia (proparacaine hydrochloride 0.5%), the central 9-mm corneal epithelium was removed, then soaked with 0.1% riboflavin–20% dextran for 30 minutes, followed by continuous instillation of the solution every 5 minutes while administrating ultraviolet A light (UV-X illumination system, version 1000; IROC AG, Zürich, Switzerland) for 30 minutes. Postoperatively, a soft contact lens was adjusted until the cornea completely re-epithelialized. Patients received topical antibiotics and steroids (gatifloxacin 0.3% [Zymar; Allergan Inc, Irvine, California, USA]) and tobramycin 0.3%–dexamethasone 0.1% (Tobradex; Alcon Laboratories, Inc, Fort Worth, Texas, USA), each 6 times daily for 1 week. After removal of the contact lens, loteprednol 0.5% eye drops (Lotemax; Bausch & Lomb, Inc, Rochester, New York, USA) were administered 5 times daily and slowly tapered over 5 weeks.

RESULTS

TWELVE PATIENTS (17 EYES; 10 MALE, 2 FEMALE) WITH MILD to severe keratoconus who underwent ICRS implantation between May 2006 and December 2015 were included in this study. The mean age was 12.3 years (range, 9–14 years). Three eyes had stage 1 keratoconus, 10 had stage 2, 1 had stage 3, and 3 had stage 4 (preoperative characteristics are shown in Table 1).

There were no problems associated with ICRS insertion and/or CXL treatment and all surgeries were well tolerated by all patients. No signs of corneal melting or infection were noted, and all rings remained in place with no migration or protrusion throughout the entire follow-up period, except for 1 ring segment that had to be removed after 2 years owing to vascularization and corneal thinning over the incision site. It was probably caused by a ring migration to the wound site that led to a secondary melting. The diagnosis was delayed because the patient's parents neglected the mild symptoms of eye irritation and redness.

The healing process after CXL was uncomplicated.

• **SIX-MONTH FOLLOW-UP:** At the 6-month follow-up after ICRS and CXL, 12 patients (17 eyes) were examined. All visual, refractive, and topographic parameters showed significant improvement compared with baseline and are displayed in Table 1. UDVA improved from 0.90 ± 0.50 logMAR preoperatively to 0.43 ± 0.31 logMAR postoperatively ($P = .001$) and CDVA improved from 0.30 ± 0.19 logMAR to 0.12 ± 0.1 logMAR postoperatively ($P = .001$). Sphere, cylinder, and SE decreased significantly by 3.18 diopters (D), 1.50 D, and 2.44 D, respectively. Keratometry (K) readings decreased significantly by 3.18 D for K_{flat}, 3.28 D for K_{steep}, and 3.77 D for K_{max} (Table 2).

• **ONE-YEAR FOLLOW-UP:** Eight patients (11 eyes) presented at the 1-year follow-up. All of the patients had attended the 6-month follow-up visit. Unfortunately, in 2 eyes of 2 patients, the topographic examination was not repeated at the 1-year follow-up. To this end, these 2 eyes were excluded from the statistical analysis of topographic parameters. None of the visual, refractive, and topographic parameters changed significantly between the 6-month and the 1-year follow-up, except for cylinder, which decreased from 2.34 ± 2.00 D to 1.52 ± 1.45 D ($P = .04$), and K_{max}, which slightly increased from 52.12 ± 5.57 D to 52.87 ± 5.84 D ($P = .04$) (Table 3).

• **TWO-YEAR FOLLOW-UP:** At the 2-year follow-up, 7 patients (10 eyes) showed up for ophthalmic examinations. All of these patients had been present at the 6-month and the 1-year follow-up. One eye of 1 patient did not have a topographic evaluation and was hence excluded from statistical analysis for these specific parameters. Between the 6-month and the 2-year follow-up, parameters showed relatively stable values, except for cylinder, which significantly decreased from 2.43 ± 2.07 D to 1.73 ± 1.84 ($P = .027$) (Table 4).

• **FOUR-YEAR FOLLOW-UP:** At the 4-year follow-up, 5 patients (7 eyes) returned to our clinic for ophthalmic evaluation. All of these patients had shown up at the 6-month visit. No long-term complications were noted in any eye and anterior slit-lamp examinations were inconspicuous.

TABLE 2. Visual, Refractive, and Topographic Parameters at the 6-month Follow-up[a] After Intracorneal Ring Segment and Corneal Cross-linking Compared With Preoperative Levels

Parameter	Number of Eyes Evaluated	Preoperative	6-month Follow-up	*P* Value
Sphere (D)	17	−5.83 ± 2.98	−2.65 ± 3.58	<.001
Cylinder (D)	17	3.68 ± 1.92	2.18 ± 1.64	.004
SE (D)	17	−4.00 ± 2.91	−1.56 ± 3.02	<.001
UDVA (logMAR)	17	0.90 ± 0.50	0.43 ± 0.31	.001
CDVA (logMAR)	17	0.30 ± 0.19	0.12 ± 0.1	.001
K_{flat} (D)	17	46.79 ± 5.83	43.61 ± 4.40	<.001
K_{steep} (D)	17	51.41 ± 7.30	48.13 ± 5.14	<.001
K_{max} (D)	17	57.47 ± 11.11	53.70 ± 6.29	.02
CCT (μm)	17	495 ± 44.41	475 ± 49.4	.001

CCT = central corneal thickness; CDVA = corrected distance visual acuity; D = diopters; K = keratometric readings; SE = spherical equivalent; UDVA = uncorrected distance visual acuity.

[a]All 17 eyes reached the 6-month follow-up and all parameters showed a significant improvement.

TABLE 3. Visual, Refractive, and Topographic Parameters Preoperatively and at the 6-month and 1-year Follow-up

Parameter	Number of Eyes Evaluated	Preoperative	6-month Follow-up	1-year Follow-up	*P* Value[a]
Sphere (D)	11	−6.05 ± 3.80	−2.84 ± 4.26	−2.43 ± 4.11	.26
Cylinder (D)[b]	11	3.30 ± 1514	2.34 ± 2.00	1.52 ± 1.45	.04
SE (D)	11	−4.40 ± 3.58	−1.67 ± 3.62	−1.60 ± 3.55	.29
UDVA (logMAR)	11	0.86 ± 0.55	0.34 ± 0.20	0.33 ± 0.28	.45
CDVA (logMAR)	11	0.40 ± 0.37	0.13 ± 0.08	0.14 ± 0.15	.77
K_{flat} (D)	9	46.52 ± 6.21	43.49 ± 5.29	43.75 ± 5.03	.34
K_{steep} (D)	9	49.58 ± 5.6	46.81 ± 4.28	47.02 ± 4.29	.14
K_{max} (D)[b]	9	55.53 ± 8.64	52.12 ± 5.57	52.87 ± 5.84	.04
CCT (μm)	9	484 ± 39.82	457 ± 49.72	468 ± 47.96	.05

CCT = central corneal thickness; CDVA = corrected distance visual acuity; D = diopters; K = keratometric readings; SE = spherical equivalent; UDVA = uncorrected distance visual acuity.

Only eyes that were examined at both the 6-month and the 1-year follow-up were included in the analysis. Two eyes did not receive topography at the 1-year visit and were hence excluded from the topographical analysis.

[a]*P* values show the significance in change between the 1-year and the 6-month follow-up.

[b]Only cylinder and K_{max} showed a significant improvement in the time between 6 months and 1 year post intervention.

In comparison to the 6-month follow-up, only UDVA showed a significant improvement, changing from 0.40 ± 0.33 logMAR to 0.23 ±0.34 logMAR ($P = .04$). All other variables showed no significant change (Table 5).

DISCUSSION

COMPARED WITH ADULTS, CHILDREN EXPERIENCE A MORE aggressive form of keratoconus, with a faster rate of progression and a higher risk of corneal scarring.[19–22] Keratoconus may cause high refractive errors, high irregular astigmatism, and a decrease in CDVA. The rapid visual deterioration can be devastating for pediatric patients, as good vision is vital for adequate functional development. Hence, an early and efficient management is essential. Conventional keratoconus treatment methods, however, have several limitations when applied to pediatric patients. In mild cases, poor CDVA and anisometropia may be addressed by hard contact lenses in adults, but in pediatric patients, lens care and fitting are an enormous challenge. Eyeglasses, on the other hand, may not adequately address anisometropia or irregular astigmatism. For advanced cases, PKP is a treatment option, but it is fraught with many complications and has a relatively high incidence of graft failure in children.[9] Considering the difficulties of a visual rehabilitation in such cases, a paper

TABLE 4. Visual, Refractive, and Topographic Parameters Preoperatively and at the 6-month and 2-year Follow-up

Parameter	Number of Eyes Evaluated	Preoperative	6-month Follow-up	2-year Follow-up	*P* Value[a]
Sphere (D)	10	−6.25 ± 3.94	−2.98 ± 4.47	−3.85 ± 4.79	.58
Cylinder (D)[b]	10	3.48 ± 1.46	2.43 ± 2.07	1.73 ± 1.84	.027
SE (D)	10	−4.51 ± 3.75	−1.76 ± 3.81	−2.99 ± 3.91	.33
UDVA (logMAR)	10	0.88 ± 0.57	0.34 ± 0.21	0.36 ± 0.42	.67
CDVA (logMAR)	10	0.40 ± 0.39	0.14 ± 0.09	0.16 ± 0.21	.54
K_{flat} (D)	9	46.74 ± 6.12	43.21 ± 5.44	43.57 ± 4.76	.62
K_{steep} (D)	9	50.40 ± 5.95	47.00 ± 4.19	47.45 ± 3.70	.21
K_{max} (D)	9	56.59 ± 9.10	52.74 ± 5.11	52.52 ± 4.58	.51
CCT (μm)[b]	9	490 ± 43.41	467 ± 56.08	481 ± 51.68	.02

CCT = central corneal thickness; CDVA = corrected distance visual acuity; D = diopters; K = keratometric readings; SE = spherical equivalent; UDVA = uncorrected distance visual acuity.

Only eyes that were examined both at the 6-month and the 2-year follow-up were evaluated. One eye did not receive topography at the 2-year follow-up and was therefore removed from topographic analysis. Compared to the 6-month follow-up, cylinder decreased significantly and central corneal thickness increased significantly at the 2-year follow-up.

[a]*P* values show the significance in change between the 2-year follow-up and the 6-month follow-up.

[b]Parameters that showed a statistically significant change.

TABLE 5. Visual, Refractive, and Topographic Parameters Preoperatively and at the 6-month and 4-year Follow-up for 7 Eyes

Parameter	Number of Eyes Evaluated	Preoperative	6-month Follow-up	4-year Follow-up	*P* Value[a]
Sphere (D)	7	−7.64 ± 5.81	−3.58 ± 5.85	−1.42 ± 2.88	.50
Cylinder (D)	7	4.36 ± 1.96	2.42 ± 2.59	0.79 ± 1.19	.08
SE (D)	7	−5.46 ± 5.19	−2.38 ± 4.98	−1.02 ± 2.75	.47
UDVA (logMAR)[b]	7	0.95 ± 0.81	0.40 ± 0.33	0.23 ± 0.34	.04
CDVA (logMAR)	7	0.55 ± 0.57	0.13 ± 0.10	0.08 ± 0.12	.52
K_{flat} (D)	7	47.81 ± 7.41	44.83 ± 4.87	44.53 ± 4.36	.92
K_{steep} (D)	7	52.64 ± 8.67	49.71 ± 7.13	48.26 ± 4.47	.55
K_{max} (D)	7	61.07 ± 14.44	54.90 ± 8.50	52.96 ± 5.33	.80
CCT (μm)	7	469 ± 36.33	442 ± 50.94	453 ± 51.62	.28

CCT = central corneal thickness; CDVA = corrected distance visual acuity; D = diopters; K = keratometric readings; SE = spherical equivalent; UDVA = uncorrected distance visual acuity.

Only eyes that were examined both at the 6-month and at the 4-year follow-up were evaluated. Compared to the 6-month follow-up, UDVA improved significantly and cylinder showed a trend in improvement at 4 years.

[a]*P* values show the significance in change between the 4-year follow-up and the 6-month follow-up.

[b]Parameter that showed statistically significant change.

recently published by our study group addressed *inter alia* an alternative approach to the visual rehabilitation of pediatric keratoconus and presented a new treatment algorithm.[3] With a good data set, the present paper analyzes the short-term and long-term outcome of a major treatment component of this new algorithm.

In the current retrospective study, outcomes of ICRS implantation followed by CXL for visual rehabilitation in pediatric keratoconus with poor CDVA and/or anisometropia are presented. Ring implantation was performed to enhance the CDVA (usually a 1-ring implantation) and/or to decrease anisometropia (usually a 2-ring implantation) and CXL was performed 1 month after ICRS implantation to prevent disease progression. Data were collected at the 6-month, 1-year, 2-year, and 4-year follow-up visits. Overall, we observed a significant improvement in all visual, topographic, and refractive parameters at the 6-month follow-up. Functionally most important parameters showed an improvement from 0.30 ± 0.19 logMAR to 0.12 ± 0.1 logMAR ($P = .001$) for CDVA and from 0.90 ± 0.50 logMAR to 0.43 ± 0.31 logMAR ($P = .001$) for UDVA (Table 1). Compared to preoperative levels,

K_{max} values significantly dropped on average by 3.7 D at 6 months, by 2.7 D at 1 year, by 4.0 D at 2 years, and by 8 D at the 4-year follow-up. (Note: sets of patients at different follow-ups are not equal. At each follow-up, only the patients that have reached this follow-up were included in the statistical analysis.) Owing to the aggressive nature of keratoconus in young ages, CXL was performed systematically in all patients.[4]

From the 6-month follow-up and thereafter, the situation remained relatively stable; only cylinder and UDVA showed significant improvements at later stages. For cylinder following the 6-month visit, data show a significant improvement at the 1-year (from 2.34 ± 2.00 D at 6 months to 1.52 ± 1.45 D at 1 year, $P = .04$) and at the 2-year visit (from 2.43 ± 2.07 D at 6 months to 1.73 ± 1.84 D at 2 years, $P = .027$) and a close to significance level at the 4-year visit (from 2.42 ± 2.59 D at 6 months to 0.79 ± 1.19 D at 4 years, $P = .08$). The results at the 4-year visit compared with the 6-month follow-up moreover showed an improvement in UDVA (0.40 ± 0.33 logMAR at 6 months compared with 0.23 ± 0.34 logMAR at 4 years, $P = .04$), indicating a possible late remodeling of the cornea with a decrease in cylinder and a subsequent improvement in UDVA. Vega-Estrada and associates reported the 5-year outcome of ICRS implantation in young patients without additional CXL; early results did not show progression of the disease, but in the longer follow-up, statistically significant regression was noted.[23] In our study, no surgical difficulties were encountered in any of the cases and no postoperative complications were observed during follow-up lasting up to 4 years, except in 1 eye, where the ICRS segment had to be removed 2 years after surgery owing to vascularization and corneal thinning above the ring. This was apparently related to neglected symptoms of irritation related to ring migration.

Male-to-female ratio in our study cohort was 5:1 and is in accordance with epidemiologic studies, which report that the disease is more common and occurs earlier in male subjects.[3,24]

The use of CXL alone for the treatment of keratoconus in children has been recently given attention.[6,7,25,26] In the short term (up to 2 years), results seem to be coherent, considering stabilization of disease progression and improvement in functional parameters. However, long-term data are still sparse and conflicting. Furthermore, the question remains whether visual gains by CXL alone are significant enough to manage keratoconus in children. Some studies in children with keratoconus stage 1 and 2 showed that CXL maintains disease stability for 3–4 years, but a study by Chatzis and associates[6] of a cohort with more advanced disease (up to stage 4) reported that disease progression and worsened visual acuity might occur as early as 2 years after CXL. The reduced CXL efficiency may be attributable to an increased turnover of collagen fibers in children.[27] In addition, the few studies providing preoperative and postoperative corneal topographic maps show a minimal corneal regularization after CXL alone.[28,29] Overall, data speak for a mild gain in CDVA following CXL in children, generally ≤1 line. Considering possible progression in the long term and minimal visual-enhancing effects, present data suggest that CXL alone is insufficient to manage more advanced keratoconus in children.

Alternatively, ICRS implantation followed by CXL, as presented in this paper, can be proposed as an option for improving CDVA in children with keratoconus. It has been proven to be safe and effective in improving CDVA in adults, it is reversible,[30] and it can be combined with CXL to stop progression. However, up to now, little is known about the effect of ICRS implantation in pediatric keratoconus. Ertan and Ozkilic[16] reported that INTACS implantation in young adolescents with keratoconus aged 13–19 years resulted in an improved UDVA, CDVA, refraction, and topographic findings similar to those in older patients. Khan and Muhtaseb[15] performed a bilateral INTACS implantation in an 11-year-old boy with progressive keratoconus and reported improvements in topographic, refractive, and visual outcomes at 15 months postoperatively (CDVA improved by 0.58 logMAR). Our study reports a similar positive effect and adds to it a positive notion of long-term stability. Visual improvement seems to be significantly more pronounced than in CXL alone. Notably, in our practice and based on our experience, results obtained in CDVA and UDVA after ICRS implantation and CXL in pediatric keratoconus are comparable to those obtained in adults.

In conclusion, ICRS implantation followed by CXL was shown to be safe and effective for visual rehabilitation of pediatric keratoconus with poor CDVA or anisometropia. Overall, ICRS implantation is a minimally invasive and reversible surgical option and improves CDVA by improving the corneal shape. This study also shows that the technique can be safely performed in children at the hands of an experienced surgeon and that in the long term no disease regression occurred. The femtosecond laser–facilitated ring implantation minimized perioperative risk and encouraged us to perform the surgery under local anesthesia. More cases examined over a longer follow-up period are needed to validate the present results.

FUNDING/SUPPORT: NO FUNDING OR GRANT SUPPORT. FINANCIAL DISCLOSURES: THE FOLLOWING AUTHORS HAVE NO financial disclosures: Youssef Abdelmassih, Sylvain el-Khoury, Ali Dirani, Rafic Antonios, Ali Fadlallah, Carole G. Cherfan, Elias Chelala, and Elias F. Jarade. All authors attest that they meet the current ICMJE criteria for authorship.

REFERENCES

1. Olivares Jiménez JL, Guerrero Jurado JC, Bermudez Rodriguez FJ, Serrano Laborda D. Keratoconus: age of onset and natural history. *Optom Vis Sci* 1997;74(3):147–151.
2. Rabinowitz YS. Keratoconus. *Surv Ophthalmol* 1998;42(4):297–319.
3. El-Khoury S, Abdelmassih Y, Hamade A, et al. Pediatric keratoconus in a tertiary referral center: incidence, presentation, risk factors, and treatment. *J Refract Surg* 2016;32(8):534–541.
4. Vazirani J, Basu S. Keratoconus: current perspectives. *Clin Ophthalmol* 2013;7:2019–2030.
5. Arora R, Jain P, Jain P, Manudhane A, Goyal J. Results of deep anterior lamellar keratoplasty for advanced keratoconus in children less than 18 years. *Am J Ophthalmol* 2016;162:191–198.e2.
6. Chatzis N, Hafezi F. Progression of keratoconus and efficacy of pediatric [corrected] corneal collagen cross-linking in children and adolescents. *J Refract Surg* 2012;28(11):753–758.
7. Vinciguerra P, Albé E, Frueh BE, Trazza S, Epstein D. Two-year corneal cross-linking results in patients younger than 18 years with documented progressive keratoconus. *Am J Ophthalmol* 2012;154(3):520–526.
8. Uçakhan ÖÖ, Bayraktutar BN, Saglik A. Pediatric corneal collagen cross-linking: long-term follow-up of visual, refractive, and topographic outcomes. *Cornea* 2016;35(2):162–168.
9. Vanathi M, Panda A, Vengayil S, Chaudhuri Z, Dada T. Pediatric keratoplasty. *Surv Ophthalmol* 2009;54(2):245–271.
10. Karadag R, Chan TCY, Azari AA, Nagra PK, Hammersmith KM, Rapuano CJ. Survival of primary penetrating keratoplasty in children. *Am J Ophthalmol* 2016;171:95–100.
11. Huang C, O'Hara M, Mannis MJ. Primary pediatric keratoplasty: indications and outcomes. *Cornea* 2009;28(9):1003–1008.
12. Alió JL, Shabayek MH, Artola A. Intracorneal ring segments for keratoconus correction: long-term follow-up. *J Cataract Refract Surg* 2006;32(6):978–985.
13. Zare MA, Hashemi H, Salari MR. Intracorneal ring segment implantation for the management of keratoconus: safety and efficacy. *J Cataract Refract Surg* 2007;33(11):1886–1891.
14. Colin J, Malet FJ. Intacs for the correction of keratoconus: two-year follow-up. *J Cataract Refract Surg* 2007;33(1):69–74.
15. Khan MI, Muhtaseb M. Intrastromal corneal ring segments for bilateral keratoconus in an 11-year-old boy. *J Cataract Refract Surg* 2011;37(1):201–205.
16. Ertan A, Ozkilic E. Effect of age on outcomes in patients with keratoconus treated by Intacs using a femtosecond laser. *J Refract Surg* 2008;24(7):690–695.
17. Jarade E, Slim E, Cherfan C, et al. Mathematical analysis of corneal remodeling after intrastromal ring surgery in keratoconus. Clinical application and topography-guided nomogram for intracorneal ring segment implantation. *Int J Ophthalmol*. (forthcoming).
18. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003;135(5):620–627.
19. Léoni-Mesplié S, Mortemousque B, Touboul D, et al. Scalability and severity of keratoconus in children. *Am J Ophthalmol* 2012;154(1):56–62.e1.
20. Tuft SJ, Moodaley LC, Gregory WM, Davison CR, Buckley RJ. Prognostic factors for the progression of keratoconus. *Ophthalmology* 1994;101(3):439–447.
21. Barr JT, Wilson BS, Gordon MO, et al. Estimation of the incidence and factors predictive of corneal scarring in the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) Study. *Cornea* 2006;25(1):16–25.
22. Al Suhaibani AH, Al-Rajhi AA, Al-Motowa S, Wagoner MD. Inverse relationship between age and severity and sequelae of acute corneal hydrops associated with keratoconus. *Br J Ophthalmol* 2007;91(7):984–985.
23. Vega-Estrada A, Alió JL, Plaza-Puche AB. Keratoconus progression after intrastromal corneal ring segment implantation in young patients: five-year follow-up. *J Cataract Refract Surg* 2015;41(6):1145–1152.
24. Ertan A, Muftuoglu O. Keratoconus clinical findings according to different age and gender groups. *Cornea* 2008;27(10):1109–1113.
25. Caporossi A, Mazzotta C, Baiocchi S, Caporossi T, Denaro R, Balestrazzi A. Riboflavin-UVA-induced corneal collagen cross-linking in pediatric patients. *Cornea* 2012;31(3):227–231.
26. Arora R, Gupta D, Goyal JL, Jain P. Results of corneal collagen cross-linking in pediatric patients. *J Refract Surg* 2012;28(11):759–762.
27. Vinciguerra R, Romano MR, Camesasca FI, et al. Corneal cross-linking as a treatment for keratoconus: four-year morphologic and clinical outcomes with respect to patient age. *Ophthalmology* 2013;120(5):908–916.
28. Soeters N, Van der Lelij A, van der Valk R, Tahzib NG. Corneal crosslinking for progressive keratoconus in four children. *J Pediatr Ophthalmol Strabismus* 2011;48 Online:e26–e29.
29. Zotta PG, Moschou KA, Diakonis VF, et al. Corneal collagen cross-linking for progressive keratoconus in pediatric patients: a feasibility study. *J Refract Surg* 2012;28(11):793–799.
30. Asbell PA, Uçakhan OO, Abbott RL, et al. Intrastromal corneal ring segments: reversibility of refractive effect. *J Refract Surg* 2001;17(1):25–31.