Safety and Visual Outcome of Visian Toric ICL Implantation After Corneal Collagen Cross-linking in Keratoconus

Ali Fadlallah, MD; Ali Dirani, MD; Hala El Rami, MD; Georges Cherfane, MD; Elias Jarade, MD

ABSTRACT

PURPOSE: To evaluate the safety and clinical outcome of phakic Visian toric implantable collamer lens (ICL) (STAAR Surgical, Monrovia, CA) insertion after corneal collagen cross-linking (CXL) in progressive keratoconus.

METHODS: A retrospective study examined the results of the two-step CXL and Visian toric ICL implantation in 16 eyes of 10 patients with keratoconus. The two procedures were done at an interval of 6 months. Data were collected preoperatively, at the 6-month follow-up visit after CXL, and at the 6-month follow-up visit after ICL implantation.

RESULTS: CXL induced a statistically significant decrease in steep keratometry (50.02 ± 4.07 at baseline to 48.74 ± 4.05 at 6 months after CXL, \( P = .001 \)) without any significant change in visual acuity or refraction. At 6-month follow-up after ICL implantation, mean \( K \) (max) was 50.49 ± 4.07 versus 52.29 ± 4.79 D at baseline (\( P = .001 \)). Mean uncorrected distance visual acuity improved from 1.67 ± 0.49 to 0.17 ± 0.06 logMAR (\( P = .001 \)) and mean corrected distance visual acuity improved from 0.15 ± 0.06 to 0.12 ± 0.04 logMAR (\( P = .023 \)). Mean spherical equivalent decreased from -7.24 ± 3.53 to -0.89 ± 0.76 D (\( P = .001 \)) and mean cylinder decreased from 2.64 ± 1.28 to 1.16 ± 0.64 D (\( P = .001 \)). The safety and efficacy indices were 1.08 ± 0.13 and 0.97 ± 0.08, respectively. No intraoperative or postoperative complications occurred.

CONCLUSIONS: Implantation of the Visian toric ICL following CXL is an effective option for improving visual acuity in patients with keratoconus.

corrected distance visual acuity (CDVA), manifest and cycloplegic refractions, and anterior and posterior segment evaluation with dilated fundus examination. All refractions were based on refined refraction using trial lenses, and the axis of astigmatism was chosen according to the best visual acuity obtained while rotating the astigmatism trial axis. Contact lens use was discontinued for at least 3 weeks for rigid lenses and 1 week for soft lenses prior to work-up and treatment.

Criteria for keratoconus diagnosis were based on a combination of computed slit-scanning videokeratography of the anterior and posterior corneal surfaces, keratometric readings, and corneal pachymetry. Keratoconus was classified into four stages based on corneal power, astigmatism, corneal transparency, and corneal thickness. All patients had best-corrected visual acuity of 20/40 or better, had well-documented progressing keratoconus in one or both eyes, and were contact lens intolerant (defined as a comfortable wearing time of less than 8 hours per day). Progression was defined as an increase in maximum keratometry of 1.00 diopter (D) or more in 1 year and/or the need for new contact lenses fitting more than once in the previous 2 years.

After CXL, the keratoconus was considered stabilized if the refraction at 4 and 6 months postoperatively was similar (and most of the time equivalent to the refraction before CXL). After attaining stable refraction, the patient was considered eligible for phakic IOL implantation. The exclusion criteria for enrollment in this study (those who could not undergo the CXL and phakic IOL procedures consecutively) were: central corneal thickness of less than 450 μm (measured by optical pachymetry [Pentacam; Oculus Optikgerate GmbH, Wetzlar, Germany]), endothelial cell count of less than 2,000 cells/mm² measured on the central part of the cornea by specular microscopy, anterior chamber depth of less than 2.8 mm from endothelium to anterior capsule measured by Pentacam, corneal opacification or scars, history of keratitis (any form), peripheral marginal degeneration, previous corneal and/or intraocular surgeries, and autoimmune and/or connective tissue disease.

The study was approved by the review board/ethics committee of the Beirut Eye Specialist Hospital, Beirut, Lebanon. All patients signed an informed consent prior to treatment. All surgical procedures were performed by the same surgeon (EJ).

CXL

The eye to be treated was anesthetized by applying proparacaine hydrochloride 0.5% drops on three occasions at 5-minute intervals. After positioning the patient under the operating microscope, an eyelid speculum was inserted and the central 9-mm corneal epithelium was removed with a blunt spatula. A mixed riboflavin 0.1%-dextran solution was instilled every 2 minutes until the riboflavin penetrated the cornea (ie, approximately 30 minutes). The ultraviolet lamp (UV-X illumination system, version 1000; IROC AG, Zurich, Switzerland) was then focused on the apex of the cornea at a distance of 5 cm for a total of 30 minutes, providing a radiant energy of 3.0 ± 0.3 mW/cm². The required irradiance of 3.0 mW/cm² was calibrated prior to each treatment using an ultraviolet A meter (LaserMate-Q; LASER 2000, Wessling, Germany). During ultraviolet A administration, riboflavin drops were applied to the cornea every 2 minutes. Thinnest and central corneal thickness were continuously monitored to ensure that neither of the two parameters dropped below 400 μm.

After treatment, the eye surface was washed with balanced salt solution and two drops of gatifloxacin 0.3% were instilled, followed by placement of a bandage soft contact lens. Postoperatively, patients received acetaminophen 500 mg twice daily for 3 days, one drop of gatifloxacin 0.3% six times daily for 7 days with one drop of tobramycin–dexamethasone 0.1% four times daily for 10 days, and one drop of loteprednol 0.5% five times daily, slowly tapered over 5 weeks.

The bandage soft contact lens was removed on postoperative day 4, and the eye examined by slit-lamp microscopy to confirm complete corneal epithelialization. Complete assessment was performed 1 and 6 months postoperatively and included visual acuity, refraction, and anterior/posterior topography. No further progression of keratoconus was noted in any eyes throughout the follow-up period.

ICL INSERTION

The implantation of the toric ICL was performed at least 6 months after CXL. ICL power was calculated using the software provided by the manufacturer. Emmetropia was selected as the target refraction except in one eye (patient 16 in Table A, available as supplemental material in the PDF version of this article). The appropriate ICL size was determined based on the horizontal white-to-white distance measured manually with a caliper, and the anterior chamber depth was measured with the Pentacam. A minor clinical adjustment of anterior chamber depth was performed by subtracting no more than 0.2 mm whenever corneal anterior bulging was advanced. Regarding the inaccuracy of the autorefractometer in predicting the K-reading in many keratoconus cases and to obtain accurate ICL choice using the online ICL calculator software, adjustment of extreme values of K-reading obtained by autorefractometer was performed by attenuating the K-reading value to reflect the magnitude
Toric ICL Implantation After CXL/Fadlallah et al

of astigmatism obtained by manifest refraction and the chosen axis of astigmatism was always the axis obtained by manifest refraction.

Laser iridotomy was performed 1 week preoperatively. The pupil was dilated with cyclopentolate and phenylephrine drops, instilled 30 minutes prior to surgery, and the horizontal axis was marked by the surgeon with the patient upright to control for cyclotorsion. General anesthesia was administered to all patients.

A 3.2-mm clear corneal tunnel incision was performed in the horizontal temporal meridian (regardless of the astigmatism axis). The anterior chamber was filled with sodium hyaluronate 1%. The ICL was inserted in the posterior chamber through the incision using the injector cartridge supplied by the manufacturer. After the ICL was gently positioned in the sulcus with the axis properly aligned, the remaining viscoelastic material was completely washed out of the anterior chamber with balanced salt solution and a miotic agent was instilled.

No intraoperative complications were encountered. Tobramycin–dexamethasone 0.1% eye drops were used four times a day for 10 days, then slowly tapered over 3 weeks. All patients were seen at 1 day, 1 week, 1 month, and 6 months postoperatively. UDVA, CDVA, manifest refraction, and keratometric readings obtained from Placido-Scheimpflug topography were recorded.

**Statistical Analysis**

Statistical analysis was performed using SPSS for Windows software (version 16.0; SPSS, Inc., Chicago, IL). The Wilcoxon signed-rank test was used to compare parameters. A two-tailed P value of .05 or less was considered statistically significant.

**RESULTS**

The study included 16 eyes of 10 patients. There were 6 men and 4 women. Mean age was 28.20 ± 12.11 years (range: 23 to 45 years). Bilateral surgery was performed in 6 patients. The Visian toric ICL was implanted in all eyes. The mean spherical power was -8.91 ± 6.10 D (range: -22 to -6 D) and the mean cylindrical power was 2.88 ± 1.33 D (range: 1 to 6 D). According to the Amsler-Krumeich classification, 1 patient had stage I, 9 patients had stage II, and 6 patients had stage III keratoconus. All patients had an endothelial cell count greater than 2,200 cells/mm². The mean central corneal thickness was 479 ± 24 μm.

**Refractive Outcome**

Individual preoperative and postoperative refractive data are reported in Table 1. Because visual acuity and corneal keratometry have shown a significant fluctuation in the first 2 months postoperatively, only the delayed results at 6 months after CXL were considered for analysis.

Visual acuity, refraction, and keratometry were compared at baseline, 6 months after CXL, and 6 months after ICL implantation (Table 1). UDVA and CDVA did not show any significant change after CXL. However, both UDVA and CDVA improved at 6 months following ICL implantation. Overall, 62.5% of eyes (10 of 16) had UDVA of 20/30 or better 6 months after ICL implantation. Seven patients gained one or two lines of CDVA (Figure 1).

The intended refraction was set to be near emmetropia for all patients. The spherical component of refraction and the spherical equivalent (SE) did not change significantly after CXL. Some statistically significant improvement was noted after CXL in the mean cylindrical component of refraction, which decreased from 2.64 ± 1.28 to 2.45 ± 1.19 D (P = .047), but this was not clinically significant.

**Table 1**

Refractive Data at Baseline, 6 Months After CXL, and 1 and 6 Months After Visian Toric ICL Implantation for Keratoconus

<table>
<thead>
<tr>
<th>Parameter (Mean ± SD)</th>
<th>Baseline</th>
<th>6 Months Post-CXL (P)</th>
<th>1 Month Post-ICL (P)</th>
<th>6 Months Post-ICL (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UDVA (logMAR)</td>
<td>1.67 ± 0.49</td>
<td>1.68 ± 0.60 (.713)</td>
<td>0.18 ± 0.07 (.001)</td>
<td>0.17 ± 0.06 (.001)</td>
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<tr>
<td>CDVA (logMAR)</td>
<td>0.15 ± 0.00</td>
<td>0.15 ± 0.06 (.180)</td>
<td>0.12 ± 0.03 (.025)</td>
<td>0.12 ± 0.04 (.023)</td>
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<tr>
<td>Sphere (D)</td>
<td>-8.56 ± 3.90</td>
<td>-8.39 ± 3.89 (.013)</td>
<td>-1.61 ± 0.97 (.001)</td>
<td>-1.47 ± 0.99 (.001)</td>
</tr>
<tr>
<td>Cylinder (D)</td>
<td>2.64 ± 1.28</td>
<td>2.45 ± 1.19 (.047)</td>
<td>1.42 ± 0.66 (.001)</td>
<td>1.16 ± 0.64 (.001)</td>
</tr>
<tr>
<td>Spherical equivalent (D)</td>
<td>-7.24 ± 3.53</td>
<td>-7.16 ± 3.58 (.307)</td>
<td>-0.91 ± 0.72 (.001)</td>
<td>-0.89 ± 0.76 (.001)</td>
</tr>
<tr>
<td>K (flat) (D)</td>
<td>46.00 ± 3.58</td>
<td>46.02 ± 2.99 (.551)</td>
<td>45.40 ± 3.20 (.009)</td>
<td>45.14 ± 3.19 (.004)</td>
</tr>
<tr>
<td>K (steep) (D)</td>
<td>50.02 ± 4.07</td>
<td>48.74 ± 4.05 (.001)</td>
<td>47.95 ± 3.68 (.001)</td>
<td>47.64 ± 3.75 (.001)</td>
</tr>
<tr>
<td>K (max) (D)</td>
<td>52.29 ± 4.79</td>
<td>51.33 ± 4.41 (.001)</td>
<td>50.79 ± 4.19 (.001)</td>
<td>50.49 ± 4.07 (.001)</td>
</tr>
</tbody>
</table>

CXL = corneal collagen cross-linking; ICL = implantable collamer lens; SD = standard deviation; UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; D = diopters; K = keratometry values

*Comparison to baseline.
The Visian toric ICL is manufactured by STAAR Surgical, Monrovia, CA.
Refraction significantly improved after ICL implantation: mean SE decreased from -7.24 ± 3.53 to -0.89 ± 0.76 D (\(P = .001\)) and mean cylinder decreased from 2.64 ± 1.28 to 1.16 ± 0.64 D (\(P = .001\)). After both procedures, 75% and 87.5% of eyes were within ± 0.5 and ± 1 D, respectively, of the intended SE correction (Figure 2).

Keratometric readings decreased after CXL: mean K (flat) changed from 46.00 ± 3.58 D at baseline to 46.02 ± 2.99 D at 6 months post-CXL (pre-ICL implantation) (\(P = .551\)) and decreased to 45.14 ± 3.19 D at 6 months post-ICL implantation (\(P = .004\)). Mean K (steep) decreased from 50.02 ± 4.07 D at baseline to 48.74 ± 4.05 D at 6 months post-CXL (\(P = .001\)) and to 47.64 ± 3.75 D at 6 months post-ICL implantation (\(P = .001\)). Mean K (max) decreased from 52.29 ± 4.79 D at baseline to 51.33 ± 4.41 D at 6 months post-CXL (\(P = .001\)) and to 50.49 ± 4.07 D at 6 months post-ICL implantation (\(P = .001\)).

Overall, the safety index (mean postoperative CDVA / mean preoperative CDVA) was 1.08 ± 0.13, and the efficacy index (mean postoperative UDVA / mean preoperative CDVA) was 0.97 ± 0.08 at 6 months post-ICL implantation. The safety and efficacy results are presented in Figure 3.

**COMPLICATIONS**

All epithelial defects healed within 4 days after CXL. No infectious keratitis and no clinically significant haze occurred during the follow-up period in all patients. No infection, lens rotation, vaulting problem, cataract formation, pigment dispersion, or pupillary block was encountered. Transient increase of intraocular pressure was observed in most patients in the first week after ICL implantation and was always successfully managed with topical drops to lower intraocular pressure.
DISCUSSION

Studies reporting on the Visian ICL and Visian toric ICL have demonstrated good efficacy and safety profiles for the correction of high ametropias in patients without keratoconus.14-21 Fewer studies have reported on the Visian toric ICL in the correction of myopia and irregular astigmatism associated with keratoconus.7,22 To the best of our knowledge, this is the first report about ICL implantation to treat refractive errors 6 months after CXL for progressive keratoconus.

In our study, visual acuity, K-reading values, and manifest refraction stabilized in most of the patients 4 months after CXL. Six-month follow-up results after CXL showed that K-readings were statistically significantly flattened or at least remained stable when compared to K-reading values before CXL. This change was not clinically significant and did not affect the manifest refraction. This finding is in accordance with another study that showed CXL did not significantly affect the refraction.23 Continuous flattening of K-reading values was also observed throughout the study period, but that did not affect the outcome of the ICL implantation procedure. The mean SE improved from -7.24 to -0.89 D and the mean cylindrical component of refraction improved from 2.64 to 1.16 D. After stabilization of keratoconus with CXL, UDVA improved significantly after ICL implantation and 62.5% of eyes achieved a UDVA of 20/30 and better.

We observed that the autorefractometer results of manifest refraction, axis of astigmatism, and magnitude of astigmatism were not always accurate and refraction was always refined with trial lenses with the same expert optometrist. The same phenomenon was observed after ICL implantation. However, UDVA and CDVA (always obtained by trial frame refraction) were considered the most important results. Online ICL calculator software is dependent on refraction, K-reading values, anterior chamber depth, and white-to-white calculation. To obtain accurate ICL choice using the online ICL calculator software, adjustment of extreme K-reading values obtained by autorefractometer was performed by attenuating the K-reading value to reflect the magnitude of astigmatism obtained by manifest refraction and the chosen axis of astigmatism was always the axis obtained by manifest refraction. The same adjustment was performed in choosing the value of anterior chamber depth.

ICL implantation was performed through a 3.2-mm clear corneal incision, which was proven to not induce any significant astigmatism; therefore, surgically induced astigmatism was not accounted for in this study and all incisions were placed at the temporal site according to the surgeon’s preference, regardless of the axis of manifest astigmatism.

Kamiya et al.24 reported 27 keratoconic eyes that significantly improved after Visian toric ICL implantation: at 6 months, 85% and 96% of the treated eyes were within 0.5 and 1.0 D, respectively, of the intended correction. The safety and efficacy indices were 1.12 ± 0.18 and 1.01 ± 0.25, respectively. Alfonso et al.22 assessed the visual outcome of 30 keratoconic eyes implanted with the Visian toric ICL. At 12 months, 86.7% of the eyes were within 0.50 D of the intended refraction and all eyes were within 1.00 D, and the safety and efficacy indices were 1.16 and 1.07, respectively. Both studies reported a safety index similar to our study and the relatively lower efficacy index observed in our study probably was attributed to the high refractive myopic power observed in one patient, which exceeded the capacity of the ICL (which is limited by -18.0 D of manifest refraction at the eyeglasses plane).

Other types of phakic IOLs have been used with success in eyes with keratoconus. Leccisotti and Fields25 evaluated the visual results and complications of angle-supported spherical phakic IOLs (ZSAL-4, Morcher, Stuttgart, Germany) in patients with stage I and II keratoconus. The spherical error was corrected within 1.00 D. However, the astigmatism did not show any significant improvement. Artisan iris-supported phakic IOLs (Ophtec USA, Boca Raton, FL) showed good results in the studies by Venter26 and Sedaghat et al.27 Both myopic and toric Artisan phakic IOLs yielded a significant improvement in visual acuity and refraction. With the increased number of reports ascertaining the efficacy and safety of phakic IOL in treating refractive errors in patients with stable keratoconus, few have addressed those results after the sequential two-step procedures (CXL followed by ICL implantation in progressive keratoconus). The only article published about a two-step CXL–Visian toric ICL implantation in unstable keratoconus is a case report by Kymionis et al. in 2011.7 The two procedures were performed at a 12-month interval with encouraging postoperative results. Visual acuity improved from counting fingers to 20/40 and CDVA improved from 20/100 to 20/30 at 3 months. In a study by Izquierdo et al.,18 11 eyes with progressive keratoconus were treated by CXL followed 6 months later by the insertion of a toric iris-fixed Artiflex phakic IOL (Ophtec USA). Results also showed a favorable outcome in terms of visual acuity, sphere, and cylinder. Güell et al.8 performed CXL on 17 keratoconic eyes followed by toric Artiflex/Artisan phakic IOL implantation to correct residual myopic astigmatism. Fourteen eyes were within 0.50 D of the attempted SE correction and 13 eyes were within 1.00 D of the attempted cylinder correction. Our study yielded favorable results compared to other studies in the literature. However, a larger number of patients and a longer follow-up period are needed to truly assess the efficacy of toric phakic IOLs in the management of kera-
toconus with high myopia and moderate-to-high myopic astigmatism. A longer follow-up period is also needed to monitor for complications such as cataract formation and pigmentary dispersion. In addition, the “quality” of vision with possible occurrence of glares and halos was not addressed in our study.

Toric ICL implantation 6 months after CXL was an effective and safe method of improving visual acuity and refraction in selected eyes with keratoconus. Patients with high myopia and moderate-to-high astigmatism seem to be the ideal candidates.

AUTHOR CONTRIBUTIONS
Study concept and design (GC, AD, HE, AF, EJ); data collection (AD, AF, EJ); analysis and interpretation of data (AD, AF); drafting of the manuscript (HE, AF); critical revision of the manuscript (GC, HE, EJ); statistical expertise (AD, AF); supervision (GC, EJ).

REFERENCES
Figure A. Dr. Jarade’s protocol for the treatment of keratoconus or ectasia after corneal refractive surgeries. Decisions are made according to the staging of keratoconus and amount of spherical equivalent of refractive errors associated. BCVA = best-corrected visual acuity; CXL = corneal collagen cross-linking; ICL = implantable collamer lens; ICRS = intracorneal ring segment (ICRS); KC = keratoconus; PRK = photorefractive keratectomy; SE = spherical equivalent; UCVA = uncorrected visual acuity.
<table>
<thead>
<tr>
<th>Eye</th>
<th>UDVA (decimal)</th>
<th>CDVA (decimal)</th>
<th>Sphere (D)</th>
<th>Cylinder (D)</th>
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<tr>
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<td>Baseline</td>
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<td>Post-ICL (6 months)</td>
<td>Baseline</td>
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UDVA = uncorrected distance visual acuity; CDVA = corrected distance visual acuity; D = diopters; CXL = corneal collagen cross-linking; ICL = implantable collamer lens

The Visian toric ICL is manufactured by STAAR Surgical, Monrovia, CA.