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CASE SERIES

Intrastromal Corneal Ring Segment with and without Collagen Corneal Crosslinking *vs* Penetrating Keratoplasty for the Treatment of Keratoconus

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ABSTRACT

Keratoconus (KC) is a noninflammatory progressive corneal degeneration that cause irregular astigmatism especially in moderate and advanced cases, the irregular astigmatism can not be corrected by glasses, contact lenses are the only optical way for improving the visual acuity (VA) in these patients. In this retrospective study, we shall present the results of eight patients suffering from KC who were treated by PKP in one eye (PKP group) and ICRS (ICRS group) with or without CXL in the second eye. All the ICRS surgeries, the CXL and the PRK were performed at the I Vision, Refractive Surgery and Keratoconus Treatment Center in Haifa, Israel, by the same surgeon (AB), the PKPs were performed elsewhere, because they were treated in our medical center after the PKP.

Keywords: Keratoconus, Intrastromal, Cornea, Rings, Intacs, Ferrara rings, Penetrating keratoplasty, Deep lamellar keratoplasty, Collagen, Cross-linking.

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INTRODUCTION

Keratoconus (KC) is a noninflammatory progressive corneal degeneration that cause irregular astigmatism especially in moderate and advanced cases, the irregular astigmatism can not be corrected by glasses, contact lenses are the only optical way for improving the visual acuity (VA) in these patients.[1]

Contact lenses (CL) are not tolerated in many patients for various reasons, among these reasons we can mention low patient motivation, atopic conjunctival diseases and conjunctival allergies which are frequently associated with keratoconus.[2,3]

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When CL are not tolerated surgery is offered to the patient, till few years ago the only option was penetrating keratoplasty (PKP).

In the last two decades new treatment modalities have emerged: Intrastromal corneal ring segments (ICRS) for VA improvement, collagen corneal crosslinking (CXL) for the arresting the disease progression, photorefractive keratectomy (PRK) in selected cases, with and without CXL.Deep anterior lamellar keratoplasty (DALK) is emerging as an alternative to PKP.

In this retrospective study we shall present the results of 8 patients suffering from KC who were treated by PKP in one eye (PKP group) and ICRS (ICRS group) with or without CXL in the second eye.

All the ICRS surgeries, the CXL and the PRK were performed at the I VISION, Refractive Surgery and Keratoconus Treatment Center in Haifa, Israel by the same surgeon (AB), the PKPs were performed elsewhere, because they were treated in our medical center after the PKP.

MATERIALS AND METHODS

This is a retrospective study on eight patients suffering from KC in both eyes, 4 males and 4 females, in one eye they underwent PKP because of advanced keratoconus. In the second eye, they underwent in our medical center ICRS implantation. In 6 eyes out of 8 eyes, the ICRS group was combined or followed later by CXL, in one eye of the same group phototherapeutic keratectomy (PTK) was performed to remove a superficial corneal scar.

PRK was performed in three of the PKP group, ICRS were inserted in one eye of the PKP group to reduce astigmatism.

Intacs Implantation

Intacs have a hexagonal shape, 150º long and 7 mm optical zone with variable thicknesses from 250 to 450 μm in a 50 μm steps (produced by Addition Technology, USA). Intacs were implanted by the mechanical way (the technique is described elsewhere) the incision was placed along the steep axis and the depth of the incision was set at 80% of the corneal thickness as measured intraoperatively by ultrasound. No sutures were placed at the incision site.

Intacs SK Implantation

Intacs SK (SK – Severe Keratoconus), available since 2007, have an oval shape, 6 mm optical zone and 400 to 450 μm thickness. The 400 μm: Indicaed for keratometry of k 55 to 62 and astigmatism of cyl < 5 D. The 450 μm: Indicated for keratometry of > 62 D and astigmatism > 5 D (produced by Addition Technology, USA). Intacs SK were implanted by the mechanical way (the technique is described elsewhere) the incision was placed along the steep axis and the depth of the incision was set at 80% of the corneal thickness as measured intraoperatively by ultrasound. No sutures were placed at the incision site.

Ferrara Rings Implantation

Ferrara Rings have a pyramidal shape (induces less glares), flat base of 600 μm, 5 mm optical zone (6 mm too, less used). Thickness:150 to 350 μm in 50 μm increments. Length 90, 120, 160 or 210º of arc, the segments are tinted in yellow, to reduce halos and glares (produced by AJL Spain), Ferrara rings were implanted by the mechanical way (the technique is described elsewhere) the incision was placed along the steep axis and the depth of the incision was set at 80% of the corneal thickness as measured intraoperatively by ultrasound. No sutures were placed at the incision site.

Collagen Corneal Cross-Linking (CXL)

Was performed according to the Dresden Protocol (described elsewhere), when the corneas were thin (< 400 um) a hypotonic riboflavin 0.1% (without dextran) until achieving the desired thickness.

Intacs were implanted in four eyes, Ferrara Rings in three eyes and Intacs SK in one eye, the ICRS were implanted using the manual technique, in two eyes the KC was associated with a superficial stromal scar, in one of these two eyes PTK was performed, in three eyes CXL was performed immediately after the implantation of Intacs, in two eyes CXL was performed few months before ICRS Implantation (one eye with Intacs and one eye with 90º Ferrara Rings), in one eye CXL was performed 5 years after Ferrara Rings implantation because of deterioration of visual acuity (VA). The final uncorrected and best spectacle corrected visual acuity (UCVA and BSCVA), Keratometry and refraction will be reported. In three of the PKP eyes we performed PRK to reduce the anisometropia, other two eyes in this group are candidates for PRK, ICRS were inserted in one eye of the PKP group to reduce astigmatism.

The patients were asked verbally to rate their satisfaction from the two procedures.

STATISTICAL ANALYSIS

We calculated mean and standard deviations for UCVA (expressed in decimals), BSCVA (expressed in decimals), the amount of cylinder and spherical correction (Diopter) as well average k (K_{ave}), minimum k (K_{min}), maximum k (K_{max}) reading before (pre ISCR) and after (post ICRS) and after PKP. The results were compared and analyzed using Fisher exact test. We are aware that this is a small case series so we performed the statistical analysis by using the Fischer test. The preoperative and the postoperative results in the ICRS were compared and analyzed. The results between the ICRS group and the PKP group were compared and analyzed.

RESULTS

The mean follow-up was 3.58 years (SD ± 3.36) in the ICRS group and 8.56 years (SD ± 3.86) in the PKP group. The mean preoperative UCVA, BSCVA, sphere, cylinder, K_{ave}, K_{min}, K_{max} in the ICRS group were respectively: 0.11 (SD ± 0.1), 0.35 (SD ± 0.2), –2.71D (SD ± 6.3), –8.25 D (SD ± 6.9) 53.81D (SD ± 6.4), 51.55 D (SD ± 6.43), 56.23D (SD ± 7.1). Post ICRS respectively : 0.49 (SD ± 0.30), 0.71 (SD ± 0.2), –0.16D (SD ± 1.9), –2.34D (SD ± 1.7) 48.14D (SD ± 4.1), 45.70D (SD ± 4.0) and 50.55D (SD ± 4.5).

The mean UCVA, BSCVA, sphere, cylinder, K_{ave}, K_{min} and K_{max} in the PKP group are respectively: 0.29(SD ± 0.3), 0.56(SD ± 0.2), –1.69D (SD ± 3.4), –3.72D (SD ± 3.2), 44. 46D (SD ± 3.8) 42.40D (SD ± 3.7) and 46.80 (SD ± 4.2).

Postoperatively improvement in UCVA, reduction of myopia and astigmatism were statistically significant in the ICRS group compared to the preoperative data, reduction of keratometry readings and improvement in BSCVA did not reach statistical significance using the Fischer test.

The data show better results in terms of UCVA, BSCVA, myopia and astigmatism in the ICRS *vs* the PKP group, the keratometry values are higher than in the PKP group but these results are not statistically significant using the Fischer test.

The detailed results are presented in Table 1. Data colored in red means statistically significant.

All the patients reported they are more satisfied from the ICRS eye than from PKP eye.

DISCUSSION

Patients suffering from KC especially in the moderate and advanced stages are frustrated by their low UCVA and BSCVA, a fact that oblige them to use CL mainly rigid gas permeable contact lenses (RGP) in order to overcome the irregular astigmatism which results from the corneal surface irregularities caused by the disease.

Table 1: The data of the eyes implanted with ICRS pre and postoperative, the data of the eyes which underwent PKP, statistical analysis of preoperative *vs* postoperative data in the eyes implanted with ICRS and the statistical analysis of the eyes implanted with ICRS *vs* the eyes which underwent PKP

	Pre ICSR	*Post ICSR*	*PKP*	*p-value (Fisher test)*	
				Pre vs Post ICSR	*Post ICSR vs PKP*
K_{ave} (SD)	53.81 (± 6.4)	48.14 (±4.1)	44.46D (±3.8)	0.27	0.83
K_{max} (SD)	56.23 (±7.1)	50.55 (±4.5)	46.80 (±4.2)	0.25	0.86
K_{min} (SD)	51.55 (±6.43)	45.70 (±4.0)	42.40 (±3.7)	0.23	0.87
Cyl (SD)	–8.25 (±6.9)	–2.34 (±1.7)	–3.72D (±3.2)	0.002*	0.11
Sph (SD)	–2.71 (±6.3)	0.16 (±1.9)	–1.69D (±3.4)	0.006*	0.14
UCVA (SD)	0.11 (±0.1)	0.49 (±0.3)	0.29 (±0.3)	0.05*	0.65
BSCVA (SD)	0.35 (±0.2)	0.71 (±0.2)	0.56 (±0.2)	0.93	0.69

*Statistically significant

Low motivation, conjunctival inflammation caused by atopic and allergic conjunctivitis which are frequently associated with KC limit the possibility of using CL in spite of the huge progress in CL industry and the introduction of soft CL for KC, piggy back CL, hybrid CL, sclera and semi scleral CL.

The only surgical option for the treatment of KC was PKP. In the last years PKP is being replaced by deep anterior lamellar keratoplasty (DALK).

PKP is a major surgery with high rate of anatomical success, S Pramanik et al report on extended long-term follow-up (FU), mean FU of 13.8 years (0.5-30.4) of PKP for KC among the 112 eyes of 84 patients, 7 eyes (6.3%) experienced graft failure. Recurrent keratoconus was confirmed clinically or histologically in 6 eyes (5.4%), with a mean time to recurrence of 17.9 years (11-27), graft survival rate of 85.4% and a rate of recurrent keratoconus of 11.7% at 25, 82 eyes (73.2%) had BSCVA of 20/40 or better.[4]

RJ Olson reported on PKP for KC with a 3.5 years FU. Allograft reaction was seen in 31% of cases but no graft failure due to allograft reaction. Mean astigmatism was 2.76 diopters (D) ± 1.99 (SD) at 24 months, with 15% > 5.00 D. Last best corrected visual acuity (BCVA) was 20/25 or better in 77% of cases.[5]

Zadok et al reported on long-term FU, 13.3 ± 2.4 years (10-17 years), in 22 eyes of 17 patients suffering from KC. At the last follow-up, 91.7% of eyes achieved BCVA of 20/40 or better.[6] Li Lim et al report on a mean FU of 46 months., BCVA in 86% of eyes was 20/40 or better at the latest FU, with 67% of eyes being corrected with spectacles.[7] Sharif et al report on a follow-up of between 4 and 16 years (mean 6.1 years), 93% of grafts remained clear and 81% achieved a final corrected VA of 6/12 or better.[8] BSCVA was 20/40 or better in 187 eyes (79.9%) and 20/20 or better in 38 eyes (16.2%) in an additional study.[9] BSCVA improved by more than two lines in 80% of KC eyes after PKP, 4% regretted PKP.[10] An other study reports a mean FU was 11.3 years, with a range of 5 to 34 years. Ninety percent of grafts remained clear, 3% were nebulous but retained 20/40 vision, and 7% failed. Seventy-three percent of the eyes out of the 326 grafts achieved 20/40 or better vision.[11] Astigmatism remain the main drawback of PKP. Progressive astigmatism was recorded in a long-term FU of 20 years (15-25) in eighty eyes were. The astigmatism was 4.05 ± 2.29 D 1 year after suture removal, 3.90 ± 2.28 D at year 3, 4.03 ± 2.49 D at year 5, 4.39 ± 2.48 D at year 7 followed by a progressive increase from 10 years after suture removal until the last FU (5.48 ± 3.11 D at year 10, 6.43 ± 4.11 D at year 15; 7.28 ± 4.21 D at year 20, and 7.25 ± 4.27 D at year 25. The mean absolute value of the difference vector (DV) calculated by vector analysis was 7.17 ± 4.35 D (0-18.33). In 70% of cases, progression of the astigmatism was evident with mean absolute DV of 9.10 ± 3.65 D. The disease severity, graft size, trephination, suture technique, and time of suture removal had no significant influence on the astigmatism.[12] 26.8% of the patients required keratorefractive surgery, which resulted in 2.9 D reduction in corneal astigmatism[13] 42 grafts (39 eyes of 38 patients) out of 201 required further surgery because of intolerable astigmatism (−3 to −18 D; mean, 8.9 D).[14] The cumulative probability of developing glaucoma, graft rejection, or graft failure was 20, 23, and 28% respectively, and 6 of the 8 graft failures after 10 years resulted from late endothelial failure.[15] An other study reports that 47% of eyes were fit with CL at 18 months.[16] Although deep anterior lamellar keratoplasty (DALK) is gaining popularity among cornea surgeons the results in terms of VA are comparable with those of PK for KC, whereas DALK surgery results in fewer postoperative complications than PKP.[17] Long-term, model-predicted graft survival and endothelial densities are higher after DALK than after PKP. The big-bubble technique gives better results than manual dissection and PKP. Compared with PKP, manual dissection provides higher survival of both the corneal endothelium and graft, but lower visual acuity[18] In a review on DALK Luz A et al reported similar VA to PK after DALK for KC and less endothelial cell loss.[19] In a review on KC recurrence after PK and DALK for KC Barbara R et al report on a recurrence rate of 1.7 to 5.4%.[20] High keratometry values may represent an under-recognized

risk group for corneal transplantation. BCVA worse than 20/40 at presentation and astigmatism are other clinical indicators of increased risk of corneal transplantation in keratoconus patients.[21]

To summarize this literature review PKP is a major surgery which can cause complications such as rejection, glaucoma and cataract and even recurrence of the KC despite high anatomical success rate in the long-term FU there is high rate of astigmatism after PKP which necessitates the use of CL and other refractive procedures such as LASIK, PRK and relaxing incisions in order to reduce the astigmatism. DALK causes less complications but yields similar results in terms of VA.

Intacs are hexagonal crescent shape implants 150º long with variable thickness of 250 μm to 450 μm with 50 μm increments made of PMMA approved since 1994 for the treatment of low myopia[22] even after LASIK or PRK[23] and approved since 2004 for the reduction of myopia and astigmatism in CL intolerant patients suffering from KC with unsatisfactory BSCVA, they were first implanted by J Colin in 1997 for the treatment of KC since then many reports were published on the effectiveness and safety of Intacs in improving UCVA BSCVA, reduction of astigmatism and keratometry readings in addition to regularization of the corneal shape[24-27] long-term results confirm the safety and the beneficial effect of Intacs for the treatment of KC[28,29] the same can be said regarding the Ferrara ICRS,[30-34] Intacs SK have similar effect to Intacs and they are indicated for severe KC,[35] ICRS are effective for the treatment of post LASIK ectasia[36-39] and pellucid marginal degeneration.[40] CXL is effective in halting the progression of KC[41-43] additive effect of CXL and ICRS was reported.[44,45]

ICRS combined with CXL are minimally invasive surgeries, have additive effect and yield positive effect on the corneal biomechanics, they improve the UCVA, BSCVA, regularize the cornea, reduce the astigmatism, the irregular astigmatism the myopia and the keratometry readings and the high order aberrations. PRK /PTK are used to further improve of VA.

There is only one study in the literature which compares Intacs ICRS with PKP, Luis A. Rodrıguez A et al report on a nonrandomized comparative study and analysis of retrospective data, the study comprised 17 patients who had PKP in 1 eye and Intacs implantation in the other eye. They were divided in 2 Groups: asymmetric (different grade of keratoconus in each eye), symmetric (same grade of keratoconus in both eyes). FU after PKP was at 24 hours and 6 and 24 months and after Intacs implantation at 24 hours and 3 and 10 months. Eyes with Intacs had a shorter recovery time than eyes having PKP. The eyes with Intacs had no complications. Complications in eyes with PKP included cataract, graft rejection, and elevated intraocular pressure. Three eyes with PKP had adverse reactions including graft rejection, vascularization, a significant decrease in endothelial cell count, and a need for long-term steroid therapy. One patient had an elevation in intraocular pressure in the PKP group and required glaucoma treatment. Two PKP patients required cataract surgery.[46]

In our series the ICRS group have a statistically significant improvement in UCVA in addition to reduction of the myopia and the astigmatism, BSCVA improvement and reduction in keratometry readings were noted but did not reach a statistical significance. Comparing the two groups the UCVA and the BSCVA are better in the ICRS group, the PKP group have more myopia and astigmatism but lower keratometry readings, all these differences were not statistically significant. Even if we deduce that the results are similar between the two groups this deduction is in favor of ICRS because it is a less invasive procedure with less post operative complications than PKP. The PKP group needed more refractive procedures to achieve the up mentioned results, three eyes in the PKP group underwent PRK in our medical center because of anisometropia, after the treatment The UCVA improved and the refractive error were reduced, in one of these three eyes. Ferrara rings were implanted in the graft to reduce the astigmatism, other two eyes in the PKP group are candidates for PRK because of anisometropia. The anisometropia in the PKP group highlights the superiority of the ICRS *vs* PKP in the treatment of keratoconus, moreover the patients in this group are more satisfied from ICRS than from the PKP. In this case series the three kinds of ICRS were used combined with CXL in most of the eyes, PTK for the removal of a superficial corneal scar was used in one eye, these minimally invasive procedures yielded similar results to PK performed in the other eye of the same patient, and there was a less need for performing other surgeries such as PRK to reduce myopia and astigmatism.

CASE REPORTS

Case 1

A female born in 1973 KC suffers from KC in the right eye (RE) and after PKP because of KC in her left eye (LE), she was CL intolerant.

Right eye: UCVA 0.05 BSCVA 0.35. The refraction was –2.5 D = –3 cylinder *70º, $K_{ave.}$ 52.6D, $K_{min.}$ 50.00D and $K_{max.}$ 55.37D, central corneal thickness (CCT) 388 um. A pair of asymmetric Ferrara ICRS, 0.25 mm –0.15 mm thickness were implanted on the first of June 2005, no intra or postoperative complications were noted.

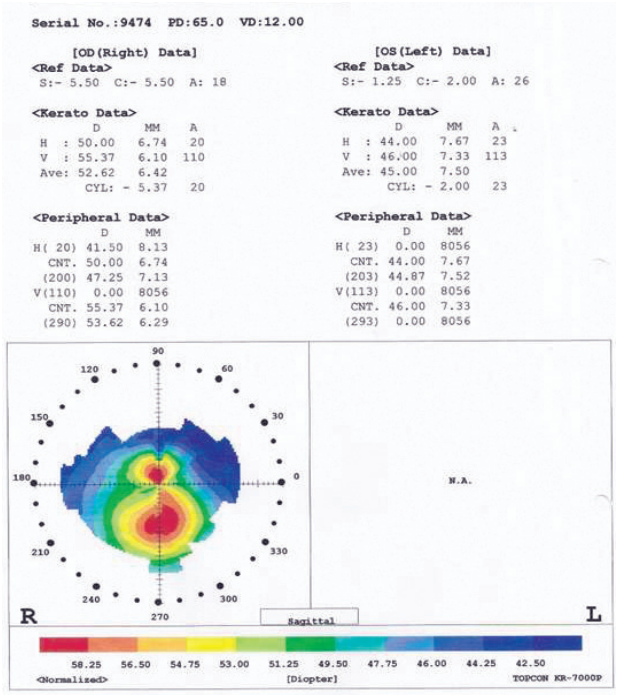

Fig. 1: Preoperative topography RE

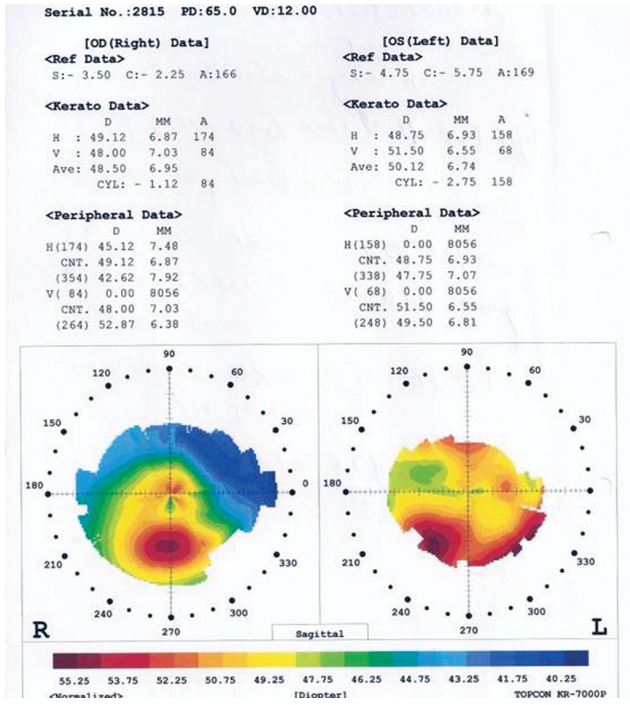

Fig. 2: Postoperative corneal topography in both eyes

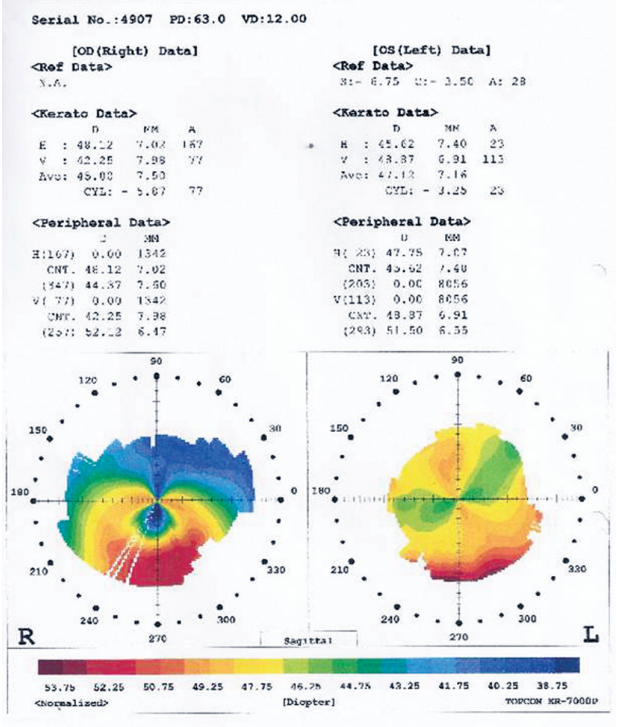

Fig. 3: Preoperative corneal topography in both eyes

Left eye: PKP was performed in 2003, arcuate cuts were performed to reduce astigmatism in the dame medical center where she was operated, laser assisted subepithelial keratomileusis (LASEK) was performed in 2006 to reduce myopia (in our medical center), Ferrara Rings 90º were implanted in 2010 (in our medical center) to reduce astigmatism.

Last FU was on the 6th of October 2011 5.200, >5 years after ICRS in the RE and 8 years after PKP in the LE.

Right eye: UCVA 0.7, no correction revealed significant improvement in her BSCVA, $K_{ave.}$ 48.5D, $K_{min.}$ 48.0D, $K_{max.}$ 49.12D.

Left eye: UCVA 0.1, BSCVA 0.35, refraction –4.5D = –6.0 cylinder *160º, $K_{ave.}$ 50.12D, $K_{min.}$ 48.75D, $K_{max.}$ 51.50D, Figures 1 and 2 (preoperative and postoperative corneal topographies).

Case 2

Male born in 1988, KC in both eyes, PKP was performed in 2007 in his LE.

Right eye: UCVA 0.1, BSCVA 0.45, refraction +3D = –7 cylinder *90º $K_{ave.}$ 45.0 D, $K_{min.}$ 42.25D, $K_{max.}$ 48.12D, CCT 439 um.

Left eye: UCVA 0.1, BSCVA 0.45, refraction –6.5D = –3.5 cylinder *28º$K_{min.}$ 45.62D, $K_{max.}$ 48.87D, $K_{aver.}$ 47.12D.

On the 20 of September 2011 one Intac segment 0.45 mm thick was implanted followed by CXL in the RE (according to the Dresden protocol, the surgical technique is described elsewhere), on the 15th of January 2013 PRK was done in the LE, the corrected refraction was –6.5D = –3 cylinder *42º, followed by the application of Mitomycin C 0.0.2 for 30 seconds. Last FU 20 June 2013, almost 2 years after ICRS + CXL in the RE and half a year after PRK in the LE

Right eye: UCVA 0.65, BSCVA 0.7, refraction +0.75D = –2.25 cylinder* 80º$K_{aver.}$ 42.75D, $K_{min.}$ 41.12D, $K_{max.}$ 44.62D.

Left eye: UCVA 0.6, BSCVA 0.75, the refraction: plano = –0.75 cylinder *45º, $K_{ave.}$ 42.5D, $K_{min.}$ 41.87D, $K_{max.}$

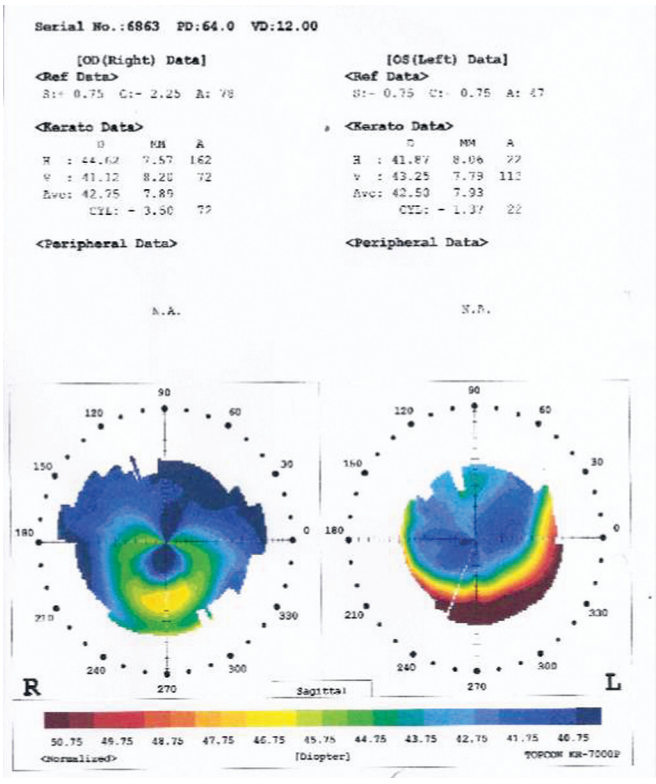

Fig. 4: Postoperative corneal topography in both eyes

43.25D, Figures 3 and 4 (preoperative and postoperative corneal topographies).

CONCLUSION

The results obtained in this unique case series in which one eye of the same patient had PKP surgery and other eye of the same patient was treated by ICRS, combined or followed by CXL in most of the eyes, confirm that these minimally invasive procedures can be an alternative to PKP or DALK in nonscared keratoconic corneas. Moreover the patients reported more satisfaction from the results obtained in the eyes implanted by ICRS than the PKP eyes. ICRS with or without CXL should be offered to patients suffering from KC and nonscared corneas who want to improve their VA before suggesting PKP or DALK. Further studies are needed to compare these two surgical techniques.

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REFERENCES

1. Rabinowitz YS. Keratoconus. Surv Ophthalmol. Elsevier; 1998;42(4):297-319.
2. Gasset AR, Hinson WA, Frias JL. Keratoconus and atopic diseases. Ann Ophthalmol 1978;10(8):991-994.
3. Donshik PC. Allergic conjunctivitis. Int Ophthalmol Clin. 1988; 28(4):294-302.
4. Pramanik S, Musch DC, Sutphin JE, Farjo AA. Extended long-term outcomes of penetrating keratoplasty for keratoconus. Ophthalmology. Elsevier; 2006;113(9):1633-1638.
5. Olson RJ, Pingree M, Ridges R, Lundergan ML, Alldredge C Jr, Clinch TE. Penetrating keratoplasty for keratoconus: a long-term review of results and complications. J Cataract Refract Surg 2000 Jul;26(7):987-991.
6. Zadok D, Schwarts S, Marcovich A, Barkana Y, Morad Y, Eting E, Avni L. Penetrating keratoplasty for keratoconus: long-term results. Cornea 2005 Nov;24(8):959-961.
7. Lim L, Pesudovs K, Coster DJ. Penetrating keratoplasty for keratoconus: visual outcome and success. Ophthalmology. Elsevier 2000;107(6):1125-1131.
8. Sharif KW, Casey TA. Penetrating keratoplasty for keratoconus: complications and long-term success. Br J Ophthalmol. BMJ Publishing Group Ltd 1991;75(3):142-146.
9. Kubaloglu A, Sari ES, Unal M, Koytak A, Kurnaz E, Cinar Y, et al. Long-term results of deep anterior lamellar keratoplasty for the treatment of keratoconus. Am J Ophthalmol 2011;151(5): 760-767.
10. Böhringer D, Schindler A, Reinhard T. Satisfaction with penetrating keratoplasty. Results of a questionnaire census. Der Ophthalmol Zeitschrift der Dtsch Ophthalmol Gesellschaft 2006;103(8):677-681.
11. Paglen PG, Fine M, Abbott RL, Webster RG Jr. The prognosis for keratoplasty in keratoconus. Ophthalmology 1982;89(6): 651-654.
12. De Toledo JA, de la Paz MF, Barraquer RI, Barraquer J. Long-term progression of astigmatism after penetrating keratoplasty for keratoconus: evidence of late recurrence. Cornea 2003;22(4): 317-323.
13. Javadi MA, Motlagh BF, Jafarinasab MR, Rabbanikhah Z, Anissian A, Souri H, et al. Outcomes of penetrating keratoplasty in keratoconus. Cornea 2005;24(8):941-946.
14. Kirkness CM, Ficker LA, Steele ADM, Rice NSC. Refractive surgery for graft-induced astigmatism after penetrating keratoplasty for keratoconus. Ophthalmol 1991;98(12):1786-1792.
15. Patel SV, Hodge DO, Bourne WM. Corneal endothelium and postoperative outcomes 15 years after penetrating keratoplasty. Am J Ophthalmol 2005;139(2):311-319.
16. Brierly SC, Izquierdo L Jr, Mannis MJ. Penetrating keratoplasty for keratoconus. Cornea 2000;19(3):329-332.
17. Han DCY, Mehta JS, Por YM, Htoon HM, Tan DTH. Comparison of outcomes of lamellar keratoplasty and penetrating keratoplasty in keratoconus. Am J Ophthalmol 2009;148(5):744-751.
18. Borderie VM, Sandali O, Bullet J, Gaujoux T, Touzeau O, Laroche L. Long-term results of deep anterior lamellar versus penetrating keratoplasty. Ophthalmol 2012;119(2): 249-255.
19. Luz A, Babosa L, Fontes BM, Ramos I, Schor P, Ambrósio Jr R. Deep anterior lamellar keratoplasty for ectatic disease.
20. Barbara R, Barbara A. Recurrent Keratoconus.
21. Reeves SW, Stinnett S, Adelman RA, Afshari NA. Risk factors for progression to penetrating keratoplasty in patients with keratoconus. Am J Ophthalmol 2005;140(4):607.e1-607.e6.
22. Schanzlin DJ, Asbell PA, Burris DJ. The intrastromal corneal ring segments: Phase II results for the correction of myopia. Ophthalmol 1997;104:1067-1078.
23. Barbara A, Shehadeh-Mashaour R, Garzozi HJ. Intacs after laser in situ keratomileusis and photorefractive keratectomy. J Cataract Refract Surg 2004;30(9):1892-1895.
24. Rabinowitz YS. Intacs for Keratoconus. Int Ophthalmol Clin 2010;50(3):63-67.

25. Sharma M BWB. Comparison of single-segment and double-segment Intacs for keratoconus and post-LASIK ectasia. 2006; 141:891-895.
26. Siganos CS, Kymionis GD, Kartakis N, Theodorakis MA, Astyrakakis N, Pallikaris IG. Management of keratoconus with Intacs. Am J Ophthalmol 2003;135(1):64-70.
27. Colin J MF. Intacs for the correction of keratoconus: two-year follow-up. J Cataract Refract Surg 2007;33:69-75.
28. Alio JL, Shabayek MH. Intracorneal ring segments for keratoconus correction: long-term follow-up. J Cataract Refract Surg 2006;32:978-985.
29. Kymionis GD, Grentzelos MA, Diakonis VF, Pallikaris. Nine-year follow-up of Intacs implantation for keratoconus. Open Ophthalmol J 2009;8(3):77-81.
30. Torquetti L, Berbel RF, Ferrara P. Long-term follow-up of intrastromal corneal ring segments in keratoconus. J Cataract Refract Surg 2009;35(10):1768-1773.
31. Torquetti L, Ferrara G, Ferrara P. Predictors of clinical outcomes after intrastromal corneal ring segments implantation.
32. Ferrara P. Clinical outcomes after implantation of a new intrastromal corneal ring with a 210 degrees arc length. J Cataract Refract Surg 2009;35(9):1604-1608.
33. El Dib RP, De Freitas D. A systematic review of Ferrara's ring in the treatment of keratoconus. J Refract Surg (Thorofare, NJ 1995). 2008;24(9):865.
34. Barbara A, Barbara R. Long-term follow-up of ferrara rings segments for the treatment of keratoconus.
35. Sansanayudh W, Bahar I, Kumar NL, Shehadeh-Mashour R, Ritenour R, Singal N, et al. Intrastromal corneal ring segment SK implantation for moderate to severe keratoconus. J Cataract Refract Surg 2010;36(1):110-113.
36. Carrasquillo KG, Rand J, Talamo J. Intacs for Keratoconus and Post-LASIK ectasia: Mechanical Versus Femtosecond Laser-Assisted Channel Creation. Cornea 2007;26(9):956-962.
37. Pokroy R, Levinger S, Hirsh A, et al. Single Intacs segment for post-LASER in situ keratomileusis keratectasia. J Cataract Refract Surg 2004;30(8):1685.
38. Piñero DP, Alio JL, Uceda-Montanes A, El Kady B. Intracorneal ring segment implantation in corneas with post-LASER in situ keratomileusis keratectasia. Ophthalmol 2009;116: 1665-1674.
39. Pokroy R, Levinger S HA. Single Intacs segment for post-LASER in situ keratomileusis keratectasia. J Cataract Refract Surg 2004;30:1685-1695.
40. Barbara A, Shehadeh-Mashaour R, Zvi F, Garzozi HJ. Management of pellucid marginal degeneration with intracorneal ring segments. J Refract Surg 2005;21(3):296-298.
41. Hafezi F, Kanellopoulos J, Wiltfang R, Seiler T. Corneal collagen crosslinking with riboflavin and ultraviolet A to treat induced keratectasia after laser in situ keratomileusis. J Cataract Refract Surg 2007;33(12):2035-2040.
42. Ashwin PT, McDonnell PJ. Collagen crosslinkage: a comprehensive review and directions for future research. Br J Ophthalmol. BMJ Publishing Group Ltd 2010;94(8):965-970.
43. Wollensak G, Spoerl E. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003;135:620-627.
44. Chan CC, Sharma M. Effect of inferior-segment Intacs with and without C3-R on keatoconus. J Cataract Refract Surg 2007;33(1):75-80.
45. Vicente LL BWB. Factors that correlate with improvement in vision after combined Intacs and transepithelial corneal crosslinking. Br J Ophthalmol 2010;94(12):1597-1601.
46. Rodríguez LA, Guillén PB, Benavides MA, Garcia L, Porras D, Daqui-Garay RM. Penetrating keratoplasty versus intrastromal corneal ring segments to correct bilateral corneal ectasia: preliminary study. J Cataract Refract Surg 2007;33(3): 488-496.