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Corneal Thickness and Topography Indices after Collagen Cross-linking for Keratoconus: 18 Months Follow-up and Literature Review

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ABSTRACT

Objective: To evaluate the changes in corneal topography indices and corneal thickness after cross-linking treatment for keratoconus.

Study Design: Retrospective Observational Study

Patients and Methods: The data of patients who underwent corneal collagen cross-linking treatment for keratoconus were retrieved. Central corneal thickness (CCT), maximum and mean keratometry (Kmax, Kmean) values and topography indices: index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus index (KI), central keratoconus index (CKI), minimum radius of curvature (Rmin), index of height asymmetry (IHA), and index of height decentration (IHD) were obtained from Pentacam and Wavelight-Allegretto Wave Topolyzer outputs. Follow-up was 18 months.

Results: The study comprised of 15 eyes of 10 patients with keratoconus. Central corneal thickness had decreased significantly 1 month after the procedure ($p=0.003$) but there were no statistically significant changes between the baseline values and last visits ($p>0.05$). Kmax and Kmean values were not statistically different from the preoperative values and at the last visits ($p>0.05$). Almost all of the corneal topography indices improved significantly after postoperative 6th month ($p<0.05$).

Conclusion: There were improvements in topography indices during 18-month follow-up period, suggesting that the cornea becomes more optically regular and symmetrical after cross-linking.

Keywords: Cornea, corneal topography, keratoconus

KERATOKONUSUN KOLLAJEN ÇAPRAZ BAĞLAMA TEDAVISI SONRASI KORNEA KALINLIĞI VE TOPOGRAFI INDEKSLERI: 18 AYLIK TAKIP VE LITERATÜR ÖZETI

ÖZET

Amaç: Keratokonusun çapraz bağlama tedavisi sonrası korneal topografi indekslerinde ve kornea kalınlığında görülen değişikliklerin değerlendirilmesi.

Çalışma Planı: Retrospektif Gözlemsel Çalışma

Hastalar ve Yöntemler: Keratokonus tedavisi için korneal kollajen çapraz bağlama tedavisi uygulanan hastaların verileri toplandı. Santral kornea kalınlığı (SKK), maksimum ve ortalama keratometri (Kmax Kort), değerleri ve topografi indeksleri: index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus index (KI), central keratoconus index (CKI), minimum radius of curvature (Rmin), index of height asymmetry (IHA) ve index of height decentration (IHD) Pentacam ve Wavelight-Allegretto Wave Topolyzer cihazlarının çıktılarından elde edildi. Takip süresi 18 aydı.

Bulgular: Çalışmada keratokonus hastalığı olan 10 hastanın 15 gözü değerlendirildi. Santral kornea kalınlığı ameliyattan 1 ay sonra istatistiksel olarak anlamlı şekilde azaldı ($p=0,003$) fakat son takip değerlerinde ameliyat öncesi değerlere göre istatistiksel olarak anlamlı bir fark yoktu ($p>0,05$). Kmax ve Kort değerleri son kontrollerde ameliyat öncesi değerlere göre istatistiksel olarak farklı değildi ($p>0,05$). Korneal topografi indekslerinin birçoğu ameliyat sonrası 6. aydan sonra istatistiksel olarak anlamlı şekilde düzeldi ($p<0,05$).

Sonuç: On sekiz aylık takip süresinde korneal topografi indekslerinde düzelme saptanmıştır. Böylece çapraz bağlama tedavisi sonrası korneanın optik olarak daha düzenli ve simetrik olduğu sonucuna ulaşmak mümkündür.

Anahtar sözcükler: Kornea, kornea topografisi, keratokonus

Keratoconus is a non-inflammatory progressive disorder of the cornea which is characterized by thinning and ectasia. The central or paracentral cornea undergoes progressive thinning and bulging, so it takes on the shape of a cone. Mild and moderate cases can be corrected with glasses or contact lenses, but the advanced cases of disease can only get benefit from either lamellar or penetrating keratoplasty. Cross-linking treatment is the first and only therapeutic option that has changed the natural course of keratoconus by stopping the progression (1).

Cross-linking arrests the progression of keratoconus by inducing the formation of new covalent crosslinks between collagen fibrils (2, 3). The improvement of patients' keratometric values and visual acuities have been demonstrated in many studies (4–6). After an initial decrease in corneal thickness (CT) after cross-linking, no difference in CT was found between the preoperative values and postoperative one-year (6, 7). Also, while some topography indices improved, others remained the same after cross-linking in different studies (6, 8).

In this retrospective study we aimed to assess the changes in corneal topography indices and central corneal thickness (CCT) 18 months after cross-linking treatment for keratoconus.

Materials and methods

The medical records of the patients who underwent cross-linking treatment for keratoconus at Acıbadem Maslak Hospital Ophthalmology Clinic between April 1st, 2008 and August 31st, 2013 were reviewed and 15 eyes of 10 patients were included in this retrospective study. The study protocol was conducted in accordance with the tenets of the Declaration of Helsinki. The inclusion criteria were; corneal topography pattern consistent with keratoconus, no history of corneal scarring or previous surgery, having had cross-linking treatment for once during the follow up period, no additional corneal surgeries during the follow up period, having at least 2 follow up visits documented during the first year follow up.

Surgical technique and postoperative management

The corneal collagen cross-linking procedure was performed by the same surgeon (CBC) as described below. After topical anesthesia with 0.5% proparacaine hydrochloride (Alcaine, Alcon Laboratories, Inc., USA) the operative eye was prepared and draped. The speculum was inserted, and the central 8.0 mm epithelium was removed with a corneal scarifier. *Standard riboflavin 0.1%* (Medio-Cross D, Medio-Haus Medizinprodukte GmbH) was instilled every 2 minutes for 30 minutes, i. e. 15 drops. The corneal penetration of riboflavin was checked with a slit-lamp using cobalt filter. After visualizing yellow colored riboflavin in the anterior chamber, the CT was measured with an ultrasonic pachymetry (Accutome AccuPach VI Pachymeter, Accutome Inc., Malvern, USA). If the corneal thickness was less than 400 µm, 1 drop of *hypotonic riboflavin 0.1%* (MedioCross H, Medio-Haus Medizinprodukte GmbH) was administered every 10 seconds for 2-minute sessions, after which ultrasound pachymetry was performed to confirm that the stroma was swollen to at least 400 µm. The procedure was proceeded by starting 365 nm UVA radiation (UV-X system, IROC AG, Zurich, Switzerland) at an irradiance of 3.0 mW/cm^2. By adjusting the aperture, only the un-epithelized cornea was irradiated and the limbal stem cells were avoided. During the application of UVA radiation *standard riboflavin 0.1%* instillation every 2 minutes was continued. For some of the patients, *isotonic riboflavin* (MedioCross M, Medio-Haus Medizinprodukte GmbH) was used in all parts of the procedure. When the 30 minutes of radiation treatment was over, the cornea was washed thoroughly with BSS. One drop of an antibiotic (Exocin®, Alcon Laboratories, Inc., USA) and a bandage contact lens (Plano B. C. : 8.6, Night & Day, Ciba Vision, USA) were put on the eye. Contact lens was removed after epithelial healing, typically 4–5 days postoperatively. Until the contact lens was removed; treatment regimen was moxifloxacin hydrochloride ophthalmic solution 0.5% (Vigamox®, Allergan Laboratories, Inc., Ireland) 3 times daily, nepafenac ophthalmic suspension 0.1% (Nevanac®, Alcon Laboratories, Inc., USA) 3 times daily and artificial tear drops (Refresh®, Allergan Laboratories, Inc., USA) every hour. After the contact lens removal loteprednol etabonate ophthalmic suspension 0.5% (Lotemax®, Bausch & Lomb, Inc., Florida, USA) was used 4 times daily and artificial tear drops were used as needed. Lotemax® was tapered and discontinued during the following 3 weeks.

The objective refraction measurements were taken by the Topcon KR 8900 Auto-Kerato-Refractometer (Topcon Corporation, Tokyo, Japan), the CCT and the keratometry values were obtained using the Pentacam (Oculus Optikgeräte GmbH, Wetzlar, Germany), corneal topography indices were obtained by Wavelight-Allegretto Wave Topolyzer (WaveLight Technologie, AG, Erlangen, Germany). The uncorrected visual acuity **(UCVA)**, best corrected visual acuity **(BCVA)** before the operation and at

the final visit; cylindrical refraction, spherical equivalent **(SEQ)**, **CCT**, **Kmax** and **Kmean** values and topography indices: **ISV**, **IVA**, **KI**, **CKI**, **Rmin**, **IHA**, and **IHD** at each visit were recorded. The abnormal and pathologic values for these indices are presented in Table 1 (9).

Table 1. Abnormal and pathological values for the topography indices (Wavelight-Allegretto Wave Topolyzer, WaveLight Technologie, AG, Erlangen, Germany).

Index	*Abnormal*	*Pathological*
ISV	≥37	≥41
IVA	≥0.28	≥0.32
KI	≥1.07	≥1.07
CKI	≥1.03	≥1.03
Rmin	<6.71	<6.71
IHA	≥19	>21
IHD	≥0.014	≥0.016

CKI: central keratoconus index, **IHA:** index of height asymmetry, **IHD:** index of height decentration, **ISV:** index of surface variance, **IVA:** index of vertical asymmetry, **KI:** keratoconus index, **Rmin:** minimum radius of curvature

Statistical analysis

Statistical analysis was performed with the IBM SPSS (Statistical Product and Service Solutions, US) Statistics Version 20. Demographic and descriptive data were expressed as mean±SD. Wilcoxon signed ranks test was used to analyze the changes in quantitative data between baseline and the following visits. At 95% confidence interval, a *p value* less than 0.05 was considered statistically significant.

Results

Out of 10 patients included in the study, six patients were men and 4 were women. The mean age was 24.4±6.8 (range: 13–36) years. The patients' data were classified in the following manner: preoperative visit (pre-op), postoperative 1st month±15 days visit (1 mo), 3rd month±15 days visit (3 mo), 6th month±15 days visit (6 mo), 12th month±2 months visit (12 mo), 18th month±2 months visit (18 mo).

Mean preoperative **UCVA** was 0.62±0.40 logMAR (log of the minimum angle of resolution), mean preoperative **BCVA** was 0.28±0.29 logMAR. The patients' final **UCVA** was 0.46±0.46 logMAR, final **BCVA** was 0.20±0.17 logMAR. The change between the preoperative and final values was significant for **UCVA** (p=0.046) but it was not for the **BCVA** (p=0.086).

The cylindrical error, **SEQ**, **CCT**, **Kmax** and **Kmean** values over time are presented in Table 2. Cylindrical error didn't change significantly during the follow-up. The change in **SEQ** between preoperative values and postoperative values was significant only in 12th month visit. **CCT** has decreased significantly after the procedure but there were no statistically significant changes between the baseline values and 12th or 18th month visits (Figure 1). **Kmax** and **Kmean** values were not statistically different from the preoperative values at the last visits (Table 2, Figure 1). **ISV, IVA, Rmin** and **IHD** values improved significantly after postoperative 6th month and **KI, CKI, IHA** values improved significantly after 12th month visit (Table 3, Figure 2).

Table 2. Postoperative changes in cylindrical error, SEQ, CCT, Kmax and Kmean measurements

	Mean±SD					
		Postoperative				
	Preop	**1mo**	**3mo**	**6mo**	**12mo**	**18mo**
Cylindrical error (D)	-3,64±2.80 (n=14)	-4,01±2.73 (n=14) (p=0.719)	-3,45±2.45 (n=10) (p=1.000)	-2.80±2.43 (n=10) (p=0.324)	-3,54±2.21 (n=12) (p=0,284)	-3,33±2.68 (n=6) (p=0.059)
SEQ (D)	-5.92±4.10 (n=14)	-5.77±4.36 (n=14) (p=0.656)	-5.30±4.83 (n=10) (p=0.138)	-4,70±4.08 (n=10) (p=0.074)	-4,89±3.98 (n=12) (p=0.006)*	-3.66±3.47 (n=6) (p=0.080)
CCT (μm)	485.23±34.19 (n=13)	442.67±38.29 (n=12) (p=0.003)*	442.50±47.44 (n=10) (p=0.012)*	472.80±34.86 (n=10) (p=0.008)*	480.92±32.74 (n=12) (p=0.894)	488.67±25.71 (n=6) (p=0.285)
Kmax (D)	48.42±4.57 (n=13)	48.41±3.85 (n=12) (p=0.023)*	48.60±4.88 (n=10) (p=0.889)	46.94±3.81 (n=10) (p=0.233)	48.19±4.42 (n=12) (p=0.171)	46.73±2.87 (n=6) (p=0.854)
Kmean (D)	46.71±3.92 (n=13)	46.64±3.03 (n=12) (p=0.091)	46.86±3.98 (n=10) (p=0.611)	45.64±3.39 (n=10) (p=0.441)	46.55±3.88 (n=12) (p=0.594)	45.46±2.78 (n=6) (p=0.465)

CCT: central corneal thickness, **Kmax:** maximum keratometry, **Kmean:** mean keratometry, **SEQ:** spherical equivalent
*Statistically significant change from preoperative measurements (p<0.05)

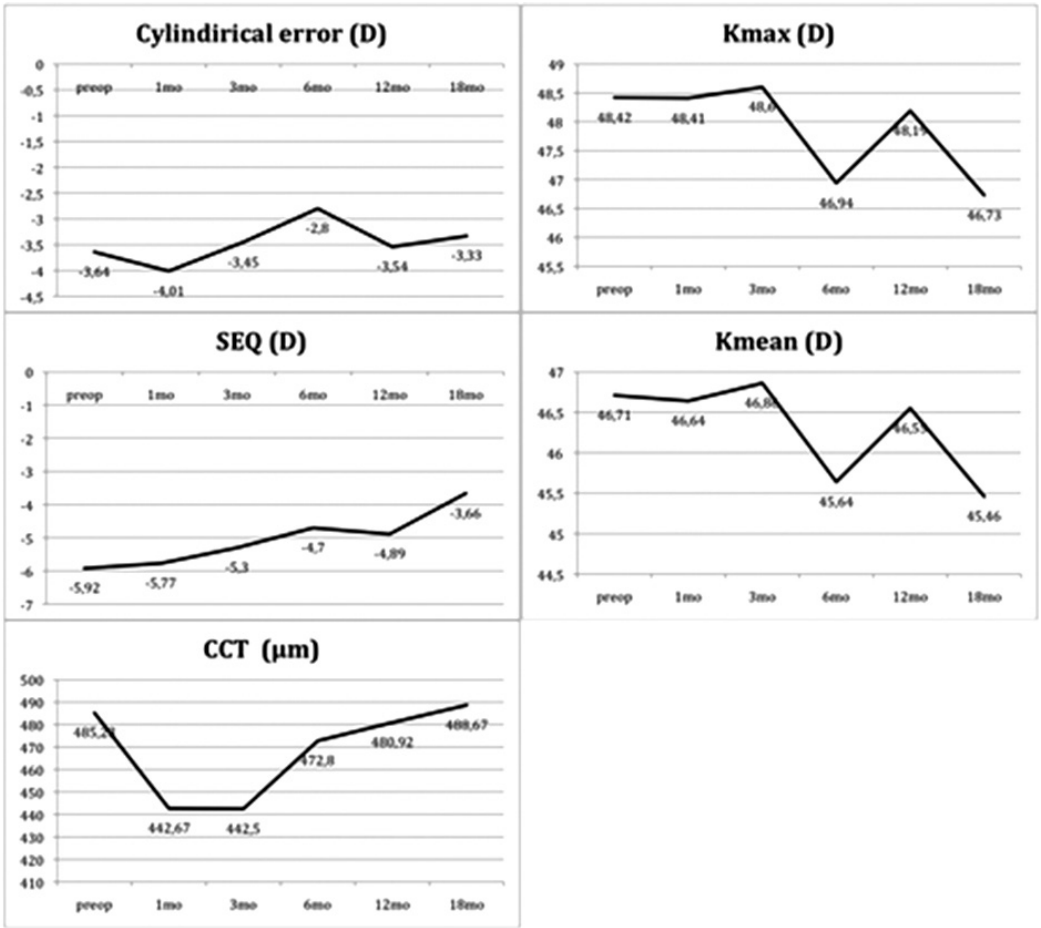

Figure 1. Change in cylindirical error, spherical equivalent (SEQ), central corneal thickness (CCT), and mean and maximum keratometry (Kmean, Kmax) values over time.

Table 3. Summary of corneal topography indices.

	Mean±SD					
		Postoperative				
Index	**Preop (n=15)**	**1mo (n=12)**	**3mo (n=8)**	**6mo (n=9)**	**12mo (n=12)**	**18mo (n=6)**
ISV (-)	72.20±39.39	67.41±35.62 (p=0.169)	78.75±40.87 (p=0.553)	65.11±44.73 **(p=0.020)***	64.33±26.55 **(p=0.002)***	67.00±48.55 **(p=0.027)***
IVA (mm)	0.78±0.50	0.67±0.39 (p=0.929)	0.82±0.48 (p=0.889)	0.70±0.56 **(p=0.015)***	0.65±0.33 **(p=0.003)***	0.77±0.62 **(p=0,042)***
KI (-)	1.20±0.14	1.18±1.12 (p=0.442)	1.18±0.14 (p=0.244)	1.17±0.15 (p=0.063)	1.14±0.07 **(p=0.004)***	1.16±0.18 **(p=0.043)***
CKI (-)	1.04±0.03	1.05±0.04 (p=0.046)*	1.06±0.04 (p=0.129)	1.04±0.03 (p=0.131)	1.04±0.02 **(p=0.024)***	1.04±0.02 **(p=0.046)***
Rmin (mm)	6.25±0.64	6.34±0.73 (p=0.969)	6.09±0.62 (p=0.778)	6.53±0.72 **(p=0.008)***	6.38±0.61 **(p=0.005)***	6.49±0.51 **(p=0.028)***
IHA (µm)	70.84±58.36	61.45±42.8 (p=0.239)	66.93±40.74 (p=0.161)	64.58±57.07 (p=0.260)	51.9±28.03 **(p=0.005)***	65.45±67.75 **(p=0.046)***
IHD (µm)	0.06±0.04	0.05±0.03 (p=0.929)	0.07±0.03 (p=0.753)	0.05±0.05 **(p=0.012)***	0.05±0.03 **(p=0.002)***	0.06±0.04 **(p=0.027)***

CKI: central keratoconus index, **IHA:** index of height asymmetry, **IHD:** index of height decentration, **ISV:** index of surface variance, **IVA:** index of vertical asymmetry, **KI:** keratoconus index, **Rmin:** minimum radius of curvature
* Statistically significant change from preoperative measurements (p<0.05)

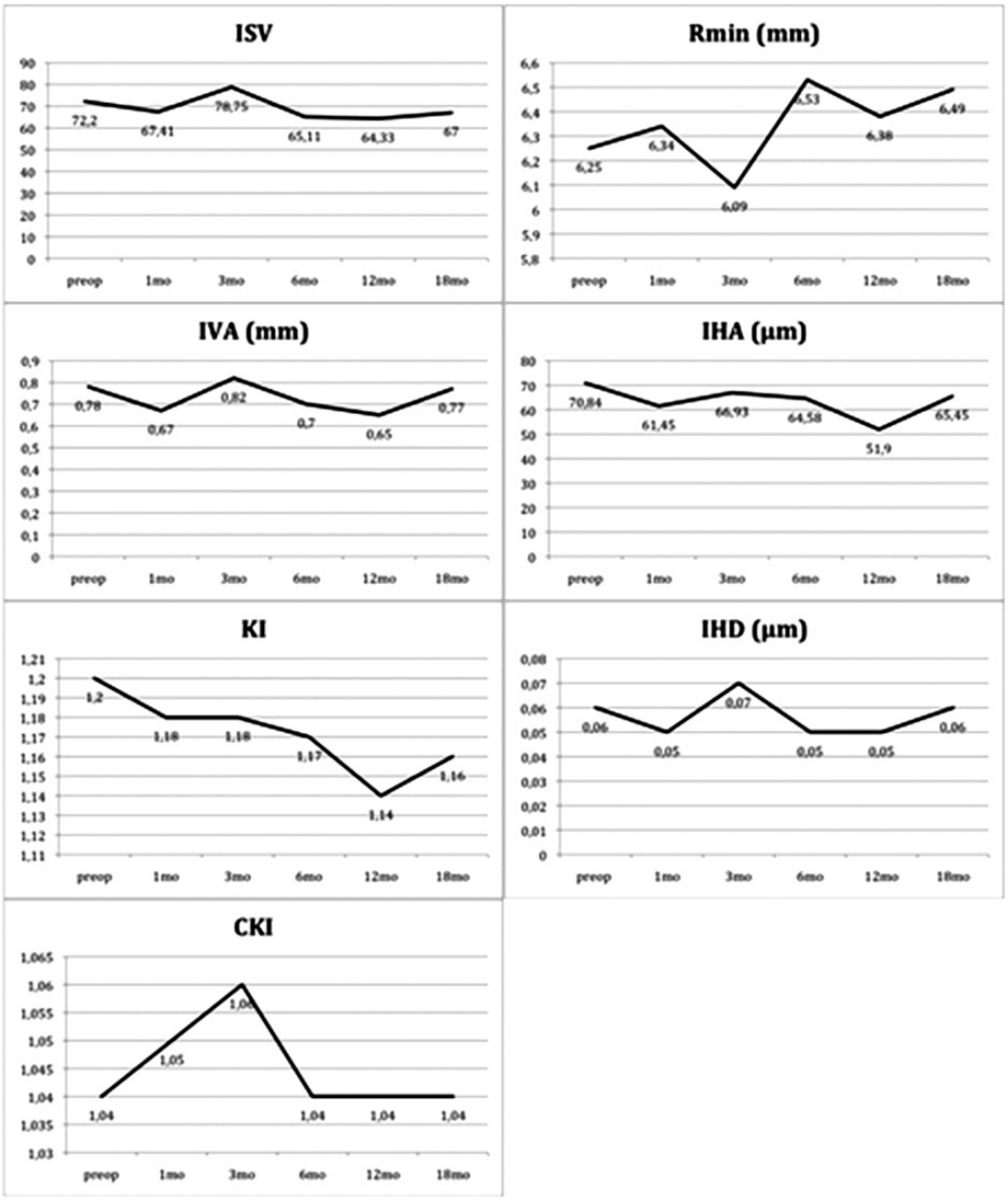

Figure 2. Change in topography indices over time after cross-linking. Index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus index (KI), central keratoconus index (CKI), minimum radius of curvature (Rmin), index of height asymmetry (IHA), index of height decentration (IHD).

Discussion

Keratoconus is an ectasic disorder in which the central or paracentral cornea undergoes progressive thinning and bulging. As keratoconus progresses the cornea gets thinner and the bulging of the cornea leads to an increase in keratometric values. Corneal collagen cross-linking treatment arrests the progression of keratoconus (1–3, 10) and the improvement can be monitored by keratometry, CT and topography indices. Arbelaez et al. found a 1.40 D decrease in maximum keratometry one year after cross-linking treatment for keratoconus when compared with preoperative values. Also, they documented a decrease in average keratometry by a mean of 1.36 D (7). Table 4 demonstrates the changes in Kmax values in different studies up to date. In our study, **Kmax** values only showed a significant decrease at the 1st month visit but there wasn't any significant change from baseline in other visits.

In the current study, preoperative mean **CCT** (485.23±34.19 µm) was decreased to 442.67±38.29 µm and 442.50±47.44 µm at postoperative 1st and 3rd month visits respectively.

At the following visits, an increase in **CCT** was observed and after 6 months the preoperative values were reached. A review of the literature about the corneal thickness changes after cross-linking for keratoconus is presented in the Table 4. Toprak et al. reported a significant decrease in corneal thickness between baseline and six months (11). Vinciguerra et al. reported that the decrease in corneal thickness at 2, 4 and 6 mm were persistent after 1 year, but they found no significant difference at 0 or 8 mm (12). Arbelaez et al. demonstrated corneal thinning and re-thickening process after cross-linking treatment (7). They found corneal thinning 3 months after the cross-linking treatment but later a steady increase was observed. This is consistent with the apoptosis after cross-linking treatment (lasting 2–3 months) and the repopulation that occurs thereafter (6 months). And the current study is concordant with this apoptosis and repopulation seen after cross-linking.

Keratoconus leads to deterioration of corneal topographic indices from normal values. Topographic indices evaluated in this study are **ISV, IVA, KI, CKI, Rmin, IHA,** and **IHD**. **ISV** is the standard deviation of individual corneal sagittal radii from the mean curvature. It is thus an expression of the corneal surface irregularity. It is unitless and elevated in all types of corneal surface irregularities (e.g., scars, astigmatism, deformities caused by contact lenses). In this study preoperative high ISV values decreased significantly starting from the 6th month visit. **IVA** is the measure (expressed in mm) of the mean difference between superior and inferior corneal curvature. It is thus the value of curvature symmetry, with respect to the horizontal meridian as the axis of reflection. Again**,** we proved a significant decrease in IVA values starting from the 6th month visit. **KI** is a unitless index expressing the ratio between mean radius values in the upper and lower segment (r sagittal superior to r sagittal inferior). **CKI** is the ratio (unitless) between mean radius values in a peripheral ring divided by a central ring: r sag (mean peripheral) to r sag mean center. In this study **KI** and **CKI** values decreased significantly after 6th month visit. **Rmin** is a measurement (mm) of the smallest radius of sagittal corneal curvature (i.e., the maximum steepness of the cone). The significant increase in **Rmin** is consistent with the decrease in **Kmax** after cross-linking treatment. We found a significant increase in **Rmin** values starting from 6th month. Although the decrease in **Kmax** in our study wasn't significant except 1st month visit, significant decreases in **Kmax** values were shown in larger study groups in literature (5, 13, 14). **IHA** is similar to the IVA but it is more sensitive because it is based on corneal elevation. It is the mean difference between height values superior minus height values inferior with horizontal meridian as mirror axis (expressed in µm). We found a significant decrease at 12th and 18th month visit in **IHA** values. **IHD** is the value of the decentration of elevation data in the vertical direction (expressed in µm), and is calculated from a Fourier analysis. This index provides the degree of decentration in the vertical direction, calculated on a ring with radius 3 mm. In this study a significant decrease was observed starting from 6th month.

In a prospective study comprising 71 eyes (49 keratoconus and 22 post-LASIK ectasia) Greenstein et al. found significant improvements in the index of surface variance, index of vertical asymmetry, keratoconus index, and minimum radius of curvature at 1 year compared with baseline. But the results were significant only in the subgroup of keratoconus patients (6). In another retrospective study Richoz et al. evaluated 26 eyes with postoperative ectasia after LASIK and PRK with a mean follow-up of 25 months and found a significant increase in **Rmin** whereas a significant decrease in index of surface variance, index of vertical asymmetry, keratoconus index and the central keratoconus index (15). Table 5 gives the summary of the literature about corneal topography index changes after corneal collagen cross-linking for keratoconus. Kanellopoulos et al. demonstrated the correlation between keratoconus severity and progression indicators, and the anterior surface topographic indices and found that **ISV** followed by **IHD** are the most sensitive and specific indices in the diagnosis, progression and surgical follow-up of keratoconus (16). In the studies presented above there were no significant changes in **IHA** and **IHD** values after cross-linking but in this study**,** we found a significant decrease of **IHA** at the 12th and 18th month visits and significant decrease of **IHD** after 6 months.

The major limitation of the present study is its small sample size, which limits extrapolation of the findings to the general population.

In conclusion, our study demonstrated the positive effect of cross-linking treatment on corneal thickness and topography indices starting from 6th month post-operatively over 18 months. The pause in corneal thinning and steepening and a decrease in corneal topography indices (except **Rmin**) may suggest the pause and the reversal of the corneal distortion during keratoconus progression. Long-term effects of cross-linking treatment on corneal parameters should be investigated.

Table 4. Literature summary for corneal collagen cross-linking in keratoconus: Keratometry and corneal thickness.

				Mean (±SD/range)	
Author	***Year***	***Follow-up[a] (months)***	***Number of eyes[b]***	***K[1], K[2]***	***CT[1], CT[2]***
Present Study	2014	18	15	48.42±4.57 46.73±2.87	485.23±34.19 488.67±25.71
Wittig-Silva[17]	2014	36	46	↓ **0.72±0.15*** 1st year ↓ **0.96±0.16*** 2nd year ↓ **1.03±0.19*** 3rd year	↓ **19.52±5.06***
Ghanem[18]	2014	24	42	**54.2±4.2** **53.3±4.1***	487±46 501±34
Toprak[19]	2014	12	96	**54.54±5.50** **53.52±5.18***	**460.11±47.15** **430.65±61.90***
Goldich[20]	2014	36	17	53.90±5.90 52.50±5.10	463±38 466±50
Sloot[21]	2013	12	53	**58.6±7.9** **57.3±7.1***	453±45 447±47
Toprak[22]	2013	12	59	**53.83±4.43** **52.67±4.33***	-
Poli[23]	2013	36	45	50.55±3.75 50.36±3.60	450.00 444.00
Toprak[11]	2013	6	47	**53.70±4.31** **52.80±4.38***	**471.30±43.54** **434.19±56.85***
Hashemi[24]	2013	60	40	49.37±3.48 49.13±3.29	483.87±29.07 485.95±28.43
Viswanathan[25]	2012	48	51	**49.65±4.91** **48.69±4.56***	470.35±39.26 467.64±43.54
Hassan[8]	2012	36	38	51.43±5.60 50.98±6.43	No statistical change
Goldich[26]	2012	24	14	**53.90±5.90** **51.50±5.40***	461±38 466±46
Asri[27]	2011	12	142	**54.09±6.07** **53.60±5.47***	468±36 459±47
Koller[28]	2011	12	151	↓ **1.0*** in 57 patients	-
Hersh[29]	2011	12	49	**60.4±9.99** **58.4±8.41***	-
Greenstein[30]	2011	12	54	-	**458.20±51.40** **450.00±52.50***
O'Brart[31]	2011	18	22	47.16 46.86	483 487
Henriquez[32]	2011	12	10	↓ **2.66***	471.5 462.8
Caporossi[13]	2010	60	44	↓ 2.0	450±14.54 451
Coskunseven[33]	2009	12	38	**54.02±4.15** **52.45±4.01***	457±21 446±26
Grewal[34]	2009	12	102	51.35±5.11 50.15±5.39	No statistical change
Vinciguerra[12]	2009	24	28	**53.59** **49.02***	490.68±30.69 479.91±32.21
Arbelaez[7]	2009	12	20	**51.89±7.99** **50.49±8.35***	463.96±27.28 463.95±37.36
Vinciguerra[14]	2009	12	28	**50.37** **44.21***	**490.68±30.69** **470.09±29.01***
Agrawal[36]	2009	12	37	53.26±5.93 -2,47±3.89 change	-
Raiskup-Wolf[5]	2008	72	241	↓ **1.46±3.76*** 1st year ↓ **1.91±4.36*** 2nd year ↓ **2.57±3.71*** 3rd year	-2±12 (1st year) **21±31*** (2ndyear)
Wittig-Silva[37]	2008	12	33	↓ **1.45±1.0***	-
Caporossi[4]	2006	6	10	↓ 1.9	431.5 (406-468) 450.6 (416-480)
Wollensak[1]	2003	48	23	↓ **2.01*** in 16 eyes no change in 5 eyes	-

a: maximum follow-up; **b:** treated eyes with keratoconus; 1: preoperative; 2: postoperative final. **K:** keratometry value, preferably Kmax; **CT:** corneal thickness, preferably central.
***:** statistically significant change from preoperative measurements ($p<0.05$)

Table 5. Literature summary for corneal collagen cross-linking in keratoconus: Topography indices.

				Mean±SD						
Author	*Year*	*Follow-up[a] (months)*	*Number of eyes[b]*	*ISV[1] ISV[2]*	*IVA[1] IVA[2]*	*KI[1] KI[2]*	*CKI[1] CKI[2]*	*Rmin[1] Rmin[2]*	*IHA[1] IHA[2]*	*IHD[1] IHD[2]*
Present study	2014	18	15	72.20±39.39 67.00±48.55*	0.78±0.50 0.77±0.62*	1.20±0.14 1.16±0.18*	1.04±0.03 1.04±0.02*	6.25±0.64 6.49±0.51*	70.84±58.36 65.45±67.75*	0.06±0.04 0.06±0.04*
Sloot[21]	2013	12	53	97±36 92±36*	0.96±0.42 0.90±0.43*	1.25±0.12 1.25±0.13	1.09±0.07 1.08±0.06*	5.81±0.72 5.97±0.69*	32.2±28.2 26.2±19.8	0.10±0.06 0.10±0.06*
Toprak[22]	2013	12	59	70.25±29.00 66.96±29.25*	0.67±0.34 0.68±0.33	1.18±0.09 1.18±0.14	1.04±0.03 1.02±0.04*	6.30±0.49 6.44±0.49*	26.68±16.51 22.87±17.12	0.06±0.03 0.06±0.03
Greenstein[6]	2011	12	49	122.2±48.2 110.3±44.9*	1.29±0.47 1.17±0.51*	1.37±0.20 1.33±0.18*	1.05±0.16 1.05±0.06	5.71±0.82 5.89±0.75*	35.2±23.5 31.0±26.7	0.12±0.06 0.12±0.13
				SAI[1] SAI[2]	SRI[1] SRI[2]	ACP[1] ACP[2]	CEI[1] CEI[2]	IAI[1] IAI[2]		
Hassan[8]	2013	36	38	2.52±1.64 1.96±1.37	0.99±0.58 0.77±0.58	47.96±3.46 47.85±4.32	0.66±0.22 0.72±0.19	0.70±0.11 0.43±0.08	(TMS-4; Tomey, Erlangen, Germany)	
Vinciguerra[12]	2009	12	28	3.02 2.83	1.64 1.61	49.61 49.23	1.13 1.09	0.62 0.62	Optical Path Difference Platform (Nidek Co Ltd, Gamagori, Japan)	
Vinciguerra[35]	2009	24	28	3.02 3.02	1.64 1.62	49.61 46.77*	1.13 1.08*	0.62 0.59	Optical Path Difference Platform (Nidek Co Ltd, Gamagori, Japan)	

a: maximum follow-up; **b:** eyes with keratoconus; 1: preoperative; 2: postoperative final
ACP: average corneal power, **CEI:** corneal eccentricity index, **CKI:** central keratoconus index, **IAI:** irregular astigmatism index, **IHA:** index of height asymmetry, **IHD:** index of height decentration, **ISV:** index of surface variance, **IVA:** index of vertical asymmetry, **KI:** keratoconus index, **Rmin:** minimum radius of curvature, **SAI:** surface asymmetry index, **SRI:** surface regularity index.
*: Statistically significant change from preoperative measurements ($p<0.05$)

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