ORIGINAL ARTICLE
(CC BY-SA)

UDC: 617.7
DOI: https://doi.org/10.2298/VSP210620079R

The effect of cross-linking procedure on corneal wavefront aberrations in patients with keratoconus

Uticaj *cross-linking* procedure na kornealne optičke aberacije kod bolesnika sa keratokonusom

Mirko Resan*, Željka Cvejić†, Philipp B. Baenninger‡, Farhad Hafezi§||¶, Horace Massa††, Miroslav Vukosavljević*, Bojan Pajić*†||††‡‡**

***University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia; †University of Novi Sad, Faculty of Sciences, Department of Physics, Novi Sad, Serbia; ‡Cantonal Hospital of Lucerne, Department of Ophthalmology, Lucerne, Switzerland; §Elza Institute, Dietikon, Switzerland; ||University of Geneva, Faculty of Medicine, Geneva, Switzerland; ¶University of Zurich, Center for Applied Biotechnology and Molecular Medicine, Zurich, Switzerland; **Wenzhou Medical University, Department of Ophthalmology, Wenzhou, China; ††Geneva University Hospitals, Department of Clinical Neurosciences, Division of Ophthalmology, Geneva, Switzerland; ‡‡Swiss Eye Research Foundation, Eye Clinic Orasis, Reinach, Switzerland**

Abstract

Background/Aim. Corneal cross-linking (CXL) treatment shows the best results in stabilizing the cornea and stopping the progress of the ectatic process. The aim of the study was to assess the impact of CXL on the keratoconus regarding higher-order aberrations (HOAs) and potential improvement of visual function. **Methods**. In 19 patients, a standard epithelium-off CXL was performed with an energy density of three mW/cm² for half an hour. The cornea was examined by Pentacam topography before CXL and one and six months after CXL. Best-corrected visual acuity (BCVA), topographic data, and aberrations were collected. **Results**. A significant reduction in vertical coma was observed from preoperative -1.03 ± 1.89 to -0.74 ± 1.73 (p = 0.004) six months after CXL, and in spherical aberration from preoperative -0.22 ± 1.05 to -0.08 ± 1.13 (p = 0.002) six months after CXL. Root mean square (RMS) HOAs six months after CXL also significantly reduced from 2.31 ± 1.82 to 2.26 ± 1.84 six months after CXL (p = 0.001). BCVA improved from preoperative 0.43 ± 0.15 to 0.71 ± 0.19 six months after surgery (p < 0.001). **Conclusion**. CXL is a very potent treatment method for keratoconus, which significantly reduces certain corneal wavefront aberrations, especially vertical coma, spherical aberration, and RMS, and leads to a significant improvement in visual acuity.

Key words:
cornea; corneal topography; keratoconus; ophthalmologic surgical procedures; visual acuity.

Apstrakt

Uvod/Cilj. Procedura *corneal cross-linking* (CXL) pokazuje najbolje efekte u stabilizovanju rožnjače i zaustavljanju napretka ektatičnog procesa. Cilj rada bio je da se ispita uticaj CXL procedure na optičke aberacije višeg reda – *higher-order aberrations* (HOAs) i poboljšanje funkcije vida u lečenju keratokonusa. **Metode**. Standardna CXL procedura sa uklanjanjem epitela rožnjače izvedena je kod 19 bolesnika korišćenjem energije jačine 3 mW/cm² u trajanju od 30 min. Kod svakog bolesnika rožnjača je snimljena na Pentacam aparatu pre procedure i jedan i 6 meseci posle CXL procedure. Ispitivani su najbolje korigovana oštrina vida, topografski podaci i vrednosti optičkih aberacija. **Rezultati**. Utvrđeno je značajno smanjenje vrednosti vertikalne kome sa -1,03 ± 1,89 preoperativno na -0,74 ± 1,73 šest meseci postoperativno (p = 0,004) i sferne aberacije sa -0,22 ± 1,05 preoperativno na -0,08 ± 1,13 postoperativno (p = 0,002). Vrednosti *root mean square* (RMS) HOAs takođe su se značajno smanjile sa 2,31 ± 1,82 preoperativno na 2,26 ± 1,84 šest meseci postoperativno (p = 0,001). Najbolje korigovana oštrina vida poboljšana je sa 0,43 ± 0,15 preoperativno na 0,71 ± 0,19 šest meseci postoperativno (p < 0,001). **Zaključak**. Procedura CXL je uspešna metoda lečenja keratokonusa koja značajno smanjuje određene aberacije talasnog fronta rožnjače, posebno vertikalnu komu, sferne aberacije i RMS, i dovodi do značajnog poboljšanja oštrine vida.

Ključne reči:
rožnjača; kornealna topografija; keratokonus; hirurgija, oftalmološka, procedure; vid, oštrina.

Correspondence to: Mirko Resan, University of Defence, Faculty of Medicine of the Military Medical Academy, Crnotravska 17, 11 000 Belgrade, Serbia. E-mail: resan.mirko@gmail.com

Introduction

Keratoconus is an ectatic dystrophic disease of the cornea that occurs in working-age people. Etiology is unknown for this generally bilateral disorder, and only 10% of patients are proven to have inherited the disease with a 1 : 2,000 prevalence. The pathohistological base of the disease shows the weakness of corneal stromal tissue caused by structural abnormalities of stromal collagen. Therefore, there is a disorganized architectonics of collagenous lamellae, which is why the cornea loses its biomechanical stability. Due to such changes cornea is progressively getting thinner and deformed in the sense that it loses its anatomical shape and assumes a cone-like form [1].

In a perfect human eye (or perfect optical system), all incoming light waves from the observed object would interfere constructively at the fovea (or focal point). The term wavefront denotes the surface obtained by joining simultaneously all the points of the propagating light wave, which have an equal phase. The wavefront shape can vary depending on the geometry of the source and can be plane (flat), spherical, cylindrical, concave, or convex. In the perfect eye, the wavefront of reflected light should still be flat, but in reality, this is not the case. Due to an imperfect crystalline lens, an irregular cornea (as in keratoconus), and a variable refractive index of ocular media, the wavefront becomes irregular. These imperfections correspond to what is known as higher-order aberrations (HOAs) in wavefront optics. Since 1999, the Optical Society of America has recommended describing wave aberrations with Zernike decomposition, and Zernike polynomials became useful for the interpretation of aberrations and the description of the wavefront error of the human eye. The slopes of the wavefront across the pupil use the least square fit with Zernike polynomials [2, 3]. Each Zernike polynomial called a mod describes a certain type of shape, a certain type of three-dimensional surface. The second-order Zernike terms represent the conventional aberrations (lower-order aberrations – LOA): myopia, hyperopia, and astigmatism. The third-order of Zernike terms are coma and trefoil (trifolio), the fourth-order includes spherical aberration, and so on [4].

The wavefront aberration function summarises all information about the monochromatic optical system. However, it is desirable to use appropriate metrics for wavefront analysis to quantitatively analyze aberrations. The most commonly used metric is the metric in the pupil plane, the so-called root mean square (RMS) wavefront error. It indicates how strongly the measured wavefront deviates from the reference wavefront. RMS gives us information about the amount of aberration between the actual and ideal wavefront for every order. The higher-order RMS error represents the vector sum of all the Zernike terms from the 3rd order and above. Aberrations are defined by either negative or positive signs as well as magnitude. A positive sign means that the aberrated wavefront is in front of the perfect wavefront, whereas a negative sign means that the aberrated wavefront is behind the perfect wavefront.

HOAs are more complex than lower-order aberrations and can be detected with an aberrometer. These aberrations can result in vision disturbances such as night vision disturbance, glare, halos, blurring, or double vision [5].

Aberration measurement was used at an early stage as a sensitive measuring method in the analysis of keratoconus. At that time, it was found that the average RMS value (total coma RMS) in a 6 mm corneal zone in healthy eyes was 0.28 ± 015 μm compared to keratoconus eyes with a value of 3.10 ± 2.28 μm [6]. The fact that an eye with keratoconus with significantly higher values of third-order RMS errors could be measured compared to a healthy eye was confirmed in other studies [7]. These results are supported by other studies, where coma-aberration in a keratoconus eye was 3.74 times higher than in a healthy control group [8]. Very similar results were reported in another paper, where higher vertical coma and RMS values were found in an early stage of keratoconus [9]. The keratoconus leads optically to increased corneal HOAs and, consequently, to increased ocular HOAs, which leads to a decrease in visual acuity. In keratoconus, the most frequently affected are the increases in corneal spherical aberration and coma [10].

To stabilize the cornea and stop the progress of the ectatic process, corneal cross-linking (CXL) treatment shows the best results. This CXL procedure saves most patients from undergoing keratoplasty (deep anterior lamellar or penetrating keratoplasty), which is the only surgical solution for the most difficult stages of the disease.

CXL procedure implies corneal treatment with riboflavin and ultraviolet-A (UVA) radiation, which creates in stroma new covalent cross-links between collagenous fibers and thus improves the firmness and biomechanical stability of the diseased cornea. Apart from this effect, the excessive corneal curvature weakened by keratoconus becomes flat a few months after the procedure, which decreases the level of astigmatism [11, 12].

The aim of the study was to determine the importance of the CXL procedure along with the effect of reducing keratometry in a decrease of levels of corneal wavefront aberrations, especially HOAs, and also in the improvement of visual function.

Methods

Study design

This retrospective, single-center study systematically collected outcome data of keratoconus patients enrolled between January 2015 and December 2018. Patients had progressive, topographically confirmed keratoconus stages 2–4 according to the Amsler-Krumeich classification

The inclusion criterion for the study was a detectable progression of keratoconus. Exclusion criteria were ocular pathology other than keratoconus and previous ocular surgery.

The study has been approved by the Ethics Committee of the Military Medical Academy, Belgrade, Serbia, with decision number 18/2020. Informed consent was obtained from all subjects involved in the study.

Clinical examination

Best-corrected visual acuity (BCVA) was assessed with Snellen charts at preoperative consultation and at one- and six-month follow-up visits. Corneal topography and tomography, as well as wavefront aberrometry assessing total RMS, HOA RMS, and lower-order aberrations (LOA) RMS, were also measured on scotopic conditions at the same time points by corneal Scheimpflug topography (Pentacam, Oculus Instruments, Wetzlar, Germany). Slit-lamp microscopic and fundoscopic examinations, as well as the measurement of intraocular pressure by applanation tonometry, were performed.

Surgical technique

The CXL procedure was performed using a modified Dresden protocol [13] under topical anesthesia (oxybuprocaine 4 mg/mL solution) in a surgery room. Using a hockey knife, the epithelial cells were removed on a diameter of 9 mm, followed by the application of iso-osmolar riboflavin solution 0.1% (10 mg riboflavin-5-phosphate in 10 mL dextran-T-500 20% solution) onto the cornea every 2 min for 30 min. Using a manual ultrasonic pachymeter (UP-100, Nidek), a minimum central pachymetry of more than 400 µm was measured immediately before the cross-linking treatment. If the corneal thickness was measured < 400 µm, additional hypoosmolar riboflavin solution 0.1% (10 mg riboflavin-5-phosphate in 10 mL physiological salt solution-sodium chloride 0.9%) was instilled every 20 sec for 2 min until the cornea had swollen to a thickness of at least 400 µm. The cornea was then irradiated for 30 min with 370 nm-UVA light from the corneal CXL system (UV-X 1000, IROC Innocross AG, Zurich, Switzerland) with a power density of 3 mW/cm^2. The riboflavin solution was further instilled every 2 min during the UVA irradiation to keep the corneal saturation in balance. After the procedure, a topical steroid combined with antibiotic (0.1% dexamethasone solution + 0.3% tobramycin solution) and soft therapeutic silicon contact lens (PureVision, Bausch&Lomb) were applied. The contact lens was usually removed on the third day after surgery if complete epithelial healing was achieved. After epithelial healing, patients used drops of a topical steroid combined with antibiotic (0.1% dexamethasone solution + 0.3% tobramycin solution) three times daily and artificial tears (0.1% sodium hyaluronate solution) eight times per day for one month.

Statistical analysis

IBM SPSS Statistics Version 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to analyze data sets, whether or not they are subject to normal distribution. A data set was considered normally distributed if p > 0.05. The parametric data sets are further analyzed using the ANOVA test, and the non-parametric data sets are further analyzed using the Friedman test. Significance exists if p < 0.05.

Results

Patients' characteristics

We performed CXL in 19 eyes of 19 progressive keratoconus patients consecutively. Their mean age was 41.7 ± 14.3 years, and 59.9% (n = 11) of patients were male. No eyes were lost to follow-up after one and six months. No intra- or postoperative complications were observed.

Overall effects of CXL

CXL improved BCVA significantly from preoperative 0.43 ± 0.15 to 0.56 ± 0.18 and 0.71 ± 0.19 after one and six months, respectively (p < 0.001). Mean spherical refraction changed after CXL from preoperative -2.14 ± 2.78 D to -1.79 ± 3.02 D, 6 months postoperatively (p = 0.002). The cylindric refraction was 2.43 ± 1.40 D preoperatively, 2.54 ± 1.58 D one month, and 2.48 ± 1.26 D six months postoperatively, which was not statistically significant (p = 0.34). The postoperative visual and refractive results are shown in Table 1.

After one month, 42.1% of eyes gained one line, and 15.8% of eyes even increased BCVA to two or more lines. In 26.2% of eyes, BCVA remained unchanged after one month. After one month, 10.5% of eyes lost two or more lines, and 5.2% of eyes lost one-line BCVA. After 6 months, there was a significant overall improvement in BCVA, i.e., 42.1% gained 2 or more lines, 31.6% gained one line, while 15.8% remained unchanged, and 10.5% lost one line of BCVA (Figure 1).

Table 1

Visual acuity, refractive and corneal parameter values before and one and six months after corneal cross-linking

Characteristics	Preoperative	One month	Six months	*p*
BCVA	0.43 ± 0.15	0.56 ± 0.18	0.71 ± 0.19	< 0.001
Spherical value D	-2.14 ± 2.78	-2.54 ± 3.38	-1.79 ± 3.02	= 0.002
Cylindrical value D	2.82 ± 2.16	2.61 ± 2.21	2.33 ± 1.76	= 0.34
Ksteep	47.04 ± 3.30	47.41 ± 3.79	46.61 ± 4.14	= 0.008
Kflat	44.70 ± 2.93	44.87 ± 3.76	44.10 ± 3.57	= 0.018
Kaverage	45.74 ± 3.02	46.09 ± 3.68	45.33 ± 3.78	= 0.002
Central corneal thickness (µm)	469.1 ± 51.52	434.6 ± 61.34	444.2 ± 58.34	< 0.001

Results are presented as mean ± standard deviation.
BCVA – best corrected visual acuity.

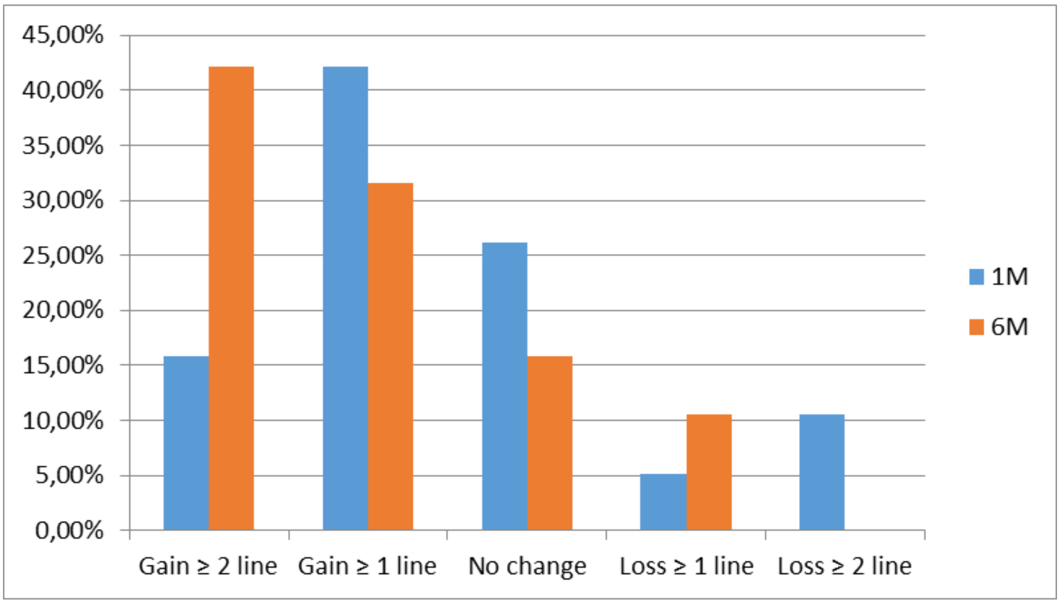

Fig. 1 – Best corrected visual acuity (BCVA) changes 1 and 6 months (M) after corneal cross-linking (CXL).

Topographic changes

Topographically, the mean value of Ksteep was 47.04 ± 3.30 D preoperatively, 47.41 ± 3.79 D one month postoperatively, and 46.61 ± 4.14 D six months postoperatively (p = 0.008). The mean value of Kflat was 44.70 ± 2.93 D preoperatively, 44.87 ± 3.76 D one month postoperatively, and 44.10 ± 3.57 D six months postoperatively (p = 0.018). Finally, the mean value of Kaverage preoperatively was 45.74 ± 3.02 D, whereas one month postoperatively the value was 46.09 ± 3.68 D, and six months postoperatively, 45.33 ± 3.78 D (p = 0.002). All three topographic values were statistically significant. The mean central pachymetry reduced from preoperative values of 469.1 ± 51.52 µm to 434.6 ± 61.34 µm one month postoperative and after 6 months to 444.2 ± 58.34 µm (p = 0.001) (Table 1). *K*average values were significantly changed in the 6-month controls (p = 0.002). One month after CXL, the value remained unchanged at 73.7%. In 21%, even a steepness of more than one diopter of the cornea was found. Only in 5.3%, a flattening of the cornea by 1-2 diopters was observed. Six months after CXL, the picture looked different: 42.1% of the corneas showed a flattening of the cornea by 1–2 diopters and 10.5% by more than 2 diopters; 36.8% remained unchanged, and only 10.5% of corneas with more than one diopter had a higher steepness (Figure 2).

Pachymetry showed a corneal thinning from preoperative 469.1 ± 51.52 µm to 434.6 ± 61.34 µm one month after CXL and 444.2 ± 58.34 µm six months after CXL, which was statistically highly significant ($p < 0.001$).

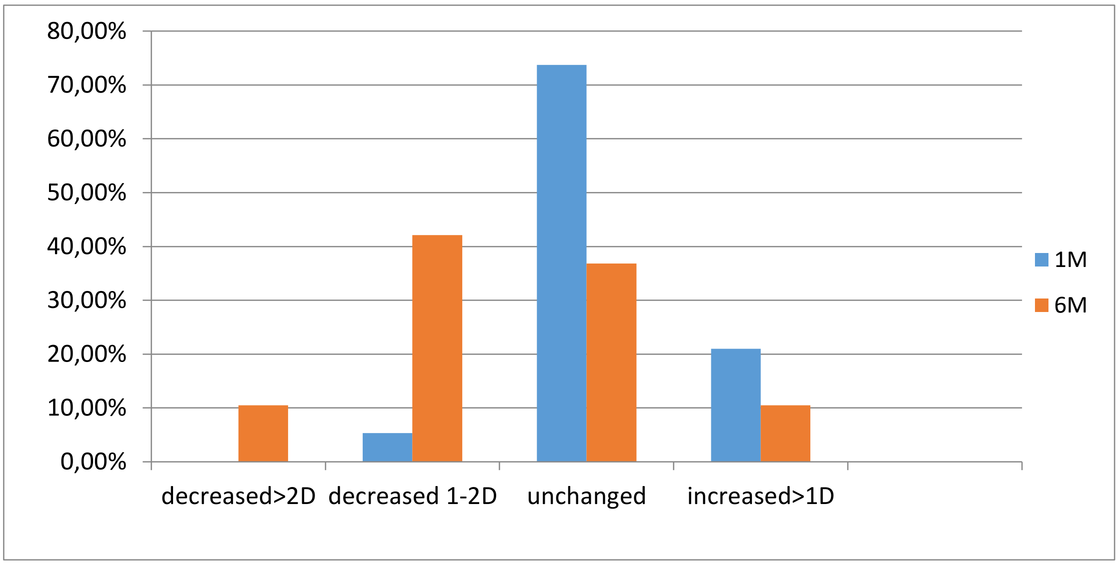

Fig. 2 – Changes of keratometry (Kaverage) 1 and 6 months (M) after corneal cross-linking (CXL).

Wavefront analysis

The wavefront analysis shows a significant reduction of vertical coma from -1.03 ± 1.89 preoperatively to -0.74 ± 1.73 six months postoperatively ($p = 0.004$) and spherical aberration from -0.22 ± 1.05 preoperatively to -0.08 ± 1.13 six months postoperatively ($p = 0.002$). The RMS values, total ($p = 0.001$), LOA ($p = 0.002$), and HOA ($p = 0.001$), decreased and improved during the 6-month postoperative course (Table 2).

All other wavefront parameters were not significant, especially those of the 5th and 6th order ($p > 0.05$). The aberration reduction per eye of the 3rd and 4th order is shown in Figure 3.

Table 2

Corneal wavefront aberrations before and one and six months after corneal cross-linking

Characteristics	Preoperative	One month	Six months	*p*
Vertical coma	-1.03 ± 1.89	-1.13 ± 1.65	-0.74 ± 1.73	0.004
Horizontal coma	0.10 ± 1.62	0.18 ± 1.72	0.12 ± 1.64	0.58
Trifolio 30°	0.10 ± 0.32	0.24 ± 0.50	0.23 ± 0.54	0.45
Trifolio 0°	0.21 ± 0.52	0.18 ± 0.86	0.11 ± 0.59	0.91
Spherical aberration	-0.22 ± 1.05	-0.38 ± 1.18	-0.08 ± 1.13	0.002
RMS total	8.63 ± 6.26	10.09 ± 6.61	8.65 ± 6.27	0.001
RMS LOA	8.31 ± 6.00	9.69 ± 6.39	8.31 ± 6.01	0.002
RMS HOA	2.31 ± 1.82	2.74 ± 1.82	2.26 ± 1.84	0.001

Results are presented as mean ± standard deviation.
RMS – root mean square; LOA – lower-order aberrations; HOA – higher-order aberrations.

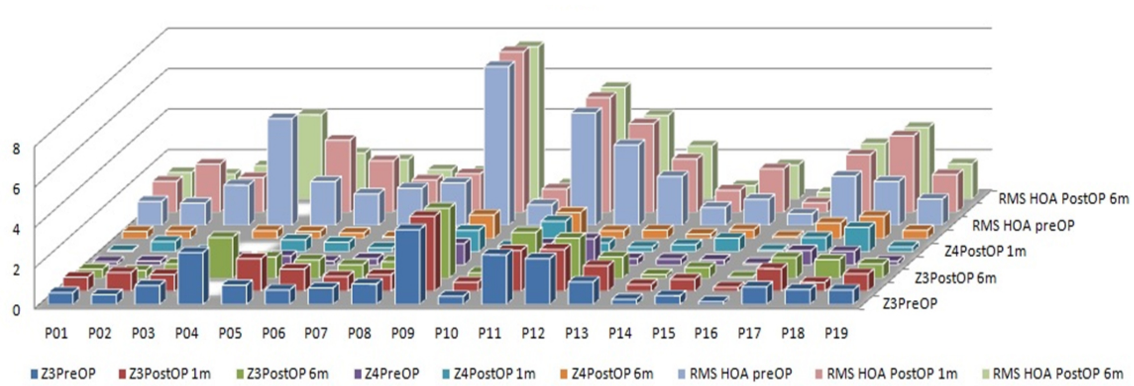

Fig. 3 – The values of root mean square (RMS) for 3rd order (Z3), RMS for 4th order (Z4) corneal wavefront aberrations, and RMS for higher-order aberrations (HOA), preoperatively (preOP), one month (1m) postoperatively (PostOP), and six months (6m) PostOP, with each patient's examined eye (P).

Discussion

Main findings

The CXL procedure not only improved BCVA and corneal topography parameters after one and six months of follow-up but also reduced corneal wavefront aberrations indicating a significant improvement of the distorted corneal shape, leading to a better visual function. The focus is on a significant improvement in spherical aberration and vertical coma.

Results in the context of the existing literature

The main therapeutic effect of the CXL procedure is increasing firmness of stroma in the diseased cornea, thus preventing or slowing further progress of the ectatic process in the diseased cornea. Besides this effect, the CXL procedure also leads to a decrease in the curvature of the diseased cornea, which was shown in our study through the results of Ksteep, Kflat, and Kaverage. According to the values of Kaverage, after 6 months, 42.1% of our patients had a flattening of 1–2 diopters, and in 10.5%, more than 2 diopters occurred. Our results are similar to the results of some other studies [14–16]. CXL procedure influences multiple corneal parameters, which has a direct positive influence on visual acuity. Two main processes lead to an improvement of the optical condition, i.e., a significant flattening of the cornea and a reduction of spherical aberration and vertical coma. The cornea thus becomes more regular and allows for a better optical system [16]. HOAs of the cornea, especially coma, are important optical parameters that say something about the image quality. The continuous analysis of these parameters can provide information about the effectiveness of CXL treatment. In analogy to our study, studies have shown that in keratoconus eyes, coma-like aberrations are dominant [7, 17]. Further studies show that CXL significantly reduces HOAs even in progressive keratoconus [18–20].

Wisse et al. [21] showed that spherical aberration was reduced significantly (-15.68%) ($p < 0.001$) at one year after CXL for keratoconus, whereas other corneal HOAs remained unchanged. Greenstein et al. [18] performed a study involving 96 eyes (64 eyes with keratoconus and 32 eyes with ectasia) and found that the mean pre-CXL total anterior corneal HOAs, total coma, 3rd order coma, and vertical coma were 4.68 µm ± 2.33 µm, 4.40 ± 2.32 µm, 4.36 ± 2.30 µm and 4.04 ± 2.27 µm respectively. One year after the CXL procedure, the mean values decreased significantly to 4.27 ± 2.25 µm, 4.01 ± 2.29 µm, 3.96 ± 2.27 µm and 3.66 ± 2.22 µm, respectively (all $p < 0.001$). There were no significant changes in posterior corneal HOAs. Bozkurt et al. [15] in their study found that total HOAs decreased from 0.54 ± 0.26 before CXL to 0.51 ± 0.28 six months after CXL, coma decreased from 0.45 ± 0.26 before CXL to 0.43 ± 0.26 six months after CXL, and spherical aberration decreased from 0.08 ± 0.06 before CXL to 0.07 ± 0.06 six months after CXL. Kosekahya et al. [19] in their study concluded that RMS total, RMS HOAs, vertical coma, and spherical aberration values significantly decreased after CXL ($p < 0.001$, $p = 0.02$, $p = 0.04$, and $p < 0.001$, respectively). The improvements in HOAs were significant at postoperative 6th months compared to the baseline measurements, while they remained the same between postoperative 6th months and 12th months. We had comparable results in our study (Table 2). It shows that the CXL has a high potential as a treatment method that should be used primarily for treating keratoconus, provided the corneal criteria are met. The aim is not only to stabilize the keratoconus but also to significantly improve the visual function.

Keratoconus patients are, in general, thought to have much larger amounts of astigmatism. The Zernike terms are significantly higher among these patients: oblique astigmatism (Z_2^{-2}), trefoil (Z_3^{-3} and Z_3^{3}), vertical coma (Z_3^{-1}), as well as secondary astigmatism (Z_4^{-2} and Z_4^{2}). Vertical coma and spherical aberration showed the highest values among higher-order Zernike coefficients. In our study, negative vertical coma was present in 16 of 19 keratoconus eyes studied. Our study showed that vertical coma and spherical aberration improved significantly after CXL. That led to a functional improvement of the eye, i.e., BCVA increased continuously from 0.43 ± 0.15 before CXL to 0.56 ± 0.18 one month and 0.71 ± 0.19 six months after surgery. At all times, the visual acuity improvement was highly significant ($p < 0.001$). Other studies confirm these results and associate BCVA improvement with the reduction of coma and keratometry values [20, 22].

Limitations

The present study has some limitations due to the retrospective design and the limited number of eyes treated. There was no formal assessment of the quality of vision, such as a standardized quality of life visual function questionnaire or assessment of contrast sensitivity as part of the routine clinical workup.

Implications for further research

In the future, a longer follow-up period is planned for further analysis, which should show the dynamics of CXL on the cornea in keratoconus eyes as a long-term minimally invasive therapy option.

Conclusion

Our study confirms previous preliminary studies showing that standard epithelium off CXL in keratoconus treatment improves BCVA and topographic parameters and significantly reduces corneal wavefront aberrations, especially vertical coma, spherical aberration, and RMS.

Funding

This research received no external funding.

Data availability statement

The data presented in this study are available on request from the authors; the datasets, in particular, are archived in the clinics treated. The data are not publicly available as they contain information that could compromise the privacy of the participants.

Conflicts of interest

The authors declare no conflict of interest.

R E F E R E N C E S

1. *Ferder RS, Kshettry P.* Noninflammatory ectatic disorders. In: *Krachmer JH, Mannis MJ, Holland EJ*, editors. Cornea. 2nd ed. Philadelphia: Elsevier-Mosby; 2005. p. 955–74.
2. *Thibos LN, Applegate RA.* Assessment of optical quality. In: *Krueger RR, Applegate RA, MacRae SM,* editors. Customized Corneal Ablation: The Quest for Super Vision. Thorofare, NJ: Slack Inc; 2001. p. 55–63.
3. *Thibos LN, Applegate RA, Schwiegerling JT, Webb R.* VSIA Standards Taskforce Members. Vision science and its applications. Standards for reporting the optical aberrations of eyes. J Refract Surg 2002; 18(5): S652–60.
4. *Bennett ES, Weissman BA.* Chapter IX in Clinical Contact Lens Practice. Philadelphia: Lippincott Williams & Wilkins; 2005.
5. *Lawless MA, Hodge C.* Wavefront's role in corneal refractive surgery. Clin Exp Ophthalmol 2005; 33(2): 199–209.
6. *Gobbe M, Guillon M.* Corneal wavefront aberration measurements to detect keratoconus patients. Cont Lens Anterior Eye 2005; 28: 57–66.
7. *Maeda N, Fujikado T, Kuroda T, Mihashi T, Hirohara Y, Nishida K,* et al. Wavefront aberrations measured with Hartmann-Shack sensor in patients with keratoconus. Ophthalmology 2002; 109(11): 1996–2003.
8. *Barbero S, Marcos S, Merayo-Lioves J, Moreno Barriuso E.* Validation of the estimation of corneal aberrations from videokeratography in keratoconus. J Refract Surg 2002; 18(3): 263–70.
9. *Jafri B, Li X, Yang H, Rabinowitz YS.* Higher order wavefront aberrations and topography in early and suspected keratoconus. J Refract Surg. 2007; 23(8): 774–781.
10. *Hefner-Shahar H, Erdinest N.* High-order aberrations in Keratoconus. Int J Kerat Ect Cor Dis 2016; 5: 128–31.

11. *Resan M, Vukosavljević M, Stanić E, Kovač B, Ristić D, Petrović M,* et al. Steep keratometry and central pachymetry after corneal collagen cross-linking procedure in patients with keratoconus. Vojnosanit Pregl 2020; 77(2): 215–9.
12. *Koller T, Pajić B, Vinciguerra P, Seiler T.* Flattening of the cornea after collagen cross-linking for keratoconus. J Cataract Refract Surg. 2011; 37(8): 1488–92
13. *Wollensak G, Spoerl E, Seiler T.* Riboflavin/ultraviolet-a-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003; 135(5): 620–7.
14. *Hersh PS, Greenstein SA, Fry KL.* Corneal collagen cross-linking for keratoconus and corneal ectasia: One-year results. J Cataract Refract Surg 2011; 37(: 149–60.
15. *Bozkurt E, Ozgurhan EB, Akcay BI, Kurt T, Yildirim Y, Günaydin ZK*, et al. Refractive, Topographic, and Aberrometric Results at 2-Year Follow-Up for Accelerated Corneal Cross-Link for Progressive Keratoconus. J Ophthalmol. 2017; 2017: 5714372.
16. *Richoz O, Mavrakanas N, Pajić B, Hafezi F.* Corneal collagen cross-linking for ectasia after LASIK and photorefractive keratectomy: long-term results. Ophthalmology 2013; 120(7): 1354–9.
17. *Alió JL, Shabayek MH.* Corneal higher order aberrations: a method to grade keratoconus. J Refract Surg 2006; 22(6): 539–45.
18. *Greenstein SA, Fry KL, Hersh MJ, Hersh PS.* Higher-order aberrations after corneal collagen cross-linking for keratoconus and corneal ectasia. J Cataract Refract Surg 2012; 38(2): 292–302.
19. *Kosekahya P, Koc M, Tekin K, Uzel M, Atilgan CU, Caglayan M*, et al. Evaluation of the shifting of the line of sight and higher order aberrations of eyes with keratoconus after corneal cross-linking. Cont Lens Anterior Eye 2017; 40(5): 311–7.
20. *Caporossi A, Mazzotta C, Baiocchi S, Caporossi T.* Long-term results of riboflavin ultraviolet a corneal collagen cross-linking for keratoconus in Italy: the Siena eye cross study. Am J Ophthalmol 2010; 149(4): 585–93.
21. *Wisse RPL, Gadiot S, Soeters N, Godefrooij DA, Imhof SM, Van der Lelij A.* Higher-order aberrations one year after corneal collagen cross-linking for keratoconus and their independent effect on visual acuity. J Cataract Refract Surg 2016; 42(7): 1046–52.
22. *Ghanem RC, Santhiago MR, Berti T, Netto MV, Ghanem VC.* Topographic, corneal wavefront, and refractive outcomes 2 years after collagen crosslinking for progressive keratoconus. Cornea 2014; 33(1): 43–8.

Received on June 20, 2021
Revised on July 31, 2021
Accepted on August 6, 2021
Online First August 2021