# Visual and topographic outcomes of accelerated corneal cross-linking in keratoconus: 1-year follow-up

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**Purpose**
The aim of this study was to evaluate the visual and topographic outcomes of accelerated corneal collagen cross-linking (ACXL) in mild and moderate progressive keratoconus.
**Patients and methods**
This retrospective study evaluated the visual and topographic outcomes of 54 eyes of 36 patients of progressive keratoconus who had ACXL (9 mW/cm; 10 min). Data were collected 12 months after corneal collagen cross-linking.
**Results**
Uncorrected distance visual acuity was improved from 0.84±0.49 logMAR preoperatively to 0.79±0.3 logMAR postoperatively which is not statistically significant ($P$=0.1). Corrected distance visual acuity was not significantly changed. The mean preoperative corrected distance visual acuity was 0.25 ±0.18 and 0.23±0.2 logMAR preoperatively and postoperatively, respectively ($P$=0.4). Manifest spherical equivalent was not significantly changed, from –4.1 ±2.77 D preoperatively to –4.02±2.4 D postoperatively, which was not statistically significant ($P$=0.4). There were no significant changes of steep $K$, flat $K$, average $K$, and $K_{max}$ compared with preoperative measurements at 12 months.
**Conclusion**
ACXL (9 mW/cm; 10 min) is effective in stabilizing the keratoconus at 1-year follow-up.

**Keywords:**
corneal cross-linking, keratoconus, maximum keratometry, visual acuity

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## Introduction

Keratoconus is a bilateral, noninflammatory, progressive corneal disorder, characterized by progressive thinning and steepening of the cornea, leading to irregular astigmatism and deterioration of visual performance with time [1]. Keratoconus affects the patients during the second decade of life, causing significant negative effect on the quality of life [2]. The changes in corneal collagen structure and organization, alterations of the extracellular matrix, and keratocyte apoptosis lead to gradual corneal biomechanical weakness [3,4].

Corneal collagen cross-linking (CXL) was first introduced by Wollensak *et al.* [5] as a technique to halt the progression of keratoconus. Riboflavin was used as a photosensitizer. The interaction between riboflavin and ultraviolet-A (UV-A) light (365 nm) leads to the formation of reactive oxygen species, which leads to the formation of additional covalent bonds between collagen molecules, with consequent increase in corneal biomechanical stiffening [6].

The purpose of this study was to assess the effects of CXL on visual and topographic measurements in patients with progressive keratoconus.

## Patients and methods

Fifty-four eyes of 36 patients were included in this retrospective study, the visual and topographic outcomes of patients with keratoconus (KC) who underwent accelerated corneal collagen cross-linking (ACXL) were investigated.

The inclusion criteria were as follows: progressive keratoconus of stages 1–3 according to the Amsler–Krumeich classification [7]; the corneal thickness was more than 400 μm at the thinnest location. Progression was defined as an increase in the maximum keratometric reading of at least 1 D or a worsening of corrected visual acuity with an increase in astigmatism of at least 1 D confirmed by at least two examinations during the preceding 6–12 months before treatment. Patients with autoimmune system disorders, as well as those who were pregnant or were breastfeeding, were excluded from the study. All participants signed an

informed consent form in accordance with the tenets of the Declaration of Helsinki.

All subjects underwent a complete ophthalmic examination which included uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) based on the logMAR chart, manifest refraction, slit lamp and dilated fundoscopy. Corneal topography was performed using the Pentacam conventional Scheimpflug system (OCULUS Optikgeräte GmbH, Wetzlar, Germany) and OPD III scan (NIDEK Inc., Gamagori, Japan). The values representing the flat, steep mean, and maximum keratometry ($K_{steep}$, $K_{flat}$, $K_{average,}$ and $K_{max}$) were recorded. These investigations were performed preoperatively and on a 1-year follow-up.

All patients underwent an epithelium-off ACXL by the KXL UV-A source (Avedro Inc., Waltham, Massachusetts, USA) of UV-A exposure at 10 min of continuous irradiation time and 9 mW/cm$^2$ UV intensity (total energy: 5.4/cm$^2$).

The corneal epithelium was partially removed from a 9.0 mm treatment zone using a rotating brush (Amoils Rotary Epithelial Scrubber; Innovative Excimer Solutions Inc., Toronto, Canada); one drop of dextran-free riboflavin 0.1% solution (VibeX Rapid; Avedro Inc.) was used every 2 min for 10 min. The eye was then rinsed thoroughly with a balanced salt solution and aligned under the UV.

Postoperatively, moxifloxacin 0.5% (Vigamox; Alcon Inc., Texas, USA) was prescribed four times daily for 2 weeks, and prednisolone acetate 1% (Pred Forte; Allergan Inc., Dublin, Ireland) was prescribed six times daily for 1 week. The dose of prednisolone was then tapered on a weekly basis over a period of 4 weeks.

#### Statistical methods

The data was revised for its completeness and consistency. Data entry was done in Microsoft Excel worksheet. Data analysis was done with the program SPSS for Windows, version 20 (IBM, New York, USA). Quantitative data was summarized by mean, SD while qualitative data was summarized by frequencies and percentages. Paired *t*-test was used in the analysis of this paper. A *P* value of less than 0.05 was considered statistically significant.

## Results

The study included 54 eyes of 36 patients, which included 22 (61%) men and 14 (39%) women. The mean age was 22.8 years (range: 14–35 years). Mean average *k* was 46.8 (range: 41.9–58.7), mean steep *K* ($K_s$) was 48.6±4.95 (range: 42.2–59.4). Mean flat *K* ($K_f$) was 45.4±3.78 (range: 40.7–58.1). Mean maximum *K* ($K_{max}$) was 54.5±8.12 (range: 47.3–69.9).

All patients (100%) underwent a complete follow-up from baseline up to 12 months after CXL. Eighteen patients underwent bilateral CXL while the remaining four patients had unilateral CXL. The mean preoperative spherical equivalent power was −4.1±2.8 D (range: −1.5 to −11.37 D).

UDVA was improved from 0.84±0.49 logMAR preoperatively to 0.79±0.3 logMAR postoperatively which is not statistically significant (*P*=0.1). Thirty-four (63%) eyes showed no change in CDVA, four (7.4%) eyes gained 1–2 lines and eight (14.8%) eyes gained more than two lines, 1 year postoperatively. Four (7.4%) eyes lost 1–2 lines and four eyes lost more than two lines.

CDVA was not significantly changed. The mean preoperative CDVA was 0.25±0.18 and 0.23±0.2 logMAR preoperatively and postoperative, respectively (*P*=0.4), while 11.1% (6/54) of the eyes gained 1–2 lines of the CDVA, 3.7% (2/54) gained more than two lines, 70.4% (38/54) had no change, and 14.8% (8/54) lost 1–2 lines.

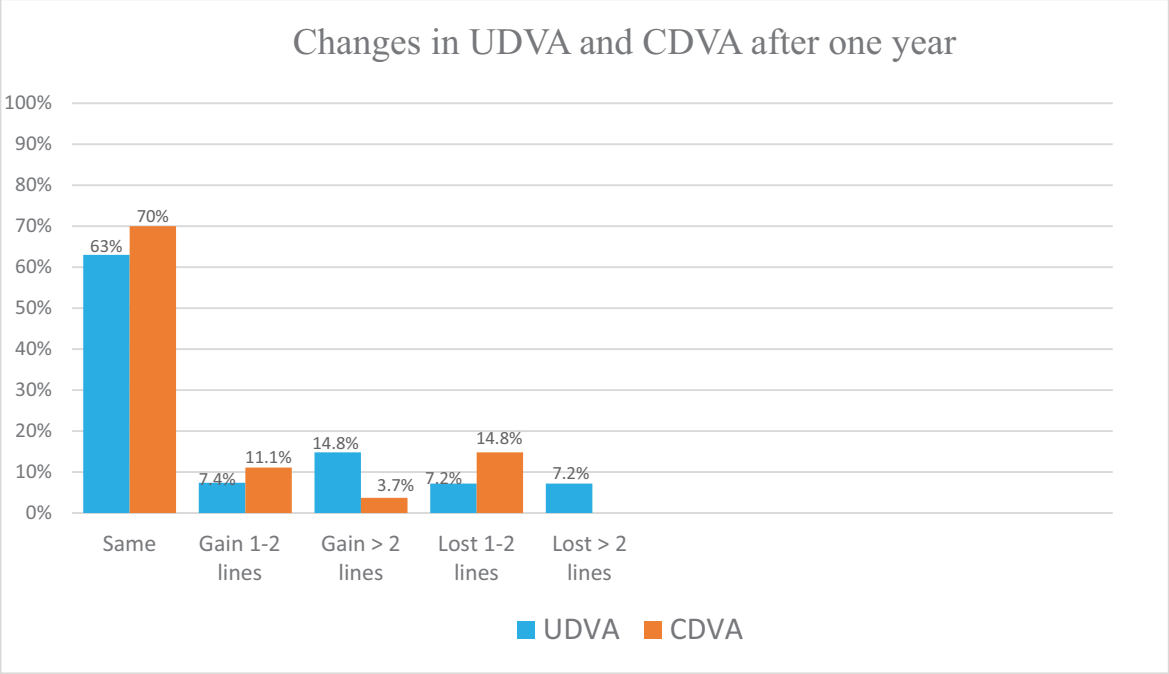
Manifest spherical equivalent (MSE) was not significantly changed, from −4.1±2.77 D preoperatively to −4.02±2.4 D postoperatively, which was not statistically significant (*P*=0.4). At 12 months after CXL, mean MSE was within 0.75 D of the preoperative value in about 66.6% (36/54) of eyes. MSE decreased by more than 0.75 D in about 26% (14/54) of eyes. MSE increased by more than 0.75 D in about 7.4% (4/54) of eyes.

There were no statistically significant changes in UDVA logMAR and CDVA logMAR. In terms of refractive outcomes, there was no significant change in SE from baseline at 1 year (Fig. 1).

Mean $K_{average}$ was 47.0±4.4 and 46.9±5.0 preoperatively and postoperatively, respectively. It remained stable in about 83.3% (45/54) of eyes, decreased by more than 1 D in about 11.1% (6/54) of eyes, and increased by more than 1 D in about 5.5% (3/54) of eyes.

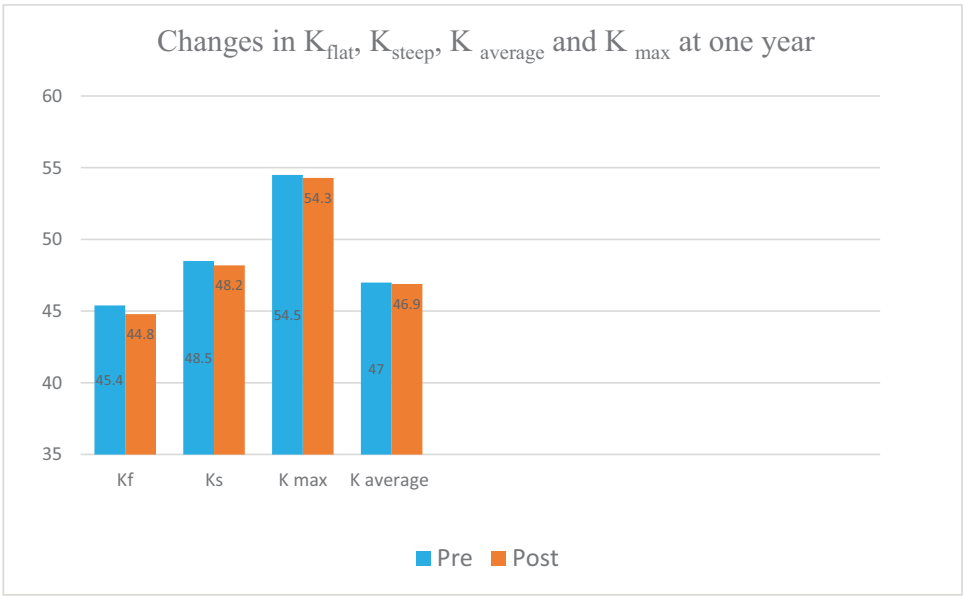
Mean $K_{steep}$ was 48.5±4.9 and 48.2±5.0 preoperative and postoperative, respectively. It remained stable in

**Figure 1**




Comparison between 2 groups regarding visual acuity after 1 year.

**Figure 2**




Comparison between 2 groups regarding keratometry readings.

about 74.1% (40/54) of eyes, decreased by more than 1 D in about 14.8% (8/54) of eyes, and increased by more than 1 D in about 11.1% (6/54) of eyes.

Mean $K_{flat}$ was 45.4±3.7 and 44.8±4.2 preoperatively and postoperatively, respectively. It remained stable in about 81.5% (44/54) of eyes, decreased by more than 1 D in about 14.8% (8/54) of eyes, and increased by more than 1 D in about 3.7% (2/54) of eyes.

Mean $K_{max}$ was 54.5±8.0 preoperatively and 54.3±8.1 postoperatively. It remained stable in about 51.9% (28/54) of eyes, decreased by more than 1 D in about 29.6% (16/54) of eyes, and increased by more than 1 D in about 18.5% (10/54) of eyes.

There were no significant changes for $K_{steep}$, $K_{flat}$, $K_{average}$, and $K_{max}$ compared with the preoperative data after 1 year (Fig. 2).

## Discussion

It has been demonstrated that CXL has shown the ability to slow or stop the progression of keratoconus by several publications.

All of our patients underwent ACXL 9 mW/cm for 10 min (5.4 J/cm$^2$). Our findings showed that there were no significant changes in UDVA and CDVA at 1 year follow-up. There were no significant changes in mean $K_{steep}$, $K_{flat}$, $K_{average}$, and $K_{max}$ before and after CXL treatment at 1 year.

In our study, the mean UDVA, 63% of the eyes remained stable with no change in preoperative CDVA, 22.2% gained at least one line of the CDVA, 14.8% lost at least one line at the end of 12 months of follow-up time. Regarding CDVA, 70.4% of the eyes remained stable with no change in preoperative CDVA, 14.8% gained at least one line of the CDVA, 14.8% lost 1–2 lines at the end of 12 months of follow-up time. There were no significant changes in UDVA and CDVA at 1 year follow-up. MSE was not significantly changed. Ozgurhan *et al.* [8] have evaluated the results of ACXL (total dose, 7.2 J/cm$^2$) on keratoconus cases at 1 year. They found a nonsignificant improvement in UDVA and CDVA at the end of the follow-up period. The mean spherical and cylindrical refractions did not significantly change. Kymionis *et al.* [9] evaluated the result of ACXL 9 mW/cm$^2$ irradiance for a duration of 10 min. They reported a nonsignificant improvement in CDVA. Elbaz *et al.* [10] reported improvement in the UDVA with ACXL (9 mW/cm; 10 min). The mean CDVA was not significantly changed. In a 2-year follow-up, Bozkurt *et al.* [11] assessed visual, refractive, and topographic results of ACXL. The mean UDVA and CDVA were significantly improved at 12 and 24 months as compared with preoperative values. The mean spherical and cylindrical refractions were not significantly changed after CXL as compared with the preoperative value.

In the current study, there was a significant reduction in average $K_{max}$ value ($P<0.05$) 12 months after CXL. The mean $K_{steep}$, $K_{flat}$, $K_{average}$, and $K_{max}$ values were not significantly changed from baseline at the 1 year visit ($P<0.05$ for all), which are consistent with the previous results. Ozgurhan *et al.* [8] revealed nonsignificant reduction in flat keratometry, steep keratometry, and apex keratometry. Chow *et al.* [12] reported more effective topographic flattening with conventional CXL as compared with ACXL (18 mW/cm$^2$ for 5 min). Kanellopoulos [13] observed a reduction in the steepest $K$ in both accelerated and Dresden protocols. Elbaz *et al.* [10] reported stabilizing topographic parameters after 12 months of follow-up in mild–moderate keratoconus. Chan *et al.* [14] demonstrated a reduction in $K_{max}$ in patients with $K_{max}$ of at least 58.0 D. They concluded that a significant correlation was found between the preoperative $K_{max}$ and postoperative change in $K_{max}$ at 1 year. Shetty *et al.* [15] evaluated the effect of three accelerated protocols of collagen cross-linking (3, 9, 18, 30 mW/cm$^2$) on visual, refractive, and tomographic parameters in patients with progressive keratoconus. They concluded that conventional CXL and ACXL with irradiations of 9 mW/cm for 10 min showed a better flattening effect at 1-year follow-up. They concluded that the flattening effect of cross-linking was reduced with higher irradiation and shorter treatment duration. Bozkurt *et al.* [11] demonstrated a significant decrease in mean $K_{steep}$, $K_{flat}$, $K_{apex}$, and $K_{average}$ values at the 12 and 24-month follow-up visits. Mita *et al.* [16] have demonstrated a significant flattening in $K_{max}$ readings at 6 months following ACXL 3-min UV-A irradiance at a level of 30 mW/cm$^2$ ($P<0.05$). On the other hand, Brittingham *et al.* [17] reported a negative effect of accelerated protocol on $K_{max}$ at 1 year, with a mean change of −0.76 D with standard protocol versus +0.72 D in the accelerated group.

## Conclusion

Our study has confirmed the previous results on the efficacy and safety of accelerated cross-linking in stabilizing the keratoconus at a 1-year follow-up. Studies with larger number of patients and longer follow-up periods are needed to confirm the findings.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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