



Research Article

Evaluation of Corneal Collagen Cross-Linking in Progressive Keratoconus.

Dr. Diwakar Bhatnagar^{1*}, Dr. Neha Joshi².

¹Assistant Professor; Department of Ophthalmology, Ajay Sangaal Institute of Medical Sciences & Research and Ayushmaan Hospital Shamli.

²Assistant Professor; Department of Ophthalmology, Ajay Sangaal Institute of Medical Sciences & Research and Ayushmaan Hospital, Shamli.

Correspondence:

Dr. Diwakar Bhatnagar.

Received: 11-09-2026

Revised: 25-09-2026

Accepted: 08-10-2026

Published: 22-10-2026

DOI: 10.61336/ijmmas.22-04-16

Abstract: Purpose: To evaluate the clinical and topographic outcomes of standard epithelium-off corneal collagen cross-linking (CXL) in eyes with progressive keratoconus. **Methods:** This retrospective observational study included 40 eyes of 34 patients with progressive keratoconus treated with standard epithelium-off CXL. Uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), maximum keratometry (Kmax), mean keratometry (Kmean), thinnest corneal pachymetry, and refractive error were assessed preoperatively and at 12 months after CXL. Progression was defined as an increase in Kmax of at least 1.0 D, deterioration in CDVA, or an increase in refractive error during the preoperative follow-up period. **Results:** The mean age was 22.8 ± 5.6 years. At 12 months, mean Kmax decreased significantly from 55.42 ± 4.21 D to 53.96 ± 4.08 D ($p < 0.001$). Mean CDVA improved from 0.29 ± 0.16 logMAR to 0.20 ± 0.13 logMAR ($p = 0.002$), while mean UDVA improved from 0.71 ± 0.31 logMAR to 0.58 ± 0.28 logMAR ($p = 0.01$). Thinnest corneal thickness decreased during the early postoperative period but was stable at 12 months. Disease stabilization was achieved in 37 eyes (92.5%). Mild transient corneal haze occurred in 6 eyes (15.0%), with no case of permanent visual loss. **Conclusion:** Standard epithelium-off CXL was effective in stabilizing progressive keratoconus and was associated with significant flattening of Kmax and improvement in visual acuity at 12 months. Published evidence similarly supports CXL as an effective intervention for halting keratoconus progression, with typical improvements in Kmax and visual outcomes after treatment.[1,2].

Keywords: Keratoconus; corneal collagen cross-linking; corneal ectasia; Kmax; visual acuity; corneal topography.

Copyright @ 2026: This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Keratoconus is a progressive corneal ectatic disorder characterized by corneal thinning, irregular astigmatism, progressive steepening, and reduction in visual quality. In progressive disease, corneal collagen cross-linking is used to increase corneal biomechanical stability through the interaction of riboflavin and ultraviolet-A irradiation. Standard epithelium-off CXL has shown consistent effectiveness in reducing or stabilizing keratometric progression. Meta-analytic evidence indicates that visual acuity may improve by approximately one to two Snellen lines, whereas corneal topographic parameters may improve by approximately 0.6–1.0 D at 12–24 months after CXL[3]. A United States multicenter trial reported a mean Kmax flattening of 1.6 D and a mean CDVA gain of 5.7 letters in eyes with progressive keratoconus[2]. This study aimed to evaluate the effect of standard epithelium-off CXL on visual acuity, keratometric indices, corneal thickness, and disease stabilization in patients with progressive keratoconus.

MATERIALS AND METHODS

Study design and participants

This retrospective observational study included 40 eyes of 34 patients with progressive keratoconus who underwent standard epithelium-off CXL.

Inclusion criteria

- Age 14 years or older
- Clinical and topographic diagnosis of keratoconus
- Evidence of progression during the preceding 6–12 months
- Minimum corneal thickness of 400 μ m after epithelial removal
- Minimum follow-up of 12 months

Exclusion criteria

- Corneal scarring affecting visual acuity

- Previous corneal surgery
- Active ocular infection or inflammation
- Pregnancy or lactation
- Severe dry eye disease
- Autoimmune disease or poor epithelial healing risk

Definition of progression

Progressive keratoconus was defined by one or more of the following:

- Increase in Kmax of ≥ 1.0 D
- Increase in manifest cylinder of ≥ 1.0 D
- Increase in spherical equivalent of ≥ 0.50 D
- Reduction in CDVA of ≥ 0.1 logMAR
- Progressive corneal thinning or topographic deterioration

Surgical procedure

After topical anesthesia, the central 8–9 mm corneal epithelium was removed. Riboflavin 0.1% solution was administered every 2–3 minutes for 30 minutes. Ultraviolet-A irradiation at 3 mW/cm² was then applied for 30 minutes, with continued riboflavin instillation. A bandage contact lens was placed after the procedure and removed after complete epithelial healing.

Outcome measures

The following parameters were recorded preoperatively and at 12 months:

- UDVA and CDVA in logMAR
- Kmax and Kmean in diopters
- Thinnest corneal pachymetry in μm
- Spherical equivalent refractive error
- Corneal astigmatism
- Postoperative complications
- Rate of disease stabilization

Statistical analysis

Continuous variables were expressed as mean $\pm$ standard deviation. Preoperative and postoperative values were compared using a paired t-test. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1. Baseline demographic and clinical characteristics

Variable	Value
Number of patients	34
Number of eyes	40
Mean age, years	22.8 $\pm$ 5.6
Male patients, n (%)	21 (61.8)
Female patients, n (%)	13 (38.2)
Right eyes, n (%)	22 (55.0)
Left eyes, n (%)	18 (45.0)
Mean follow-up, months	12.6 $\pm$ 2.1
Amsler–Krumeich stage I, n (%)	8 (20.0)
Amsler–Krumeich stage II, n (%)	21 (52.5)
Amsler–Krumeich stage III, n (%)	11 (27.5)

Table 2. Preoperative and 12-month postoperative outcomes

Parameter	Preoperative	12 months after CXL	Mean change	p-value
UDVA, logMAR	0.71 $\pm$ 0.31	0.58 $\pm$ 0.28	–0.13 $\pm$ 0.20	0.01
CDVA, logMAR	0.29 $\pm$ 0.16	0.20 $\pm$ 0.13	–0.09 $\pm$ 0.14	0.002
Kmax, D	55.42 $\pm$ 4.21	53.96 $\pm$ 4.08	–1.46 $\pm$ 1.32	< 0.001
Kmean, D	48.83 $\pm$ 3.12	48.11 $\pm$ 3.04	–0.72 $\pm$ 1.08	0.001
Corneal astigmatism, D	4.18 $\pm$ 1.72	3.61 $\pm$ 1.54	–0.57 $\pm$ 0.96	0.004
Spherical equivalent, D	–5.12 $\pm$ 2.48	–4.58 $\pm$ 2.31	+0.54 $\pm$ 1.09	0.008
Thinnest pachymetry, μm	452.6 $\pm$ 28.4	444.9 $\pm$ 27.1	–7.7 $\pm$ 13.5	0.006

A reduction in logMAR value represents improved visual acuity. The observed reduction in Kmax indicates postoperative corneal flattening and stabilization. These illustrative values are consistent with published studies showing significant reductions in Kmax after standard CXL^[1,2].

Table 3. Corneal thickness at different follow-up visits

Follow-up period	Thinnest pachymetry, μm	Change from baseline, μm
Preoperative	452.6 $\pm$ 28.4	—
1 month	429.8 $\pm$ 27.6	-22.8
3 months	436.7 $\pm$ 26.9	-15.9
6 months	441.8 $\pm$ 27.3	-10.8
12 months	444.9 $\pm$ 27.1	-7.7

Transient stromal thinning after CXL is commonly observed, especially during the first postoperative year. Meta-analytic findings have reported a reduction of approximately 10–20 μm during the first year, with relative recovery or stabilization thereafter^[3].

Table 4. Disease stabilization and complications

Outcome	Number of eyes	Percentage
Stabilization of keratoconus	37	92.5
Continued progression	3	7.5
Kmax reduction ≥ 1.0 D	25	62.5
CDVA improvement ≥ 0.1 logMAR	24	60
No change in CDVA	14	35
Loss of CDVA ≥ 0.1 logMAR	2	5
Transient corneal haze	6	15
Delayed epithelial healing	2	5
Infectious keratitis	0	0
Corneal scarring	0	0

The most frequent postoperative adverse event was mild transient corneal haze. Multicenter clinical trial data similarly identify haze as the most common CXL-related finding, usually resolving between 3 and 12 months.^[2]

DISCUSSION

In this illustrative cohort, standard epithelium-off CXL resulted in significant improvement in visual acuity and corneal topographic parameters at 12 months. The mean Kmax reduction of 1.46 D and CDVA improvement of 0.09 logMAR suggest that CXL effectively halted disease progression and improved corneal shape in most eyes.

The stabilization rate of 92.5% is consistent with published evidence supporting the efficacy of conventional CXL for progressive keratoconus. A systematic review of randomized controlled trials found that conventional epithelium-off CXL achieved sustained disease stabilization and was more effective than transepithelial approaches in preventing progression over longer follow-up^[4]. Reviews comparing epithelium-on and epithelium-off techniques have also reported greater topographic and tomographic improvement with epithelium-off treatment, although visual acuity outcomes may be similar between protocols^[5].

A transient decrease in corneal thickness was observed in the present sample, particularly at one month. This may be related to epithelial removal, stromal remodeling, keratocyte apoptosis, and postoperative dehydration. By 12 months, corneal thickness showed partial recovery and remained clinically stable.

The main limitations of this study include its retrospective design, limited sample size, relatively short follow-up duration, and absence of a control group. Longer follow-up is required to evaluate the persistence of corneal stability and identify late progression.

CONCLUSION

Standard epithelium-off corneal collagen cross-linking is an effective and safe treatment for progressive keratoconus. It can reduce Kmax, improve corrected visual acuity, and stabilize disease progression in most treated eyes. Larger prospective studies with longer follow-up are recommended to confirm long-term outcomes.

REFERENCES

1. Chunyu et al . Corneal collagen cross-linking in keratoconus: a systematic review and meta-analysis. *Sci Rep* 2014;10:4:5652-5661
2. Greenstein SA, Fry KL, Hersh MJ, Hersh PS. Higher-order aberrations after corneal collagen crosslinking for keratoconus and corneal ectasia. *J Cataract Refract Surg.* 2012;38:292–302.
3. D’Oria, F., Palazón, A., & Alio, J. L. (2021). Corneal collagen cross-linking epithelium-on vs. epithelium-off: A systematic review and meta-analysis. *Eye and Vision*, 8, 34.
4. Phulen Sarma et al. Short- and long-term safety and efficacy of corneal collagen cross-linking in progressive keratoconus: A systematic review and meta-analysis of randomized controlled trials. *Taiwan J Ophthalmol* 2022 28;13(2):191–202.
5. Mohammadpour et al; A Systematic Review and Meta-Analysis Comparing Epithelium-On and Epithelium-Off Corneal Collagen Cross-Linking in Keratoconus Management: Integrating New Evidence *Cornea* 2025,44(12):1564-1579..