Original Article

Effect of Accelerated Epi-Off Crosslinking on Optical Quality, Corneal Aberrations, and Epithelial Wavefront During Adolescence

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Abstract

Objectives: To examine the effect of accelerated epi-off crosslinking (A-CXL) on visual acuity and quality in adolescent patients with progressive keratoconus.

Materials and Methods: The study included 109 eyes of 109 patients (mean age 16.24±2.55 years). MS-39 anterior segment optical coherence tomography images from before A-CXL and 1 month, 6 months, and 12 months after A-CXL were analyzed. Corneal tomographic parameters, total corneal aberrations, corneal epithelial aberrations, and optical quality indicators such as modulation transfer function (MTF) and Strehl ratio of the point spread function (PSF) were recorded.

Results: A significant improvement in corrected distance visual acuity was observed at 6 and 12 months after A-CXL (0.23±0.10 and 0.22±0.10 logarithm of the minimum angle of resolution [logMAR]) compared to the pre-A-CXL value (0.30±0.12 logMAR) ($p<0.001$ for both). MTF-5 and MTF-15 values were significantly higher at 12 months after A-CXL compared to before A-CXL ($p<0.001$). However, almost all MTF and PSF values were significantly lower at 1 month after A-CXL than at the other visits ($p<0.05$). Significant improvements were seen in root mean square higher-order aberrations (RMS-HOAs), vertical coma, and vertical trefoil values at 12 months after A-CXL compared to before A-CXL. A significant improvement was also detected in corneal epithelial aberrations, specifically in the vertical coma value. The change in corrected distance visual acuity at 12 months after A-CXL was significantly correlated with changes in keratometry values, with total corneal RMS-HOAs, vertical coma, and vertical trefoil, and with corneal epithelial RMS-HOAs (all $p<0.05$).

Conclusion: Besides total corneal aberrations, corneal epithelial aberrations may also influence the improvement of visual acuity and quality after A-CXL.

Keywords: Accelerated epi-off crosslinking, corneal aberration, corneal epithelial wavefront, modulation transfer function, point spread function

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Introduction

Keratoconus is the most common form of corneal ectasia, a serious condition that causes progressive thinning and steepening of the cornea, leading to deterioration of the corneal refractive surface.[1] The progressive decline in visual acuity and quality associated with the disease poses a major visual health concern, especially in adolescents. Individuals diagnosed before age 18 are often identified at a later stage and tend to experience more progression than those diagnosed in adulthood.[1,2] Therefore, early diagnosis and treatment are essential.

Corneal crosslinking (CXL) is the leading treatment for stopping keratoconus progression, with proven safety and effectiveness.[1] CXL treatment involves saturating the corneal stroma with the photosensitizer riboflavin, which reacts with ultraviolet A (UVA, 315-400 nm) to increase corneal stromal rigidity. While some studies have demonstrated the importance of improved anterior curvature parameters for visual recovery after CXL, others have highlighted the role of reduced higher-order aberrations (HOAs).[3,4,5,6] Indicators of impaired visual quality in patients with keratoconus include corneal HOAs and optical quality indices such as the modulation transfer function (MTF) and point spread function (PSF). Optical quality indicators are affected by the severity and progression of keratoconus.[7,8] The few available studies on changes in optical quality indicators following CXL have reported inconsistent findings.[3,9,10]

Anterior segment optical coherence tomography (AS-OCT) is a current imaging technique that enables assessment of the corneal layers. Epithelial wavefront analysis using the MS-39, which combines Placido disk technology with AS-OCT, is a recent development that has not yet gained sufficient coverage in the literature. Ning et al.[11] reported that epithelial aberrations were significantly higher in patients with keratoconus compared with a healthy control group. Studies analyzing changes in optical power due to epithelial remodeling after keratorefractive surgery have highlighted the importance and reproducibility of the epithelial wavefront.[12,13] Previous studies have also shown that epithelial remodeling occurs after CXL.[14,15] However, to our knowledge, no research has been conducted to examine the impact of corneal epithelial aberrations on the level and quality of vision, which can change after CXL.

This study aimed to investigate the effects of accelerated CXL (A-CXL) performed during adolescence on visual quality by analyzing changes in and relationships between optical quality, corneal aberrations, and corneal epithelial aberrations.

Materials and Methods

This retrospective study was conducted in the cornea unit within the ophthalmology department of a tertiary referral hospital. The study protocol was approved by a University of Health Sciences Türkiye, Ankara Etlik City Hospital Ethics Committee (decision no: AEŞH-BADEK1-2025-289, date: 27.08.2025) in accordance with the Declaration of Helsinki.

Patient Selection

The study included adolescent patients who were referred to the cornea and contact lens unit for keratoconus, were diagnosed with progressive keratoconus during follow-up, and were subsequently treated with A-CXL. A total of 109 eyes from 109 patients were included in this study. One eye of each patient who underwent bilateral A-CXL treatment was randomly selected.

Patients with a ≥1 diopter (D) increase in the maximum keratometry (Kmax) value, ≥1 D increase in corneal astigmatism, and ≥25 µm decrease in the thinnest corneal thickness at 1-year follow-up were classified as having progressive keratoconus.[1,16] Additionally, all patients under 18 years of age were considered to have progressive keratoconus because they were identified as having a very high risk of progression at the time of diagnosis.[2,17]

Inclusion criteria were as follows: patients under 20 years of age who were treated with A-CXL for progressive keratoconus and who had regular follow-up measurements at 1, 6, and 12 months after A-CXL. An important reason for selecting patients aged <20 years is that studies comparing adults and pediatric patients in the literature have shown that improvements in corrected distance visual acuity (CDVA) and anterior curvature parameters are more pronounced in the pediatric group.[16,18] Exclusion criteria were as follows: patients who developed keratitis, sterile corneal infiltrates, or greater than grade 2 haze after A-CXL; patients with preexisting corneal opacities such as sequelae of hydrops, apical scars, or sequelae of keratitis; patients with ocular surface diseases; patients who were pregnant or breastfeeding; and patients who wore contact lenses during the 1-year follow-up before or after A-CXL.

CDVA values measured with spectacle lenses using the Early Treatment Diabetic Retinopathy Study logarithm of the minimum angle of resolution (logMAR) chart were recorded retrospectively from the patients' digital records from before A-CXL and at 1, 6, and 12 months after A-CXL treatment.

Surgical Procedure

A total of 87 of 109 patients received topical anesthesia, while the remaining 22 received general anesthesia. After an 8-mm debridement of the corneal epithelium, a riboflavin solution containing 0.1% riboflavin and 1.1% hydroxypropyl methylcellulose was applied every 2 minutes for 20 minutes (MedioCROSS® M, Glaukos Company). Using a crosslinking device (CRS-X®, YURATEK), 370 nm UVA light was directed at the intersection of the target beams at the corneal apex for 10 minutes at an intensity of 9 mW/cm^2 (5.4 J/cm^2). UVA radiation was maintained while applying riboflavin drops every minute. The procedure was completed with cold irrigation and placement of a bandage contact lens. Postoperative management consisted of 0.5% moxifloxacin drops (Moxai, Abdi İbrahim İlaç San. ve Tic. A.Ş., İstanbul, Türkiye), 0.5% loteprednol etabonate drops (Lotemax, Bausch & Lomb Inc., Tampa, FL, USA) and artificial tears.

MS-39 Combined Placido Disk and High-Resolution AS-OCT

The MS-39 AS-OCT (software Phoenix version 4.1.1.5; CSO, Firenze, Italy) combines a Placido disk with a spectral domain (SD)-OCT system. The device uses an infrared superluminescent diode source emitting at 850 nm to acquire slices over a 16-mm diameter with an axial resolution of 3.6 µm. The SD-OCT scan consisted of 1024 A-scans and 25 B-scans across 16-mm sections, each captured in approximately 1 s. In our study, all AS-OCT images were acquired in the "12 × 5 @ 10 mm" mode by an experienced technician due to its higher resolution. Kmax, flat keratometry (Kflat), steep keratometry (Ksteep), average keratometry (Kavg) values, thinnest pachymetry, minimum and maximum epithelial thicknesses (ET) in the central 6-mm zone, along with maximum anterior and posterior elevation values and anterior astigmatism measurements in the 6-mm and 3-mm zones, were obtained from pre-A-CXL and 1-month, 6-month, and 12-month post-A-CXL images.

Total corneal aberrations, PSF, MTF, and corneal epithelial aberrations were calculated by selecting a 4.5-mm virtual pupil diameter, centered on the corneal vertex. The PSF value is expressed as the Strehl ratio (SR), which is the ratio between the peak intensity of the PSF of the optical system under study and the peak intensity of a flat wavefront that passes through the same pupil. MTF values were expressed at different spatial frequencies (5, 10, 15, and 20 cpd).

The MS-39 software automatically converts the anterior and posterior corneal elevation profiles into corneal wavefront data based on Zernike polynomials up to a seventh-order expansion. Total corneal aberrations and HOAs were recorded as root mean square (RMS) values. Documented third- and fourth-order HOAs derived from the Zernike polynomials included vertical trefoil (Z_3^{-3}), vertical coma (Z_3^{-1}), horizontal coma (Z_3^1), oblique trefoil (Z_3^3), and spherical aberration (Z_4^0). Corneal epithelial aberrations, specifically epithelial wavefront errors, were calculated using virtually refracted rays via the MS-39 software. The epithelial optical wavefront was simulated by modeling the interaction of light with the epithelial layer and its interfaces, including the air-tear film interface and the epithelium-stroma interface. A collimated beam of light with a specific diameter was virtually projected onto the epithelium, deflected according to the corneal curvature, and finally influenced by the Bowman layer curvature. For corneal epithelial aberrations, total aberrations and HOAs were similarly recorded as RMS values, including the same third- and fourth-order aberrations mentioned above for the total cornea.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). We used the Kolmogorov-Smirnov test to evaluate the normality of quantitative variables. Repeated measures from the same individuals were compared using the repeated-measures one-way analysis of variance (ANOVA) with Bonferroni multiple comparison tests for normally distributed data and with the Friedman test followed by the Wilcoxon test with Bonferroni correction for non-normally distributed data. Pearson's or Spearman's correlation coefficients were employed to analyze the relationships between variables, depending on data normality. Statistical significance was defined as a p value less than 0.05.

Results

This study evaluated 109 eyes of 109 patients, including 46 females and 63 males. The average age was 16.24±2.55 years (range, 11-20 years). The patients' mean CDVA values were 0.30±0.12 logMAR before A-CXL, 0.29±0.12 logMAR at 1 month after CXL, 0.23±0.10 logMAR at 6 months after CXL, and 0.22±0.10 logMAR at 12 months after CXL. Significant improvements were observed at 6 and 12 months compared to pre-CXL values (p<0.001 for both) (Table 1).

Following A-CXL, substantial flattening was observed in Kmax (p<0.001) and Ksteep (p=0.004) values at 12 months after the procedure compared to before A-CXL and at 1 and 6 months post-procedure. Significant flattening was also observed in Kavg values at 12 months after A-CXL compared to pre-treatment (p=0.020). The minimum ET in the central 6-mm zone was significantly thicker at 6 and 12 months post-A-CXL compared to before A-CXL (p=0.037). The maximum ET in the central 6-mm zone was significantly thicker at 1 month post-A-CXL compared to before and at 6 and 12 months post-A-CXL (p=0.002). The difference between the maximum and minimum ET in the central 6-mm zone was significantly lower at 6 and 12 months post-A-CXL compared to before and at 1 month post-A-CXL (p<0.001). Anterior elevation decreased significantly at 6 and 12 months post-A-CXL compared to pre-treatment (p<0.001). Additionally, corneal astigmatism within the central 3-mm zone decreased significantly at 12 months after A-CXL compared to pre-treatment and 1 month post-treatment values (p=0.003 and p<0.001, respectively). No significant changes were observed in Kflat, thinnest pachymetry, posterior elevation, or corneal astigmatism values (p>0.05) (Table 1).

When we examined optical quality markers, SR-PSF was significantly lower at 1 month than at 6 and 12 months after A-CXL (p=0.006 and p<0.001, respectively). The MTF-5 value at 12 months after A-CXL was significantly higher than that before and at 1 month after A-CXL (p=0.033 and p=0.001, respectively). MTF-10 and MTF-20 values were significantly lower at 1 month than at 12 months after A-CXL (both p=0.001). The MTF-15 value at 12 months after A-CXL was significantly higher than that before and at 1 and 6 months after A-CXL (p=0.022, p=0.004, and p=0.005, respectively). However, no significant differences were observed in the SR-PSF, MTF-10, and MTF-20 values at 12 months post-A-CXL compared to baseline (p>0.05) (Table 2).

Total corneal aberrations showed significant decreases in RMS-HOAs and vertical coma at 6 and 12 months after A-CXL compared to pre-A-CXL levels ($p=0.034$ and $p<0.001$ for RMS-HOA; $p=0.006$ and $p<0.001$ for vertical coma, respectively). Vertical trefoil showed significant improvement at 12 months after A-CXL compared to pre-A-CXL levels ($p=0.017$). No significant differences were observed in horizontal coma, oblique trefoil, or spherical aberration values ($p>0.05$) (Table 3).

Regarding corneal epithelial aberrations, only the vertical coma value improved at 1, 6, and 12 months after A-CXL compared to before A-CXL ($p=0.004$, $p=0.038$, and $p=0.003$, respectively). No significant differences were observed in other corneal epithelial aberrations ($p>0.05$) (Table 3).

The change in the difference between maximum and minimum ET in the central 6-mm zone from baseline to 12 months after A-CXL was significantly correlated with the changes in corneal epithelial RMS-HOAs ($r=0.423$, $p<0.001$) and vertical coma ($r=-0.252$, $p=0.008$) at 12 months after A-CXL (Figure 1).

The change in CDVA at 12 months after A-CXL compared to baseline was significantly correlated with the changes in Kmax ($r=0.640$, $p<0.001$), Kflat ($r=0.566$, $p<0.001$), Ksteep ($r=0.670$, $p<0.001$), Kavg ($r=0.637$, $p<0.001$), and corneal astigmatism within the central 3-mm zone ($r=0.457$, $p<0.001$). Change in CDVA was also significantly correlated with changes in total corneal RMS-HOAs ($r=0.606$, $p<0.001$), vertical coma ($r=0.506$, $p<0.001$), and vertical trefoil ($r=-0.541$, $p<0.001$) values. Among the corneal epithelial aberration changes, only the RMS-HOA value was significantly correlated ($r=0.224$, $p=0.019$). The changes in optical quality indicators SR-PSF, MTF-5, MTF-10, MTF-15, and MTF-20 from baseline to 12 months after A-CXL were not significantly correlated with the change in CDVA ($p>0.05$) (Table 4).

Table 1. Changes in corrected distance visual acuity and topographic and tomographic data after accelerated corneal crosslinking (A-CXL)

	Before A-CXL	1 month after A-CXL	6 months after A-CXL	12 months after A-CXL	p
CDVA (logMAR)	0.30±0.11^{a}	0.30±0.12^{a}	0.23±0.10^{b}	0.22±0.10^{c}	**<0.001**
Kmax (D)	53.79±5.82$^{a, b}$	53.73±5.08^{a}	52.95±4.57^{b}	52.38±4.49^{c}	**<0.001**
Kflat (D)	44.96±2.76	45.05±2.65	44.76±2.44	44.73±2.50	0.064
Ksteep (D)	48.94±3.74$^{a, b}$	49.01±3.66^{a}	48.67±3.45^{b}	48.49±3.29^{c}	**0.004**
Kavg (D)	46.87±3.06$^{a, b}$	46.90±2.95^{a}	46.61±2.75$^{b, c}$	46.51±2.72^{c}	**0.020**
Thinnest pachymetry (µm)	453.38±35.42	449.53±36.37	449.13±36.89	451.02±39.17	0.058
Min. ET (µm)	42.79±5.56^{a}	43.42±5.39$^{a, b}$	43.77±5.07^{b}	43.84±6.15^{b}	**0.037**
Max. ET (µm)	62.53±4.43^{a}	64.70±7.61^{b}	62.88±5.61^{a}	62.34±5.46^{a}	**0.002**
Max.-min. ET (µm)	19.74±0.70^{a}	21.28±0.81^{b}	18.57±0.61^{c}	18.21±0.61^{c}	**<0.001**
Anterior elevation	26.32±14.42^{a}	24.58±13.89^{a}	22.42±12.95^{b}	20.62±12.56^{c}	**<0.001**
Posterior elevation	40.59±17.86	40.74±21.47	39.45±19.33	38.74±18.93	0.099
Corneal astigmatism (3 mm) (D)	4.24±2.30^{a}	4.22±2.25^{a}	3.93±2.11^{a,b}	3.80±2.00^{b}	**<0.001**
Corneal astigmatism (6 mm) (D)	3.19±1.66	3.14±1.60	3.01±1.53	2.99±1.53	0.055

Different lowercase letters indicate statistically different groups. CDVA: Corrected distance visual acuity (with spectacle lenses), logMAR: Logarithm of the minimum angle of resolution, K: Keratometry value, D: Diopters, Kmax: Maximum keratometry, Kflat: Flat keratometry, Ksteep: Steep keratometry, Kavg: Average keratometry, ET: Epithelial thickness, Min.: Minimum, Max.: Maximum

Table 2. Changes in the Strehl ratio of the point spread function (SR-PSF) and the modular transfer function (MTF) after accelerated corneal crosslinking (A-CXL)

	Before A-CXL	1 month after A-CXL	6 months after A-CXL	12 months after A-CXL	p*
SR-PSF	0.077±0.06$^{a, b}$	0.071±0.04^{a}	0.079±0.05^{b}	0.080±0.05^{b}	**<0.001**
MTF-5 (cpd)	0.229±0.20$^{a, b}$	0.217±0.18^{a}	0.243±0.20$^{b, c}$	0.256±0.21^{c}	**<0.001**
MTF-10 (cpd)	0.122±0.13$^{a, b}$	0.104±0.11^{a}	0.118±0.12$^{a, b}$	0.135±0.13^{b}	**0.003**
MTF-15 (cpd)	0.075±0.09^{a}	0.072±0.07^{a}	0.073±0.08^{a}	0.083±0.08^{b}	**0.001**
MTF-20 (cpd)	0.063±0.07$^{a, b}$	0.052±0.07^{a}	0.060±0.07$^{a, b}$	0.068±0.08^{b}	**0.001**

*Friedman test. Different lowercase letters indicate statistically different groups. cpd: Cycles per degree

Table 3. Changes in total corneal aberrations and corneal epithelial aberrations after accelerated corneal crosslinking (A-CXL)

	Before A-CXL	1 month after A-CXL	6 months after A-CXL	12 months after A-CXL	p
Total corneal aberrations					
RMS-HOAs (µm)	1.41±0.93^{a}	1.38±0.74^{a}	1.26±0.67^{b}	1.17±0.64^{c}	**<0.001**
Vertical coma (µm)	1.05±0.77^{a}	0.99±0.70^{a}	0.92±0.64^{b}	0.85±0.60^{c}	**<0.001**
Horizontal coma (µm)	0.03±0.40	0.01±0.40	0.03±0.36	0.01±0.34	0.861*
Vertical trefoil (µm)	-0.48±0.38^{a}	-0.46±0.38$^{a, b}$	-0.43±0.35$^{a, b}$	-0.41±0.32^{b}	**0.009**
Oblique trefoil (µm)	0.00±0.44	-0.006±0.37	0.00±0.35	0.025±0.19	0.746*
Spherical aberration (µm)	0.046±0.25	0.058±0.23	0.027±0.21	0.025±0.19	0.200*
Corneal epithelial aberrations					
Total aberrations-RMS (µm)	1.22±0.54	1.28±0.60	1.23±0.54	1.20±0.50	0.370
RMS-HOAs (µm)	0.78±0.39	0.85±0.46	0.79±0.39	0.77±0.36	0.207
Vertical coma (µm)	-0.38±0.36^{a}	-0.30±0.38^{b}	-0.32±0.39^{b}	-0.29±0.38^{b}	**<0.001**
Horizontal coma (µm)	0.02±0.34	0.02±0.29	-0.03±0.27	-0.02±0.31	0.537
Vertical trefoil (µm)	0.10±0.17	0.09±0.24	0.12±0.19	0.14±0.19	0.067
Oblique trefoil (µm)	0.01±0.19	0.02±0.26	0.01±0.20	-0.01±0.19	0.700
Spherical aberration (µm)	-0.10±0.21	-0.07±0.26	-0.09±0.20	-0.08±0.21	0.398

*Friedman test. Different lowercase letters indicate statistically different groups. RMS-HOAs: Root mean square higher-order aberrations

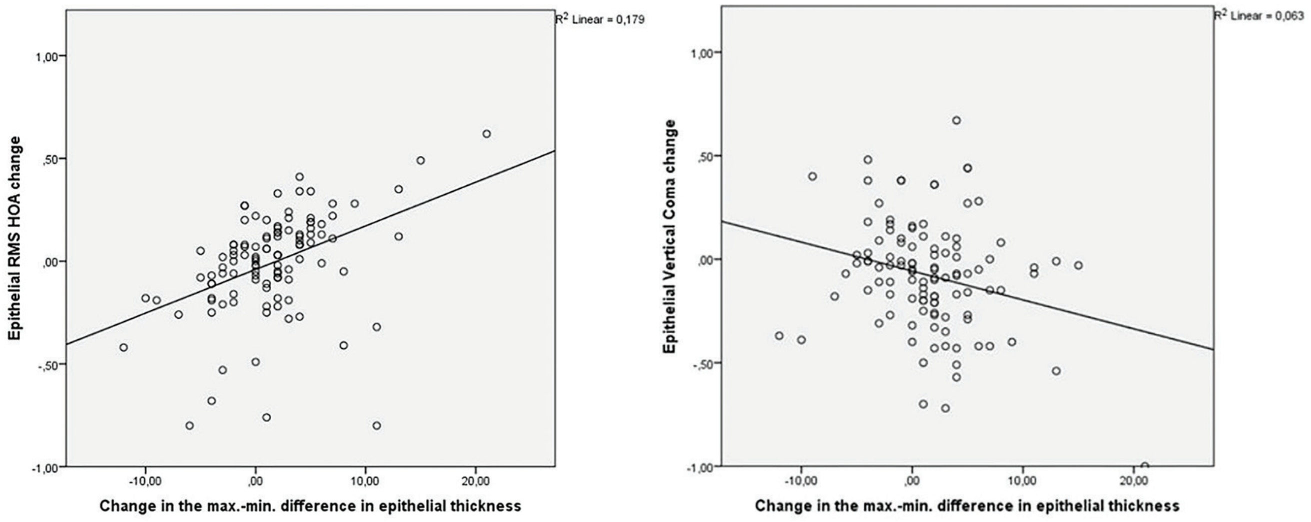

Figure 1. Correlations between the change in the difference of maximum and minimum corneal epithelial thicknesses in the central 6-mm zone from baseline to 12 months after A-CXL and the change in corneal epithelial RMS-HOA and vertical coma aberration from baseline to 12 months after A-CXL

A-CXL: Accelerated corneal crosslinking, RMS-HOA: Root mean square higher-order aberrations, max.: Maximum, min.: Minimum

Table 4. Correlations between change in corrected visual distance acuity at 12 months after accelerated corneal crosslinking (A-CXL) vs. baseline and changes in corneal topometric parameters, Strehl ratio of the point spread function, modular transfer function, and total and epithelial corneal aberrations

Change at 12 months after A-CXL	**Change in CDVA at 12 months after A-CXL**	
	r	**p**
Age (years)	-0.130	0.177
Kmax (D)	0.640	**<0.001**
Kflat (D)	0.566	**<0.001**
Ksteep (D)	0.670	**<0.001**
Kavg (D)	0.637	**<0.001**
Corneal astigmatism (3 mm) (D)	0.457	**<0.001**
SR-PSF	0.022	0.817*
MTF-5 (cpd)	-0.055	0.573*
MTF-10 (cpd)	-0.067	0.487*
MTF-15 (cpd)	0.005	0.955*
MTF-20 (cpd)	-0.054	0.580*
RMS-HOAs (µm)	0.606	**<0.001**
Vertical coma (µm)	0.506	**<0.001**
Vertical trefoil (µm)	-0.541	**<0.001**
Epithelial RMS-HOAs (µm)	0.224	0.019
Epithelial vertical coma (µm)	-0.152	0.116
Epithelial vertical trefoil (µm)	0.102	0.291

*Spearman correlation analysis. CDVA: Corrected distance visual acuity, D: Diopters, Kmax: Maximum keratometry, Kflat: Flat keratometry, Ksteep: Steep keratometry, Kavg: Average keratometry, SR-PSF: Strehl ratio of the point spread function, MTF: Modulation transfer function, RMS-HOAs: Root mean square higher-order aberrations, r: Correlation coefficient

Discussion

Many studies have investigated the impact of corneal CXL treatment on visual quality and function employing various parameters, including CDVA, corneal and ocular aberrations, optical quality indicators, and contrast sensitivity.[3,9,10,19,20,21] To our knowledge, our study is the first to evaluate corneal epithelial aberrations following A-CXL. Consistent with many studies in the literature, we observed significant improvements in CDVA, the anterior curvature parameters Kmax, Ksteep, and Kavg, corneal astigmatism in the central 3-mm area, and anterior elevation from baseline to 12 months after A-CXL.[1,16,20,22,23,24] This may be related to remodeling of the anterior cornea caused by A-CXL through the reorganization of stromal collagen lamellae.[1,25]

Most studies evaluating corneal aberration changes after CXL have found significant reductions in third- and fourth-order aberrations, such as vertical coma, spherical aberration, vertical trefoil, and secondary astigmatism. While some studies have argued that reductions in HOAs after CXL are associated with visual improvement, others have found no such association.[3,6,19,20,23,26] In the 5-year follow-up results after standard CXL, Taşçı et al.[27] found an improvement in visual acuity and a decrease in HOAs, but no change in vertical coma as found in our study. Together with RMS-HOAs, we observed significant reduction in vertical coma and vertical trefoil values at 12 months post-A-CXL compared to baseline levels. Moreover, we determined that this improvement correlated significantly with the improvement in CDVA. The reduction in aberrations after CXL is primarily a result of the anterior corneal reshaping induced by A-CXL. This creates a smoother optical surface and explains the linear relationship between decreased aberrations and improved CDVA.

While aberrations play a crucial role in assessing visual quality, they are insufficient on their own. Optical quality indicators, such as the PSF and MTF, are used to describe how an image is formed at the fovea and the relationship between the image and the object. The MTF is an objective reflection of vision under different contrast conditions. The SR-PSF represents the ratio of the light intensity at the fovea in an eye with aberration (scattering) to that of a perfect optical system with no scatter. Previous studies have emphasized the importance of optical quality indicators in distinguishing eyes with keratoconus from those of healthy eyes and in assessing the severity and progression of keratoconus.[7,8] However, there are very few publications on how optical quality indices change after CXL. Uysal et al.[3] found no significant difference in MTF and SR-PSF values when they compared 111 patients before and 12 months after CXL using a standard protocol. Similarly, Kaya Ergen et al.[10] found no significant change in SR-PSF values from baseline to 12 months after transepithelial CXL in 110 eyes. Ozdas et al.[9] found a significant improvement in SR-PSF values after A-CXL in a 3-year follow-up of 110 patients.

In our study, we observed a worsening in almost all SR-PSF and MTF values at 1 month after A-CXL, whereas we found a significant improvement in MTF-5 and MTF-15 values at 12 months after A-CXL compared to baseline. This deterioration in optical quality indicators at 1 month after A-CXL may have resulted from early subclinical haze during the healing period due to incomplete stromal healing.[9,28] The improvement we achieved in MTF-5 and MTF-15 values compared to other studies may be due to our lower mean age and the fact that we worked with adolescent patients (11-20), which allowed us to observe the effectiveness of A-CXL differently. Similarly, studies comparing the effects of CXL in pediatric and adult groups have reported that the improvements in CDVA and changes in anterior curvature were more pronounced in the pediatric group.[16,18] This indicates that CXL is more effective in this group.

However, we observed no significant correlation between the changes in optical quality indicators from baseline to 12 months post-A-CXL and the change in CDVA. This may be because the limited change in visual acuity was insufficient to correlate with the change in optical quality indicators. Indeed, a study conducted in 20 eyes of 16 patients treated using the Cretan protocol (a procedure that includes CXL and limited refractive correction) demonstrated greater improvements in PSF and MTF values, as well as in CDVA.[28]

The ability to examine corneal layers in detail with AS-OCT has made ET maps an important tool in the clinical practice of both refractive surgery and the diagnosis and treatment of corneal ectasia. Epithelial remodeling can cause undercorrection, particularly in refractive surgery. This highlights the importance of epithelial optical power. Epithelial wavefront analysis, a novel technology, allows for better examination of the effects of epithelial optical power and epithelial remodeling. Indeed, some studies have suggested that epithelial remodeling after CXL results in a more uniform corneal optical surface.[14,15]

In our study, total epithelial aberrations did not change significantly, but among the epithelial HOAs, we observed a significant improvement in the vertical coma values 12 months after A-CXL compared to baseline. This result in particular indicates that the vertical coma value, which is often the corneal aberrometric result of the inferotemporal displacement of the cone in keratoconus, is similarly reflected in the epithelium. Indeed, studies have shown that the epithelial layers in patients with keratoconus are thinner, particularly in the inferotemporal and inferior regions, compared to those in healthy controls, and this correlates with posterior elevation on the steepest keratometry readings.[29,30] Furthermore, differences between the maximum and minimum ET, an indicator of epithelial uniformity, have been reported to be more pronounced in keratoconic patients.[30,31] Lautert et al.[15] demonstrated that this difference decreased after CXL, indicating that epithelial remodeling resulted in a more uniform epithelium. In our study, we also observed that the differences between the maximum and minimum ET decreased after A-CXL.

The improvement in the epithelial vertical coma value observed in our study, as well as our finding that the improvement in CDVA was correlated with the change in epithelial RMS-HOAs, may indicate that A-CXL provides a more uniform structure to the epithelial layer, resulting in a more regular refractive surface in the epithelium, thus improving the optical power. Furthermore, the correlation we found between the changes in corneal epithelial RMS-HOAs and vertical coma and the changes in the difference between maximum and minimum ET in the central 6-mm zone may indicate that epithelial remodeling plays a role in the change of the corneal epithelial wavefront after A-CXL.

Study Limitations

Our study has some important limitations. First, we examined only corneal and corneal epithelial aberrations and did not evaluate whole-eye ocular aberrations. Indeed, a significant portion of corneal aberrations is neutralized by internal aberrations. Another important limitation is the one-year follow-up period. With longer follow-up periods, the effects of A-CXL on total corneal and corneal epithelial aberrations, as well as optical quality indicators, can be assessed more clearly.

Conclusion

In conclusion, A-CXL is an effective treatment for adolescent patients with progressive keratoconus, playing a significant role in improving vision and reducing total corneal and corneal epithelial HOAs. The association between visual improvement after A-CXL and the reduction in total corneal and corneal epithelial aberrations may be a consequence of anterior corneal remodeling after A-CXL. Longitudinal studies with longer follow-up periods could contribute to a clearer understanding of the effects of CXL on optical quality indicators as well as total and epithelial corneal aberrations.

Ethics

Ethics Committee Approval: The study protocol was approved by a University of Health Sciences Türkiye, Ankara Etlik City Hospital Ethics Committee (decision no: AEŞH-BADEK1-2025-289, date: 27.08.2025) in accordance with the Declaration of Helsinki.

Informed Consent: Retrospective study.

Declarations

Authorship Contributions

Surgical and Medical Practices: B.D.Y.E., B.K., Concept: B.D.Y.E., B.K., Design: B.D.Y.E., B.K., Data Collection or Processing: B.D.Y.E., B.K., Analysis or Interpretation: B.D.Y.E., Literature Search: B.D.Y.E., B.K., Writing: B.D.Y.E., B.K.

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