

# Evaluation of changes in corneal volume, volume and angle of anterior chamber in keratoconus patients using Pentacam after CXL

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## ABSTRACT

**Introduction and Objective:** Corneal collagen cross-linking (CXL) with riboflavin and ultraviolet-A (UVA) is a new technique of mechanical stability of the cornea and prevention of keratoconus progression. The present study aimed at the evaluation of the changes in the corneal volume (CV), volume, and the angle of anterior chamber in keratoconus patients using the Pentacam after CXL. **Methods:** This prospective study was performed on 48 eyes of 24 patients (including 12 men, 17–33 years old) with progressive keratoconus undergoing CXL treatment at collagen cross-linking Imam Khomeini Hospital in Ahvaz in 2019. The CV (CV) and anterior chamber parameters such as anterior chamber volume (ACV) and anterior chamber angle (ACA) were measured using the Pentacam before CXL and at 6 and 12 months after CXL. Also, all of the patients were evaluated in terms of best-corrected visual acuity (BCVA), during the follow-up. **Results:** The pre-CXL values of BCVA was significantly lower than the post-CXL values in 6 and 12 months ( $0.18 \pm 0.11$ ,  $0.15 \pm 0.10$ , and  $0.11 \pm 0.10$ , respectively,  $P < 0.0001$ ). In general, there was a significant improvement in the BCVA ( $P < 0.0001$ ), a significant decrease in the CV ( $P = 0.001$ ), and a significant increase in the ACV ( $P < 0.0001$ ), and angle ( $P < 0.0001$ ) 6 and 12 months after CXL. **Conclusion:** It seems that CXL has a positive effect on the anterior chamber parameters (ACV and ACA) and CV after 6 months and 1 year in the treatment of keratoconus patients. In addition, the visual acuity improves after CXL. Finally, further studies with a higher sample size and longer follow-up periods are recommended.

**Keywords:** Anterior chamber, cornea, cross-linking, keratoconus

## Introduction

Keratoconus is a bilateral asymmetric disorder that affects the corneal stroma selectively. This disorder causes protrusion, thinning, and progressive biomechanical instability of the cornea and manifests itself in the form of keratoconus. Finally, this process can reduce vision due to unacceptable levels of irregular astigmatism.<sup>[1]</sup> The prevalence of keratoconus varies in different

countries based on diagnostic techniques. According to a recent meta-analysis, the prevalence of keratoconus was reported to be 1.38 cases per 1,000 people worldwide.<sup>[2]</sup> Keratoconus usually occurs in adolescence and progresses until the third or fourth decade of life.<sup>[3,4]</sup> The economic costs of keratoconus for patients have caused considerable concerns.<sup>[5]</sup>

It is estimated that if left untreated, about 12–20% of the patients will need corneal transplantation to restore their vision.<sup>[6]</sup> This will lead to problems such as rejection and graft failure, which will prolong the time required to improve the vision.<sup>[7]</sup> Keratoconus is one of the most common causes of keratoplasty.<sup>[8]</sup> Nowadays,

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corneal collagen cross-linking (CXL) is offered as a new, minimally invasive method for treating keratoconus. This method is fast and relatively painless which has good results in stopping the disease progression.<sup>[9]</sup> In this procedure, a few drops of riboflavin (vitamin B2) are injected into the patient's eye and exposed to ultraviolet light, where riboflavin is absorbed by the cornea. This substance leads to corneal strength by binding the collagen fibers inside the corneal stroma to each other.<sup>[10,11]</sup> CXL prevents the development of keratoconus, improves ectasia, reduces refractive errors, and also improves visual acuity by about 1–2 lines.<sup>[12,13]</sup> Studies have shown that the weakening of corneal tissue in the keratoconus causes changes in the corneal parameters such as corneal strength and corneal astigmatism. Some studies have also shown that CXL causes changes in the corneal apex thickness, corneal volume (CV), anterior chamber angle (ACA), anterior chamber volume (ACV), and depth compared to the preoperative.<sup>[14,15]</sup> However, a few studies have been performed on the effect of CXL on the anterior chamber parameters; therefore, the aim of this study was to compare the changes in the CV, volume, and angle of the anterior chamber in patients with keratoconus using the Pentacam before and after collagen cross-linking.

## Method

The present case series study was performed on the patients with progressive keratoconus who were candidates for the CXL operation in the Imam Khomeini Medical Center in Ahvaz in 2019. This study was conducted after obtaining permission from the Research Council and approval of the ethics committee of the Ahwaz University of Medical Sciences (code: IR.AJUMS.REC.1399.373). At first, informed and written consent was obtained from the participating patients or their legal guardians, and the provisions of the ethics statement were observed in all the stages of this research. The exclusion criteria included pregnancy and lactation, patients with a history of corneal surgery, patients with any complications during and after surgery, people with diabetes or collagen-tissue diseases, severe dry-eye syndrome, visual acuity  $\geq 20.25$ , and cornea thickness (TCT) less than 400 microns.

At the beginning and before surgery, the CXL, CV, ACV, and angle were measured by the Pentacam. Before the surgery, pilocarpine drops were injected to narrow the pupil and reduce damage to the lens and retina. Then, surgery was performed under sterile conditions and local anesthesia with tetracaine drops. First, the central epithelium of the cornea was removed with a diameter of 9 mm, and then a drop of 0.1% riboflavin was injected into the surface of the cornea every 2–3 min for 30 min. After ensuring that riboflavin enters the anterior segment, ultraviolet radiation with a wavelength of 370  $\mu\text{m}$  and a power of 3  $\text{mw}/\text{cm}^2$  at a distance of 1 cm from the cornea for 30 min at a dose of 4.5 J per  $\text{cm}^2$  began using a slit-lamp. The riboflavin drops were injected every 2–3 min at intervals of this process. A dressing lens was then inserted, which remains on the cornea until the epithelium was completely healed. Prophylactic antibiotics

and topical betamethasone drops were used for 4 weeks after epithelial repair. The CV, ACV, and ACA were measured by the Pentacam (Oculus Pentacam, Oculus Optikgerate GmbH, Germany) at 6 and 12 months postoperative. Also, the BCVA was assessed using an E chart in the follow-up period. All the examinations were conducted by a corneal fellowship.

## Statistical analysis

The SPSS software version 22 was used for statistical analysis. The normality of the data was checked by Kolmogorov–Smirnov. The Wilcoxon test was used to compare the variables and Spearman's correlation test was used to examine the relationship between the variables. The analysis of variance test with repeated measures was also used to compare the changes in the parameters at different times. The significance level in the tests was considered as 0.05.

## Results

This study was performed on 12 men and 12 women including 48 eyes (24 right eyes and 24 left eyes). The mean age of the patients was  $24.71 \pm 4.28$  years (between 17 and 33 years). The results of measuring the CV, volume, and angle of the anterior chamber in the patients with keratoconus before and after cross-linking are presented in Tables 1-3. The results showed that the CV showed significant changes at different times before and after CXL ( $P = 0.001$ ). The CV decreased significantly at 6 and 12 months after CXL compared to before the operation ( $P = 0.031$  and  $P = 0.028$ , respectively). However, the CV at 12 months after the CXL did not show a significant change compared to 6 months after CXL ( $P = 0.576$ ). The ACV showed significant changes at different times before and after CXL ( $P < 0.0001$ ). The ACV showed a significant increase in 6 and 12 months after CXL compared to before the operation ( $P = 0.021$  and  $P = 0.001$ , respectively). The ACV also increased in 12 months after CXL compared to 6 months after CXL ( $P < 0.0001$ ). The ACA showed significant changes at different times before and after CXL ( $P < 0.0001$ ). The ACA increased at 6 and 12 months after CXL compared to before operation ( $P < 0.0001$ ). The ACA was also increased 12 months after CXL compared to 6 months after CXL ( $P = 0.001$ ). The visual acuity showed significant changes at different times before and after CXL ( $P < 0.0001$ ). The visual acuity increased at 6 and 12 months after CXL compared to before surgery ( $P < 0.0001$ ).

**Table 1: Corneal volume, volume, and angle of anterior chamber in patients with keratoconus before and 6 months after cross-linking surgery**

Variable	Preoperative (T0)	6 months after surgery (T1)	P
CV ( $\text{mm}^3$ )	55.11 $\pm$ 3.08	54.62 $\pm$ 3.13	0.031
ACV ( $\text{mm}^3$ )	187.18 $\pm$ 32.39	188.59 $\pm$ 30.51	0.021
ACA ( $^\circ$ )	37.44 $\pm$ 5.36	38.32 $\pm$ 5.20	<0.0001
BCVA (log MAR)	0.18 $\pm$ 0.11	0.15 $\pm$ 0.10	<0.0001

CV: Corneal volume; ACV: anterior chamber volume; ACA: anterior chamber angle; BCVA: best-corrected visual acuity

**Table 2: Corneal volume, volume, and angle of anterior chamber in patients with keratoconus before and 12 months after cross-linking surgery**

Variable	Preoperative (T0)	12 months after surgery (T2)	P
CV (mm <sup>3</sup> )	55.11±3.08	54.53±3.15	0.028
ACV (mm <sup>3</sup> )	187.18±32.39	190.94±30.55	0.002
ACA (°)	37.44±5.36	38.62±4.92	<0.0001
BCVA (log MAR)	0.18±0.11	0.11±0.10	<0.0001

CV: Corneal volume; ACV: anterior chamber volume; ACA: anterior chamber angle; BCVA: best-corrected visual acuity

**Table 3: Corneal volume, volume, and angle of anterior chamber in patients with keratoconus 6 and 12 months after cross-linking surgery**

Variable	6 months after surgery (T1)	12 months after surgery (T2)	P
CV (mm <sup>3</sup> )	54.62±3.13	54.53±3.15	0.576
ACV (mm <sup>3</sup> )	188.59±30.51	190.94±30.55	<0.0001
ACA (°)	38.32±5.20	38.62±4.92	0.001
BCVA (log MAR)	0.15±0.10	0.11±0.10	<0.0001

CV: Corneal volume; ACV: anterior chamber volume; ACA: anterior chamber angle; BCVA: best-corrected visual acuity

The visual acuity was also increased in 12 months after CXL compared to 6 months after CXL ( $P < 0.0001$ ).

## Discussion

The results of the present study showed that the CV at 6 and 12 months after CXL was significantly reduced compared to before surgery. However, the CV did not change significantly 12 months after CXL compared to 6 months after surgery. A significant reduction in the CV in patients with keratoconus after CXL has been reported in other previous studies. In a study of 97 progressive keratoconus eyes treated with CXL surgery, Sedaghat *et al.*<sup>[14]</sup> reported that the CV measured by the Pentacam decreased significantly after a 1-year follow-up compared to the preoperative value (55.97 mm<sup>3</sup> vs. 56.66 mm<sup>3</sup>, respectively). In a study by Omar *et al.*,<sup>[16]</sup> the CV before surgery was 57.97 mm<sup>3</sup>, which reduced significantly to 56.91 mm<sup>3</sup> after the CXL surgery. In the Alifa study,<sup>[8]</sup> the total CV at 3 and 6 months after surgery showed a significant decrease compared to before surgery. Other studies also reported a significant reduction in the CV in the short term (1, 3, and 6 months) and long term (12 and 24 months) after the CXL surgery measured by different methods.<sup>[13,17-19]</sup> Therefore, it seems that the decrease in the CV is global and has been observed in all areas where CXL surgery has been used. However, further studies are needed to determine the effect of CXL on selected corneal areas such as the apex or in a thinner area. Although the results of many studies have shown that CXL surgery reduces CV compared to preoperative in keratoconus patients, on the other hand, the results of Polat *et al.*<sup>[15]</sup> showed that the CV at 12 months postoperative was significantly increased compared to the amount of preoperative and 6-month postoperative. In this study, it was reported that the reason for the increase in the postoperative CV was due

to continued remodeling and concluded that the main corneal remodeling and recovery after CXL occur from 6 to 12 months after surgery.<sup>[15]</sup> Also, the study of Salman *et al.*<sup>[20]</sup> showed that the CXL operation had no significant effect on CV (measured by the Pentacam). The authors report that the stability of corneal biomechanical parameters confirms the effectiveness of CXL treatment without adversely affecting corneal elasticity.<sup>[20]</sup> In addition, Grewal *et al.*<sup>[21]</sup> showed that CXL did not cause significant edema, the CV and thickness remained constant for up to 1 year after surgery. The differences in the number and characteristics of samples and disease severity can be the cause of this difference in results.

In the present study, the CV decreased significantly after 6 months and this decrease remained unchanged until 12 months after CXL surgery. The probable cause of this reduction in CV is collagen shrinkage, which occurs after CXL surgery. Also, the re-accumulation of stromal keratocytes (SKs) along with the disappearance of stromal edema reduces the volume of the cornea in the 6<sup>th</sup> month and maintains it until 1 year after surgery.<sup>[13]</sup> In the present study, the ACV and angle were significantly increased at 6 and 12 months after CXL compared to before surgery. Also, the volume and angle of the anterior chamber increased significantly 12 months after CXL compared to 6 months after surgery. Consistent with the results of the present study, Polat *et al.*<sup>[15]</sup> showed that the values of the ACA, ACV, and anterior chamber depth immediately after surgery were significantly lower than 6 and 12 months postoperative. Also, the angle of the anterior chamber, the volume of the anterior chamber, and the depth of the anterior chamber were increased at 12 months after the operation compared to 6 postoperative. In previous studies, it has been reported that keratoconus increases the volume and angle of the anterior chamber.<sup>[22,23]</sup> This effect increases with disease progression and may be due to the anterior corneal protrusion.<sup>[22]</sup> The relationship between the corneal curvature and anterior chamber parameters in keratoconus patients has been shown in previous studies.<sup>[24]</sup> The corneal curvature is likely to increase in the central conical region, which is compensated by the flattening of the peripheral cornea, resulting in a decrease in ACA.<sup>[25]</sup> However, very limited studies have examined the effect of CXL on the anterior chamber parameters in keratoconus patients.

A study of 47 keratoconus eyes during the 6-month follow-up period after CXL showed no significant change in ACA and ACV.<sup>[18]</sup> Although the measurement tools and sample size were similar to our study, these results do not agree with the findings of the present study. The reason for this could be related to the differences in the other parameters such as K values and disease stage in the two studies. The results of another study showed that CXL with riboflavin in the keratoconus patients significantly reduced the CV after 24 months, but had no significant effect on the ACV and depth.<sup>[13]</sup> In the Vinciguerra study,<sup>[17]</sup> the CV decreased significantly during the 12 months after CXL, but the ACV did not change significantly. The results of the Salman study<sup>[20]</sup> also showed that CXL surgery in adolescents with

progressive keratoconus during 12 months of follow-up had no significant effect on the changes in the CV, volume, and depth of the anterior chamber.

In the present study, the improvement in the anterior chamber parameters (ACV and ACA) was observed after CXL at 6 months postoperative and this improvement continued for up to 1 year after surgery. The biomechanical stability of the cornea after CXL has already been reported<sup>[24]</sup> Accordingly, it appears that the corneal stability may alter the anterior chamber parameters through corneal contraction and indirect pressure on the iris—lens aperture. The CXL-induced shrinkage of the cornea in keratoconus patients may restore the peripheral corneal flattening and increase the corneal tilt, resulting in increased ACA values. We also believe that the pressure exerted on the anterior chamber by the stiffened cornea due to CXL can tighten the iris-lens aperture backward, thereby, increasing the ACA values. Further studies on iris-lens aperture position measurement before and after the CXL can be helpful in this regard. It also appears that an increase in the ACV may be due to an increase in ACA. Therefore, based on what has been said, CXL impact monitoring can be done by examining the anterior chamber parameters.

The results of the present study also showed that visual acuity was significantly improved at 6 and 12 months after CXL compared to before surgery. A significant improvement in the visual acuity was also observed at 12 months after CXL compared to 6 months postoperatively. This improvement in visual acuity after CXL has also been reported in many previous studies. For example, in one study, CXL improved the visual acuity from 0.95 log MAR before surgery to 0.68 after 12 months.<sup>[20]</sup> The results of another study showed that the visual acuity (BCVA and Uncorrected visual acuity (UCVA)) significantly improved after a 1-year follow-up compared to preoperative.<sup>[14]</sup> The study by Bernardo *et al.*<sup>[13]</sup> also showed that the treatment of patients with keratoconus using CXL significantly improved the visual acuity (BCVA) after 24 months. This improvement in the visual acuity (both UCVA and BCVA) 1 year after CXL has been reported in other studies.<sup>[16,27]</sup> A meta-analysis also reported a significant improvement in the visual acuity for keratoconus patients at 12 months after CXL.<sup>[28]</sup> In the Tiveron study,<sup>[29]</sup> the visual acuity decreased significantly 12 months after CXL in patients with keratoconus. A significant improvement in the visual acuity after CXL surgery in keratoconus patients has been reported in other studies.<sup>[30,31]</sup> Although CXL treatment is not considered to improve visual acuity, its effect on corneal topography can also improve visual acuity.

The present study also had some limitations, including the fact that in this study, the effects of the surgery were examined for 1 year and the effects of CXL on changes in the corneal and anterior chamber parameters were not studied for longer periods. The other limitations of the study include the small number of samples studied. The lack of a control group to monitor keratoconus patients without treatment due to ethical issues was another limitation of this study. Finally, more multicenter

studies with larger sample size and longer follow-up period can have better results.

## Conclusion

The results of the present study showed that CXL has positive effects on the anterior chamber parameters and CV in the treatment of keratoconus patients for a 1-year follow-up. The CXL decreased the CV and increased the ACV and angle at 6 and 12 months postoperative. Collagen cross-linking is also an effective method to improve visual acuity. The improvement and stability of the corneal parameters in keratoconus patients after CXL surgery can also have positive effects on the anterior chamber parameters. These changes in the anterior chamber parameters after CXL can be important in any refractive surgery or cataract surgery required in keratoconus patients.

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## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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