Original Article

Corneal Biomechanical Changes after Corneal Cross-Linking in Patients with Keratoconus

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Abstract

Purpose: To evaluate the changes in biomechanical properties of the cornea using the Corvis ST device after the treatment of keratoconus patients with ultraviolet-A/riboflavin corneal cross-linking (CXL).

Methods: Thirty-seven eyes from 37 consecutive patients with progressive keratoconus were included in this prospective observational case series. Corneal biomechanical parameters including the length of the applanated cornea (L1 and L2), corneal movement velocity during applanation (V1 and V2) at the moment of the first and second applanation, deformation amplitude (DA), distance between bending points of the cornea points of the cornea (PD), and concave radius of curvature (R) at the point of the highest concavity were recorded using the Corvis ST at baseline, 3 months, and 1 year after CXL.

Results: The mean age of the patients was 23.27 years (range, 19–31 years). Among CorVis ST corneal biomechanical parameters, L1, DA, PD, and R at the point of the highest concavity did not change significantly. The length of the applanated cornea at the moment of second applanation (L2) showed a significant change 3 months after CXL, but no significant difference was found between the 3-month and 1-year values of this parameter. Corneal movement velocity during applanation (V1 and V2) did not change 3 months after doing CXL, but the changes in these parameters were significant 1 year after CXL.

Conclusions: Although the CorVis ST device may detect changes in some biomechanical properties of cornea after the treatment of keratoconus patients with CXL, many parameters remain unchanged, and this device cannot readily be used to find the effects of CXL.

Keywords: Corneal biomechanical properties, Corneal cross-linking, CorVis ST, Dynamic imaging, Keratoconus

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Introduction

Keratoconus, as the most common ectatic corneal disorder, is characterized by a progressive noninflammatory thinning of the cornea. It is a usually bilateral, but asymmetrical cone-like ectasia of the cornea, which results in corneal thinning, corneal protrusion, irregular astigmatism, and ultimately decreased vision.[1] The precise etiology of keratoconus has not been elucidated yet; however, a reduced number of collagen cross-links, a pepsin digestion higher than normal, increased levels of lysosomal and proteolytic enzymes, and decreased concentration of protease inhibitors have been shown in keratoconus. These changes result in structural weakness of the corneal tissue.[2-6] Changes in the biomechanical properties of the cornea due to decreased mechanical corneal stability play an important role in the pathogenesis of keratoconus that ultimately results in irregular astigmatism, progressive myopia, corneal thinning, and central corneal scarring.[7,8]

In the recent years, corneal cross-linking (CXL) with ultraviolet-A (UVA) and riboflavin has gained a widespread

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acceptance in the management of keratoconus. Through several mechanisms including changes in the physicochemical properties of the collagen and increasing resistance of cornea to enzymatic degradation, it is believed that CXL stabilizes the cornea and stops the progression of the disorder. Several studies provide evidence regarding the beneficial effects of this procedure in management of keratoconus.[7,9-17]

Measurement of the biomechanical properties of the cornea is important in the assessment of therapeutic interventions in ectatic disorders of the cornea, and different instruments have been recently developed for this purpose. Ocular Response Analyzer (ORA) and CorVis ST are devices that evaluate *in vivo* the biomechanical response of the cornea to an air-puff–induced deformation. These instruments are the only two devices commercially available for *in vivo* assessment of corneal biomechanical properties. There are a very few studies investigating the biomechanical changes of the cornea using CorVis in keratoconic eyes,[18-21] The main purpose of our study was to prospectively assess *in vivo* the changes in biomechanical properties of cornea using CorVis ST after the treatment of keratoconus patients with UVA/riboflavin CXL. The changes in corneal pachymetry after CXL were also evaluated using both CorVis ST and Pentacam.

Methods

In this prospective, observational case series study, 37 eyes of 37 consecutive patients with progressive keratoconus were enrolled. Corneal biomechanical parameters were recorded using the CorVis ST device at baseline, 3 months, and 1 year after CXL. Complete ophthalmic examination including Snellen visual acuity measurement, slit-lamp biomicroscopy, and fundus examination was performed. Refraction was measured using an autorefractometer (Canon R-50; Canon Inc., Tokyo, Japan) and refined by manual retinoscopy subjective refraction. Final refinement was performed using subjective refraction. Pentacam HR (OCULUS Optikgeräte GmbH, Wetzlar, Germany) was used to compute keratometry measurements. Patients with a history of previous eye surgery or other eye disorders such as uveitis, glaucoma, corneal opacities, or scars, retinal vascular occlusive disorders, and diabetic retinopathy were excluded from the study. Other exclusion criteria were systemic diseases, autoimmune disorders, or inability to cooperate with measurement devices. Informed consent was obtained from all patients. Protocol of the study was approved by the local Ethics Committee of Shiraz University of Medical Sciences (ID: 9423456). The tenets of the Declaration of Helsinki were followed in this study.

Intraocular pressure (IOP), central corneal thickness (CCT), and ocular biomechanical parameters were measured using CorVis ST device (OCULUS Optikgerate GmbH, Germany).

CorVis ST corneal biomechanical parameters comprise the length of the applanated cornea (L1 and L2) and corneal movement velocity during applanation (V1 and V2) at the moment of the first and second applanation, respectively. The other measured parameters were deformation amplitude (DA), distance between bending points of the cornea (PD), and concave radius of curvature (R) at the point of the highest concavity. All CXL procedures were performed using the method described by Wollensak *et al*. previously.[10] After topical anesthesia with application of tetracaine 1% drops, the epithelium was removed over the central 8–9 mm mechanically or with alcohol (ethanol 20%) application for 20 s. After epithelial removal, riboflavin 0.1%–dextran 20.0% solution was applied every 3 min for 30 min. Then, the central cornea was irradiated using UVA light through the 8.0 or 9.0 mm aperture 5 cm from the cornea for 30 min. The UVA light had a wavelength of 370 nm and an irradiance of 3 mW/cm^2. Riboflavin drops were applied every 5 min during the UVA irradiation. Centration was monitored continuously during the procedure and adjusted accordingly. After treatment, one eye drop of chloramphenicol was applied, and betamethasone 0.5% eye drops were given 4 times a day with chloramphenicol eye drop for every 8 h administered until complete re-epithelialization occurred. After the contact lens was removed, fluorometholone acetate 0.1% was used in a tapered dose over 6 weeks if the corneal haze was detected. All measurements were performed by experienced operators following the criteria provided by the manufacturers. Pretreatment and posttreatment variables were recorded and analyzed using IBM SPSS statistics software, version 21 (SPSS Inc., Chicago, IL, USA). Descriptive statistical results were expressed as mean ± standard deviation. Paired sample *t*-test was used to compare pre- and post-CXL measurement. Corneal biomechanical parameters were compared using repeated measurement analysis of variance test. *P* value was considered statistically significant when it was < 0.05.

Results

Measurements from 37 eyes of 37 patients were analyzed. The mean age of the patients was 23.27 years (range, 19–31 years). Eighteen patients (48.6%) were male. At baseline, the mean keratometry and keratometric astigmatism were 47.939 D and 3.6222 D, respectively. The mean keratometry and astigmatism 1 year after CXL were 47.931 and 3.927, respectively.

The mean minimum keratometry measured by Pentacam was 46.128 at baseline and changed to 45.967 ± 3.79 after 1 year (P: 0.05). Furthermore, the mean maximum keratometry at baseline and 1 year after CXL was 49.75 and 49.894 ± 3.88, respectively (P: 0.94).

The mean IOP values before, 3 months, and 1 year after CXL were 13.92 ± 2.05, 13.21 ± 2.04, and 13.47 ± 1.99, respectively ($P = 0.32$). The mean CCT as measured by Pentacam before, 3 months, and 1 year after CXL were 448.78 ± 34.92, 388.70 ± 81.36, and 435.00 ± 42.03, respectively (*P*: 0.032 and *P*: 0.042, respectively). The mean CCT as measured by CorVis ST before, 3 months, and 1 year after CXL was 452.87 ± 43.07, 377.14 ± 90.16, and 419.65 ± 59.8, respectively ($P < 0.001$ and *P*: 0.005, respectively). Three-month and 12-month follow-up

results of CCT obtained by CorVis and Pentacam devices showed a significant reduction when compared to baseline values ($P < 0.001$ and 0.032 after 3 months and 0.005 and 0.042 after 1 year, respectively) [Table 1].

CorVis ST results showed nonsignificant changes of L1 length, DA, PD, and R at the point of the highest concavity, 3 months, and 1 year after CXL [Table 2]. Compared to baseline values, L2 showed a significant change 3 months (P: 0.026) and 1 year (P: 0.042) after CXL, but no significant difference was seen between 3-month and 1-year values of this parameter (P: 0.428). Corneal movement velocity during applanation (V1 and V2) did not change significantly 3 months after CXL. However, V1 and V2 changes were significant 1 year after CXL [P: 0.010 and P: 0.025, respectively, Table 2]. The changes in V1 and V2 parameters were also significant when comparison between 3- and 12-month measurements was performed ($P = 0.013$ and 0.007, respectively).

Discussion

In the current research, our results showed significant changes of L2, V1, and V2 biomechanical parameters of cornea after 1-year follow-up. However, CorVis ST device was not able to detect significant alteration of L1 length, DA, PD, and R at the point of the highest concavity.

According to our results, some biomechanical parameters of cornea changed after the treatment of keratoconus patients with UVA/riboflavin CXL as demonstrated by measurements obtained by CorVis ST. However, several corneal biomechanical parameters as measured by CorVis ST device remained unchanged.

Since its introduction for management of keratoconus,[10,11] CXL has been used in the management of keratectasia to halt the progression of the disease and to postpone the surgical intervention. A long-term increase in corneal biomechanical rigidity after CXL has been demonstrated in several experimental and clinical studies.[7,12-17] These effects subsequently result in corneal stabilization and improvement of vision. By stiffening the human cornea by more than 300%, CXL results in a long-term increase in corneal biomechanical rigidity.[12] The primary treatment effect of CXL is in the anterior 300 microns of the corneal stroma.[12] CXL induces the formation of high-molecular-weight collagen polymers resulting to increment of chemical stability.[13] In addition, CXL increases the collagen fiber diameter in the anterior corneal stroma by 12.2%.[14]

Clinical studies with long follow-up time have also demonstrated the effectiveness of this procedure. The results have been promising with the long-term improvement of uncorrected and best spectacle-corrected visual acuity and pachymetric and keratometric indices.[16,17] Improvement of corneal wavefront aberration profiles has also been shown after CXL.[15,16]

Assessment of the beneficial effects of treatment modalities in patients with keratoconus is of paramount importance. The measurement of corneal thickness and corneal curvature using different devices such as corneal topographers, keratometers, and autokeratometers has been used conventionally to evaluate the effectiveness of treatment modalities in keratoconus. A few techniques such as ultrasonic elastography and high-frequency ultrasonographic analysis have also been developed for the assessment of corneal biomechanics *in vitro*. In the recent years, there has been an interest and attempt for *in vivo* characterization of corneal biomechanics in patients with keratoconus.[7,8]

CorVis ST has been introduced recently for *in vivo* investigation of corneal biomechanical properties; dynamic Scheimpflug imaging analysis is incorporated in a noncontact tonometer

Table 1: Corvis and Pentacam thickness in baseline and follow-up points

	Baseline	3-month	*P*	1 year	*P*
Thickness CorVis	452.476±43.07	377.14±90.16	<0.001	419.65±59.80	0.005
Thickness Pentacam	448.78±34.92	388.70±81.36	0.032	435.00±42.03	0.042

Paired sample T test was done for comparison.

Table 2: Corneal biomechanical parameters measurements obtained by CorVis ST at the baseline and postcorneal cross-linking

Parameters	Baseline	3 months	*P* value between baseline and 3 months	12 months	*P* value between baseline and 12 months results
L1	1.724±0.052	1.68±0.030	0.199	1.640±0.035	0.152
L2	1.151	0.751	0.026	0.836	0.042
V1	0.141	0.151	0.735	0.159	0.010
V2	1.065	1.122	0.580	1.193	0.025
Deformation amplitude	1.212	1.266	0.052	1.265	0.182
Peak distance	4.651	4.810	0.162	4.479	0.578
Radius of curvature	5.460	5.447	0.782	5.545	0.514

L1, L2: Length of the applanated cornea at the moment of the first and second applanation, V1, V2: Corneal movement velocity during applanation at the moment of the first and second applanation. Paired sample T test was done for comparison

in CorVis ST. There are a few studies investigating CorVis ST in the evaluation of changes of corneal biomechanical properties in keratoconus patients.[18-25] Bak-Nielsen *et al*. examined nine eyes of eight patients before and after CXL. Patients were measured with CorVis ST before and about 3 months after CXL. They found a significant difference in the highest concavity DA, highest concavity time, and A2 time. When the authors considered their findings with regard to the direction of change, only highest concavity time followed their expectation as it increased after CXL. The change in the highest concavity DA and A2 time was opposite the values in the normal corneas. Authors concluded that the standard parameters of the CorVis ST cannot readily be used for diagnosing keratoconus or documenting the effect of CXL in postoperative examinations.[22]

In a study by Tomita *et al*., outcomes of accelerated CXL to conventional corneal CXL have been compared.[23] Their results showed that from CorVis ST printouts, they only compared DA, distance between corneal bending points, and radius of the curvature between preoperative and post-CXL values. From the parameters they evaluated and compared, no variable was changed significantly in the conventional CXL group, and distance between corneal bending points in accelerated CXL group was the only parameter that showed a statistically significant change.[23] In a recent study by Jabbarvand *et al*. on progressive keratoconus patients, 6-month outcomes of CXL procedure were assessed using CorVis ST device. They found statistically significant changes of L1 and V1 and increment of the highest concavity after 6 months of follow-up. Furthermore, they documented a significant lower DA and integrated radius as well as higher stiffness of L1 parameter.[18] In another study by Pedrotti *et al*., significant changes of DA, V1, V2, and L1 stiffness were reported after 1 year CXL in progressive recurrent keratoconus patients.[24] Salouti *et al*. compared the corneal biomechanical parameters of 48 keratoconus patients using ORA and CorVis devices 4 months following CXL intervention.[25] They found considerable changes of L2 and V2 as well as corneal resistance factor and waveform score in CorVis and ORA findings after four postoperation.

In the present study, when a comparison was made between measurements obtained preoperatively and 3 months and 1 year after CXL, among the CorVis ST corneal biomechanical parameters, L1 length, DA, PD, and R at the point of the highest concavity did not change significantly after 1 year of follow-up. Furthermore, L2 showed a significant change 3 months after CXL, but no significant difference was seen between 3-month and 1-year values. In addition, V1 and V2 did not change 3 months after CXL, but changes were significant 1 year after CXL. When a comparison between 3- and 12-month points was made, further analysis showed significant changes of V1 and V2. Results of our study with a follow-up of 1 year on 37 eyes with keratoconus indicated that CXL influenced some parameters and did not influence many corneal biomechanical parameters of CorVis ST device. Several explanations might be proposed for the nonsignificant change of these parameters. The first explanation is that these beneficial changes might have occurred, but are subtle to be measured. As the length of the applanated cornea at the moment of the second applanation at 3-month examination and corneal movement velocity at the moment of the first and second applanation at 3- and 12-month examinations showed a statistically significant change after CXL in our study, conducting more studies with a larger sample size may show significant changes in other parameters. Another explanation is that the current device's parameters are incapable of showing beneficial effects of treatment on cornea biomechanics. Interobserver and intraobserver repeatability in the measurement of biomechanical parameters is another concern in keratoconic eyes. This subject has previously been assessed in ORA.[26]

Repeatability of CorVis ST measurements has also been assessed by the recent studies. Hon and Lam studied intraexaminer repeatability and intersession reproducibility of CorVis ST measurements on the normal subjects.[27] They concluded that HC, DA and L1 time showed a good repeatability and intersession reproducibility, whereas the remaining CorVis ST parameters had a poor repeatability. In another study, HC radius and HC deflection amplitude have also been identified as having a reasonable level of repeatability in the normal subjects. As the authors stated, these repeatability analyses have been performed in normal patients, and these measurements in patients with keratoconus may be more complicated because the auto-release function of the air puff may not be possible and may affect the repeatability of the measurements in keratoconic corneas.[22] In another study on healthy and keratoconic cornea by Ali *et al*., DA and length of the applanated cornea in first second have been fairly repeatable.[28] Averaging multiple nonrepeatable measurements influences the accuracy and may hide beneficial effects of CXL on biomechanical parameters. Improving repeatability indices through optimizing the device and its parameters seems necessary. Combining multiple biomechanical parameters into a logistic regression equation has also been demonstrated that increase the sensitivity and specificity of the device for distinguishing keratoconic from normal eyes.[29] New Scheimpflug dynamic *in vivo* curve analyses to demonstrate distinct changes of the biomechanical properties of the cornea have also been suggested as an important next step for characterizing corneal biomechanics.[26] Further optimization of device for better characterization of cornea biomechanics is of paramount importance and is a research goal.

Our study had limitation in investigating some corneal biomechanical parameters including Corvis Biomechanical Index, stiffness parameter, and integrated radius indices because the available CorVis device software at the beginning of our study did not include these parameters in its printout. Another limitation of the present study was its relatively small sample size.

Therefore, we suggest future larger sample size studies that evaluate CBI, stiffness parameter, and integrated radius indices in addition to the parameters that we investigated in the present

study to more clarify the changes of biomechanical corneal parameters after CXL surgery.

In conclusion, the CorVis ST device shows changes in some biomechanical properties of cornea after the treatment of keratoconus patients with CXL. However, several parameters remain unchanged. Given the widespread use of CXL and the importance of measuring corneal biomechanics, there is clearly a demand for further optimization of device and future studies to investigate this subject.

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Conflicts of interest

There are no conflicts of interest.

References

1. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. Surv Ophthalmol 1984;28:293-322.
2. Kenney MC, Nesburn AB, Burgeson RE, Butkowski RJ, Ljubimov AV. Abnormalities of the extracellular matrix in keratoconus corneas. Cornea 1997;16:345-51.
3. Sawaguchi S, Yue BY, Sugar J, Gilboy JE. Lysosomal enzyme abnormalities in keratoconus. Arch Ophthalmol 1989;107:1507-10.
4. Rehany U, Lahav M, Shoshan S. Collagenolytic activity in keratoconus. Ann Ophthalmol 1982;14:751-4.
5. Kao WW, Vergnes JP, Ebert J, Sundar-Raj CV, Brown SI. Increased collagenase and gelatinase activities in keratoconus. Biochem Biophys Res Commun 1982;107:929-36.
6. Andreassen TT, Simonsen AH, Oxlund H. Biomechanical properties of keratoconus and normal corneas. Exp Eye Res 1980;31:435-41.
7. Edmund C. Corneal elasticity and ocular rigidity in normal and keratoconic eyes. Acta Ophthalmol (Copenh) 1988;66:134-40.
8. Nash IS, Greene PR, Foster CS. Comparison of mechanical properties of keratoconus and normal corneas. Exp Eye Res 1982;35:413-24.
9. Spoerl E, Wollensak G, Seiler T. Increased resistance of crosslinked cornea against enzymatic digestion. Curr Eye Res 2004;29:35-40.
10. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. Am J Ophthalmol 2003;135:620-7.
11. Wollensak G, Spörl E, Seiler T. Treatment of keratoconus by collagen cross linking. Ophthalmologe 2003;100:44-9.
12. Wollensak G, Spoerl E, Seiler T. Stress-strain measurements of human and porcine corneas after riboflavin-ultraviolet-A-induced cross-linking. J Cataract Refract Surg 2003;29:1780-5.
13. Zhang Y, Conrad AH, Conrad GW. Effects of ultraviolet-A and riboflavin on the interaction of collagen and proteoglycans during corneal cross-linking. J Biol Chem 2011;286:13011-22.
14. Wollensak G, Wilsch M, Spoerl E, Seiler T. Collagen fiber diameter in the rabbit cornea after collagen crosslinking by riboflavin/UVA. Cornea 2004;23:503-7.
15. 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.
16. 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;33:43-8.
17. Hashemi H, Seyedian MA, Miraftab M, Fotouhi A, Asgari S. Corneal collagen cross-linking with riboflavin and ultraviolet a irradiation for keratoconus: Long-term results. Ophthalmology 2013;120:1515-20.
18. Jabbarvand M, Moravvej Z, Shahraki K, Hashemian H, Ghasemi H, Berijani S, *et al.* Corneal biomechanical outcome of collagen cross-linking in keratoconic patients evaluated by Corvis ST. Eur J Ophthalmol 2021;31:1577-83.
19. Ren S, Xu L, Fan Q, Gu Y, Yang K. Accuracy of new Corvis ST parameters for detecting subclinical and clinical keratoconus eyes in a Chinese population. Sci Rep 2021;11:4962.
20. Yang K, Xu L, Fan Q, Zhao D, Ren S. Repeatability and comparison of new Corvis ST parameters in normal and keratoconus eyes. Sci Rep 2019;9:15379.
21. Elham R, Jafarzadehpur E, Hashemi H, Amanzadeh K, Shokrollahzadeh F, Yekta A, *et al.* Keratoconus diagnosis using Corvis ST measured biomechanical parameters. J Curr Ophthalmol 2017;29:175-81.
22. Bak-Nielsen S, Pedersen IB, Ivarsen A, Hjortdal J. Dynamic scheimpflug-based assessment of keratoconus and the effects of corneal cross-linking. J Refract Surg 2014;30:408-14.
23. Tomita M, Mita M, Huseynova T. Accelerated versus conventional corneal collagen crosslinking. J Cataract Refract Surg 2014;40:1013-20.
24. Pedrotti E, Caldarella G, Fasolo A, Bonacci E, Gennaro N, Gregorio A, *et al.* Topographic and biomechanical changes after application of corneal cross-linking in recurrent keratoconus. Int J Environ Res Public Health 2019;16:3872.
25. Salouti R, Khalili MR, Zamani M, Ghoreyshi M, Nowroozzadeh MH. Assessment of the changes in corneal biomechanical properties after collagen cross-linking in patients with keratoconus. J Curr Ophthalmol 2019;31:262-7.
26. Steinberg J, Frings A, Mousli A, Casagrande MK, Druchkiv V, Katz T, *et al.* New scheimpflug dynamic *in vivo* curve analyses to characterize biomechanical changes of the cornea after cross-linking for progressive keratoconus. J Refract Surg 2016;32:34-9.
27. Hon Y, Lam AK. Corneal deformation measurement using Scheimpflug noncontact tonometry. Optom Vis Sci 2013;90:e1-8.
28. Ali NQ, Patel DV, McGhee CN. Biomechanical responses of healthy and keratoconic corneas measured using a noncontact scheimpflug-based tonometer. Invest Ophthalmol Vis Sci 2014;55:3651-9.
29. Mercer RN, Waring GO 4th, Roberts CJ, Jhanji V, Wang Y, Filho JS, *et al.* Comparison of corneal deformation parameters in keratoconic and normal eyes using a non-contact tonometer with a dynamic ultra-high-speed scheimpflug camera. J Refract Surg 2017;33:625-31.