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Direct measurement of anterior corneal curvature changes attributable to epithelial removal in keratoconus

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Purpose: To compare the tomography of the corneal epithelium and Bowman layer in eyes with moderate to severe keratoconus before and after epithelial debridement.

Setting: University hospital tertiary referral center.

Design: Prospective case series.

Methods: Dual-channel Scheimpflug combined with Placido-disk tomography was used to measure the corneal variables in eyes with keratoconus having corneal crosslinking immediately before and after epithelial debridement. The differences in pachymetry, axial keratometry, astigmatism magnitude, asphericity, total corneal power, and spherical aberrations were computed.

Results: The study comprised 30 eyes of 30 patients. After epithelial removal, the central (0.0 to 4.0 mm) and midperipheral (4.0 to 7.0 mm) corneal zones were significantly thinner mean (21 μm ± 14 [SD] and 35 ± 44 μm, respectively). The mean anterior axial flat keratometry (K) (+1.71 diopters [D]), steep K (+2.14 D), maximum K (+2.13 D), corneal astigmatism (+1.11 D), asphericity (−0.31), and total corneal power changes (+2.03 D) were significantly different after epithelial debridement. There were no significant changes in posterior corneal flat K or steep K, posterior corneal astigmatism, or posterior asphericity. There were no significant differences in the mean astigmatic axis (anterior or posterior corneal surface) or spherical aberration after epithelial debridement.

Conclusions: In eyes with moderate to severe keratoconus, the tomography of Bowman layer was significantly steeper than that of the epithelium; thus, epithelial debridement increased the magnitude of anterior corneal keratometry, astigmatism, and prolateness. These data suggest that the corneal epithelium smooths the underlying Bowman layer irregularity in keratoconus.

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The corneal epithelium is a moldable, nonkeratinized stratified layer with a reported thickness of between 48 μm and 53 μm.[1,2] It has an asymmetric thickness profile, being slightly thicker inferiorly and nasally than superiorly and temporally. There is a larger inferosuperior difference than a nasotemporal difference in epithelial thickness.[3] The corneal epithelial thickness profile has a demonstrable effect on the total corneal power. It governs the shape of the air–tear film[4] and affects the tomographic analysis of this interface. The epithelium is thought to account for an average of 1.03 diopters (D) of central corneal power (2.0 mm diameter zone)[5] and contributes to the power and axis of the corneal astigmatism.[6]

In keratoconic eyes, the corneal epithelium shows a localized thinning over the cone that is surrounded by an annulus of epithelial thickening.[7] It has been postulated that epithelial thickness mapping can be a sensitive means for the diagnosis of keratoconus.[8–12]

The contribution of the epithelium to corneal refractive power in keratoconus is of special importance because in recent years, corneal surface reshaping procedures have been developed to improve the corneal shape by combining transepithelial photorefractive keratectomy (PRK) and corneal crosslinking (CXL).[13–15]

The present study sought to determine the differences between the tomographic features of the corneal epithelium and Bowman layer in eyes with keratoconus. To our knowledge, there has been only 1 previous in vivo study (using specular corneal topography) characterizing the role of the corneal epithelium on the anterior corneal shape and curvature in eyes with keratoconus.[16] In the present study, a dual rotating Scheimpflug combined with Placido

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tomography analyzer (Galilei G2, version 6.1.3, Ziemer Ophthalmic Systems AG) was used to assess the tomographic changes induced by the removal of the corneal epithelial layer in keratoconic patients having CXL.

PATIENTS AND METHODS

This prospective study enrolled patients with keratoconus having CXL from August 2016 to April 2017 who were attending the University of Auckland Cornea and External Eye Disease Service, Greenlane Hospital, Auckland District Health Board, Auckland, New Zealand. The study was approved by the local Health and Disability Ethics Committee, a branch of the Ministry of Health in New Zealand. Written informed consent was obtained from all patients after they voiced understanding of the purpose and the procedures of the study in accordance with the tenets of the Declaration of Helsinki.

The inclusion criterion was progressive keratoconus diagnosed based on clinical and associated tomographic findings. Progressive keratoconus was defined as 1 or more of the following changes over 12 months: an increase of 1.00 diopter (D) or more in the steepest keratometry (K) measurement, an increase of 1.00 D or more in the manifest cylinder, or an increase of 0.50 D or more in manifest refraction spherical equivalent. The keratoconus stage was assessed using the Krumeich et al. classification.[17] Exclusion criteria were contraindications to CXL, including corneal scarring or edema visible on slitlamp examination a history of contact lens wear, ocular surgery, or trauma. One eye of each patient was included in the study.

Patient Assessment

All patients received a complete ocular assessment before surgery including slitlamp biomicroscopy and ocular fundus examinations. Corneal tomography was obtained using the Galilei Dual Scheimpflug Analyzer. The Galilei dual Scheimpflug analyzer combines dual rotating Scheimpflug cameras and a Placido disk. The flash illumination is an output from a 475 nm wavelength blue light–emitting diode (ultraviolet free); it measures more than 122 000 datapoints per scan. Height data acquired from the Scheimpflug edges and slope data from the Placido images are transformed into height data. The combined height data are merged and used to create a surface fit of the anterior cornea through a proprietary algorithm.[18,19]

Measurements and Surgical Technique

Ten minutes before the planned CXL procedure, a preoperative tomography scan was performed in the operative eye using the dual Scheimpflug analyzer, which was located in the same room as the crosslinking unit. Three consecutive scans were performed by the same experienced examiner. All measurements were performed without pupil dilation and under identical lighting conditions between 1:00 PM and 5:00 PM to limit the influence of overnight corneal swelling.[20] With their chins on the chinrest, patients were asked to fixate on the target light; they were also asked to blink completely immediately before each measurement to allow for adequate tear-film coverage over the corneal surface. The examiner checked each scan and its quality before recording it; only scans of acceptable quality were included.

Immediately after data acquisition, 2 drops of proxymetacaine hydrochloride 0.5% were administered and a speculum was placed between the eyelids. Under an operating microscope, an ethanol 20.0% solution was applied over 20 seconds in the central 8.0 mm corneal zone using a cornea well. The epithelium was then removed using a blunt spatula. The corneal surface was rinsed with a balanced salt solution and inspected to ensure that all epithelial remnants had been removed. The lid speculum was removed, and a further 3 consecutive tomography scans were acquired. No eyedrops were administered after epithelial debridement; however, the patient was asked to blink to optimize the tear film. The examiner checked each scan and its quality before recording it; only scans of acceptable quality were included. The patient returned to the surgical bed, and the CXL procedure resumed with the application of riboflavin solution composed of dextran-free riboflavin 0.1% with hydroxylpropyl methylcellulose (Vibex Rapid, Avedro, Inc.), with 10 minutes of corneal soaking. Corneal crosslinking was performed using an ultraviolet-A (UVA) source system (KXL, Avedro, Inc.) with 4 minutes of continuous UVA exposure at 30 mW/cm^2 and an energy dose of 5.2 J/cm^2. Treated eyes were dressed with a soft contact lens bandage for 3 days and medicated with ciprofloxacin and fluorometholone eyedrops 4 times a day for 3 days.

Measurements Variables

The average value of 3 consecutive high-quality scans were recorded for the following anterior and posterior corneal surface variables:

- Corneal dioptric power in the flattest and steepest meridian of the 3.0 mm central zone.
- Maximum K power on the anterior axial or anterior instantaneous curvature map.
- Corneal astigmatism in the 3.0 mm central zone (toricity).
- Asphericity in the 8.0 mm diameter central zone aligned to the first Purkinje $q = (-e)^2$.
- Pachymetry at the central (0.0 to 4.0 mm), midperipheral (4.0 to 7.0 mm), peripheral (7.0 to 10.0 mm), and thinnest points of the cornea.
- Total cornea power calculated using ray tracing from a zone of 1.0 to 4.0 mm.
- Spherical aberration in the 6.0 mm diameter central zone aligned to the pupil.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows software (version 19.0, IBM Corp.). When data had a normal distribution, as shown by the 1-sample Kolmogorov-Smirnov test, parametric analysis (2-sided t test) was used. A P value less than 0.05 was considered statistically significant.

RESULTS

Demographics

The study comprised 30 eyes of 30 patients. Twenty-eight eyes (93%) were graded as stage II and 2 eyes (7%) were graded as stage III on the Amsler-Krumeich classification system. The mean quality of the scan before epithelial debridement versus after debridement was 88.38% and 86.86%, respectively ($P = .13$). There were no intraoperative or postoperative complications, and the epithelialization rate was within normal limits in all patients after CXL. Table 1 shows the patients' demographics.

Keratometry

Table 2 shows the anterior K values of the patients. There was significant steepening of the anterior axial corneal curvature after epithelial debridement in the central and midperipheral corneal zones but not in the peripheral zone ($P < .01$, $P < .02$, and $P < .72$, respectively) (Figures 1 and 2).

Table 3 shows the posterior K values of the patients. There was no significant difference between the posterior axial corneal curvature before and after epithelial