7-YEAR OUTCOMES OF EPITHELIUM-OFF CORNEAL COLLAGEN CROSSLINKING IN PROGRESSIVE KERATOCONUS

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ABSTRACT

Purpose: To evaluate the clinical results of epi-off corneal collagen crosslinking (CXL) during a 7-year follow-up.

Methods: Retrospective non-randomized single-center interventional study enrolling 34 consecutive eyes of 24 patients with progressive keratoconus undergoing CXL surgery with epithelium removal. Visual, refractive, corneal topography, pachymetric and anterior segment changes were evaluated at 1, 3 and 7 years after surgery.

Results: Significant reduction of refraction was observed at 1 year postoperatively ($p \leq 0.006$), with an additional significant reduction between the 1-year and 3-year postoperative visits ($p \leq 0.002$) and no significant changes afterwards (≥ 0.156). Regarding corrected distance visual acuity (CDVA), a significant improvement was detected at 1 year after surgery ($p < 0.001$), with an additional improvement between 1 and 3 years postoperatively ($p = 0.001$), and no significant changes at the end of the follow-up ($p = 0.518$). Significant corneal flattening was observed at 1, 3 and 7 years after surgery ($p \leq 0.041$). Likewise, a significant central thinning was observed at 1 year postoperatively ($p < 0.001$), with no significant changes afterwards ($p \geq 0.112$). Anterior maximum elevation only changed significantly between 1 and 3 years after surgery ($p = 0.002$), whereas the posterior maximum elevation changed significantly at all time points of the follow-up ($p \leq 0.034$). No significant changes with surgery in anterior segment volume ($p \geq 0.377$) and in anterior chamber depth ($p \geq 0.142$) were detected.

Conclusion: The effect of epi-off CXL in progressive keratoconus is maintained 7 years after surgery. Long term corneal changes after this procedure may be influenced by age-related corneal stiffening process.

Keywords: corneal collagen crosslinking; keratoconus; pachymetry; corneal topography; corneal ectasia

INTRODUCTION

Corneal collagen crosslinking (CXL) with riboflavin and ultraviolet A (UVA) 370 nm radiation is capable of arresting the progression of keratoconus, with significant improvements in visual, keratometric, and topographic measurements.[1] However, most of studies report clinical improvements and stability in a short or medium-term follow-up,[2-9] with very few studies reporting the real capability of CXL of maintaining the corneal shape and structure in the long term.[10] Raiskup et al[10] reported the outcomes in terms of visual acuity, refraction, corneal curvature and endothelial cell count changes 10 years after CXL surgery with epithelium removal, confirming that a stabilization of the ectatic process was achieved. However, in spite of this long-term evidence of stabilization, epi-off CXL failure, retreatment rates, and need for transplantation have been reported to be up to 33, 8.6, and 6.25%, respectively.[11] Good levels of efficacy and safety have been reported for CXL retreatments in eyes with previous CXL, but showing signs of keratoconus progression associated to allergic conjunctivitis and eye rubbing.[12] The aim of the current study was to evaluate the clinical results of epi-off CXL during a 7-year follow-up, evaluating not only visual, refractive, corneal curvature and pachymetric changes, but also potential corneal elevation and anterior segment alterations.

Material and methods

Patients

This retrospective non-randomized single-center interventional study included a total of 34 consecutive eyes of 24 patients with keratoconus and undergoing CXL surgery. All cases were examined, diagnosed and treated at Horus Vision Correction Center, Alexandria, Egypt. Inclusion criteria were presence of keratoconus according to the Rabinowitz criteria,[13] evidence of keratoconus progression manifested by continuous deterioration of vision, increase of central keratometric readings by 1.0 D or more over a period of 1 year and frequent readjustment of contact lenses (more than twice a year). Exclusion criteria were pachymetric measurements of less than 400 microns, severe dry eyes, corneal scarring, previous ocular surgeries, chronic ocular inflammations, and autoimmune diseases. Pregnant and nursing women were also excluded. This study was revised and approved by the ethics committee of the Faculty of Medicine of the University of Alexandria. A consent form was signed by all patients following the recommendations of the Declaration of Helsinki.

Surgical procedure

The surgical procedure was performed under sterile conditions in the operating theater. Two drops of topical anaesthesia were instilled twice before surgery (benoxinate hydrochloride 0.4%) and then a lid speculum was inserted. The corneal epithelium was removed over an entire area of 9 mm in the center of the cornea using the Amoils brush (Amoils Brush Epithelial Scrubber, Innovative Excimer Solutions, Toronto, Canada). Before UVA irradiation, the riboflavin 0.1% solution (Ricrolin®, Sooft, Montegiorgio, Italy) was applied onto the cornea every one minute for 10 to 15 minutes to achieve adequate penetration of the solution into the corneal stromal lamellae. These drops contain 12.7 mg of riboflavin phosphate, which is equivalent to 10 mg of basic riboflavin in 20% 10 ml solution dextran-T-500. The cornea was then exposed to UVA light emanating from a solid-state laser system (VEGA System, CSO Ophthalmic, Italy), which emitted UVA rays at a wavelength of 370 ± 5 nm and energy of 3

mW/cm^2 or 5.4 J/cm^2. The cropped light beam had an 8.0-mm diameter. A calibrated UVA meter (LaserMate-Q; Laser 2000, Wessling, Germany) was used before treatment to check the irradiance at 1.0-cm distance. Exposure was maintained for 30 minutes, a period in which the riboflavin solution was applied again, but this time once every 5 minutes. Likewise, topical anaesthesia was also instilled whenever needed to ensure the maximum patient's comfort. Fixation and centration during irradiation was achieved by instructing the patient to fixate at the central light-emitting diode of the probe.

A soft bandage contact lens was applied at the end of the procedure until re-epithelialization was complete. Topical moxifloxacin hydrochloride drops (Vigamox, Alcon, USA) were prescribed to be applied 4 times daily for 7 days, prednisolone acetate 1% drops (Econopred plus, Alcon, USA) 3 times daily for 20 days, and 0.3 % hydroxypropyl methylcellulose drops (Tears Naturale, Alcon, USA) 6 times daily for two months.

Clinical protocol

In all patients, a complete preoperative examination was performed that included manifest refraction, uncorrected (UDVA) and corrected distance visual acuity (CDVA) testing, slit lamp anterior segment examination, corneal topography and anterior segment imaging using the Pentacam-HR system (Oculus Inc., Wetzlar, Germany), applanation tonometry, and funduscopy. With the Pentacam topography system, the following topographic and pachymetric parameters were recorded and evaluated: flattest and steepest keratometric readings (K1 and K2), maximum keratometry (Kmax), magnitude of corneal astigmatism in the central 3-mm zone (AST), central corneal thickness (CCT), minimum corneal thickness (MCT) and Cartesian coordinates of its position (X-MCT, Y-MCT), maximum anterior corneal elevation (AE) for an 8-mm diameter and

Cartesian coordinates of its position (X-AE, Y-AE), maximum posterior corneal elevation (PE) for an 8-mm diameter and Cartesian coordinates of its position (X-PE, Y-PE), anterior chamber volume (ACV) and corneal volume (CV), and anterior chamber depth (ACD).

Postoperatively, patients were examined the day after surgery, at 1 week, 1 month, 3 months, and 1 year postoperatively. After this, all patients were examined once per year during a 7-year follow-up. During the first week after surgery, the corneal status was re-evaluated carefully. After complete epithelization, the therapeutic contact lens fitted at the completion of surgery was removed. Thereafter, the same clinical protocol used preoperatively was followed for all postoperative visits. In order to simplify the analysis, we have analysed and compared in the current study the results at 1, 3 and 7 years after surgery.

Statistical analysis

Data analysis was performed using the software SPSS for Windows version 19.0 (SPSS Inc., Chicago, USA). Normality of data samples was evaluated by means of the Kolmogorov-Smirnov test. When parametric analysis was possible, the Student t test for paired data was used for data comparisons between the consecutive visits, whereas the Wilcoxon rank sum test was applied to assess the significance of such differences when parametric analysis was not possible. Differences were considered to be statistically significant when the associated p-value was <0.05.

RESULTS

A total of 34 eyes from 24 patients (15 females, 9 males) with progressive keratoconus were included in the study. Mean age of the sample was 24.7 years (SD: 7.4; median: 22.0; range: 16 to 44 years). A total of 19 (55.9%) right eyes and 15 (44.1%) left eyes were included. All patients completed the 7-year follow-up.

Visual and refractive outcomes

Table 1 summarizes the preoperative and postoperative visual and refractive outcomes obtained in the current study. As shown, a significant reduction of manifest sphere, cylinder and spherical equivalent was observed at 1 year after surgery ($p \leq 0.006$), with an additional small but statistically significant reduction between the 1-year and 3-year postoperative visits ($p \leq 0.002$). No significant changes in refraction were observed during the 4 last years of the follow-up (≥ 0.156). Regarding CDVA, a significant improvement was detected at 1 year after surgery ($p<0.001$), with an additional significant improvement between 1 and 3 years postoperatively ($p=0.001$). No significant changes in CDVA were detected at the end of the follow-up ($p=0.518$). Gains of lines of CDVA were found in a total of 67.55, 73.53 and 73.53% of eyes at 1, 3 and 7 years after surgery, respectively (Figure 1).

Corneal topographic and tomographic changes

Table 2 summarizes the corneal morphologic changes occurring after surgery in the analysed sample. As shown, progressive significant changes were observed during the whole follow-up in the keratometric readings, with a flattening effect at 1, 3 and 7 years after surgery

($p \leq 0.041$) (Figure 2). In contrast, changes in the magnitude of keratometric astigmatism did not reach statistical significant at any time point of the follow-up ($p \geq 0.118$). Regarding pachymetry, a significant central thinning was observed at 1 year after surgery ($p < 0.001$), with no significant changes afterwards ($p \geq 0.112$). Similarly, a significant change in corneal volume was only observed at 1 year postoperatively ($p = 0.016$). Likewise, a significant change was observed in the X ($p = 0.040$) and Y ($p = 0.022$) coordinates of the point of minimum thickness between 1 and 3 years after surgery (Figure 3).

Anterior maximum elevation only experienced a significant change between 1 and 3 years after surgery ($p = 0.002$), whereas the posterior maximum elevation experienced significant changes at all time points of the follow-up ($p \leq 0.034$) (Figure 3). The position of anterior maximum elevation also experienced a significant change, with X coordinate changing significantly at 1 year ($p = 0.034$), and Y coordinate between 3 and 7 years postoperatively ($p = 0.042$) (Figure 3). Furthermore, the X coordinate of the point of maximum posterior elevation also changed significantly at 1 year after surgery ($p = 0.002$) (Table 2) (Figure 3).

Anterior segment changes

Table 3 summarizes the anterior segment changes occurring after surgery in the analysed sample. No significant changes with surgery were detected in anterior segment volume ($p \geq 0.377$) and anterior chamber depth ($p \geq 0.142$).

DISCUSSION

Since the first experiences reported, corneal collagen crosslinking using riboflavin and ultraviolet A (UVA) 370 nm radiation with epithelium removal has been shown to be an effective procedure to halt the progression of keratoconus.[14] Several topographic, refractive, aberrometric and pachymetric changes have been described in the short term after this procedure.[2-4,6,7,9,14] However, long-term studies are still limited as the technique was developed and implemented in clinical practice in the last decade.[5,8,10] There is evidence of topographic keratoconus progression despite stability for a long-term period after CXL.[15] The current study was aimed at evaluating the clinical outcomes, including visual acuity, refraction, and topographic and tomographic anterior segment changes of epi-off CXL during a 7-year follow-up.

In our sample, besides the visual and refractive improvement found at 1 year after surgery, we observed an additional small but statistically significant reduction of the refractive error between the 1-year and 3-year postoperative visits, with an associated improvement in CDVA. No significant changes in visual and refractive parameters were detected afterwards, although there was an additional significant flattening of the cornea between 3 and 7 years after surgery. This significant additional flattening in the long term was small in magnitude, generating minimal impact on manifest refraction and not inducing significant refractive changes. In any case, it should be considered that the determination of refraction in keratoconus eyes is not as reliable as in healthy eyes, with some problems of repeatability.[16] All these outcomes suggest that long-term visual and refractive changes, even 3 years after surgery, can occur after CXL. These changes are related to topographic changes occurring also in the long term in variables such as keratometry or corneal elevation. Ghanem and colleagues[8] found at 2 years after CXL that there were significant improvements in UDVA, CDVA, topographic metrics, and most corneal high order aberrations. However, these authors did not analyse changes between different periods of the follow-up. Similarly, Raiskup et al[10] found a statistically significant decrease of apical keratometry and a significant improvement in CDVA at 10 years of follow-up after CXL, but the authors did not compare changes occurring between different visits of the follow-up. Besides refractive and keratometric changes, a rate of loss of CDVA of 3% was found in our series. This may be related to changes in high order aberrations limiting the eye resolution and even to increase in ocular scattering due to local changes in corneal transmittance. It should be mentioned that no corneal scar or leukoma was visible at slit lamp examination during the long term follow-up. Likewise, no corneal infection or any other severe complication was reported.

Several factors may have accounted for those changes found during the follow-up in our series, such as a long-term induced reorganization of corneal collagen lamellae or structural modifications leading to enhanced mechanical properties of the cornea, or epithelial changes. Although there are several studies evaluating the microscopic structural changes occurring after CXL in the initial postoperative period,[17-20] there are no studies analysing these potential changes in the long term. Among initial changes after CXL, the following are the most notable: stromal collagen compaction and remodelling leading to temporary haze of the anterior-mid stroma, loss of keratocytes with honeycomb oedema and apoptotic bodies, keratocyte regeneration starting at 3 months and being completed at 6 months postoperatively, and loss of subepithelial and stromal nerves, with a complete regeneration at 12 months after surgery and fully restored corneal sensitivity.[17-20] Likewise, a thinner and more homogeneous remodelled epithelium has been observed in keratoconic eyes treated with CXL.[21] All these modifications have been shown to induce an initial significant corneal thinning after surgery, with the corresponding reduction of corneal volume.[22] However, the cornea tends to recover its original volume during the 24 months after CXL with a persistence of the efficacy of surgery.[5] This trend was also observed in our series.

Besides pachymetric modifications, significant changes were found in our series during the follow-up in the position of the points of minimum thickness and maximum anterior and posterior elevation. An initial change was observed in the X coordinate of the point of maximum anterior and posterior elevation in favor of re-centering the cone, this being one of the major benefits of CXL beside keratoconus halting and stabilisation. This would generate a lower level of irregularity of the cornea, allowing the clinician to obtain a more reliable refraction. Besides this, changes in Y coordinate of the point of anterior maximum elevation occurred in the last period of the follow-up. This suggests that ageing may have also influenced the outcomes reported in this study. The stiffness of the human cornea is demonstrated to increase by a factor of approximately two between the ages of 20 and 100 years.[23] In our sample, most of patients were within this range of age and therefore age-related corneal stiffness changes should have influenced the outcomes and may explain those changes occurring in the long term after CXL. Elsheikh et al[24] demonstrated that considerable stiffening occurred with age, with a behavior closely fitting an exponential power function. These authors suggested that this age-related increase in stiffness could be related to age-related non-enzymatic cross-linking affecting the stromal collagen fibrils.[24] Therefore, it is difficult to define the specific factors contributing to the changes occurring after CXL in the long term as it is influenced by a multifactorial process. However, in our series, it was clear that no significant deterioration of visual, refractive and topographic outcomes compatible with keratoconus progression was present in the 7-year follow-up. Therefore, this study confirms that epi-off CXL is able to stabilize the corneal structure in keratoconus, with a potential additional crosslinking effect related to age-related stiffness modifications in the long term. Besides changes in the position of the points of maximum anterior and position elevation, significant changes were detected during the follow-up in the magnitude of these maximum elevation values. Specifically, there was a reduction in MAE between 1 and 3 years after surgery and also in MPE at 1, 3 and 7 years postoperatively. This confirms that the corneal structure is changing after CXL in the long term possibly due to, as previously mentioned, age-related stiffness. The analysis of MAE and MPE allows the clinician to monitor those changes occurring in ectatic corneas in more detailed way than with refractive or corneal curvature data. This analysis may be possibly a better and more objective evaluation of keratoconus progression.

This article has some drawbacks that should be considered. First, no control group or comparison with other type of treatments used in keratoconus was performed. Future comparative studies should be performed to confirm the long-term efficacy of CXL effect compared to other options. Second, no questionnaire evaluating the patient's satisfaction with the outcomes of the surgery was used. This would have allowed us to confirm if the improvements observed in some visual, refractive and topographic parameters were consistent with the subjective perception of the patient.

In conclusion, the efficacy of epithelium off corneal collagen crosslinking using riboflavin and ultraviolet A (UVA) 370 nm in progressive keratoconus is maintained until 7 years after surgery, confirming the benefit of this therapeutic option to halt the progression of this disease. Concerning refractive measurements, they should be interpreted with caution as the reliability and repeatability of manifest refraction in keratoconus has been shown to be limited,[16] and can be also have been affected by accommodative changes especially in the younger patients with strong accommodation capacity. The long term CXL effect is combined with the natural age-related corneal stiffening, providing a satisfactory outcome and corneal stability. Future studies should be conducted to evaluate the long term microscopic structural changes occurring after CXL.

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Figure legends

Figure 1.- Distribution of changes in corrected distance visual acuity (CDVA) at 1, 3 and 7 years after surgery in the analysed sample.

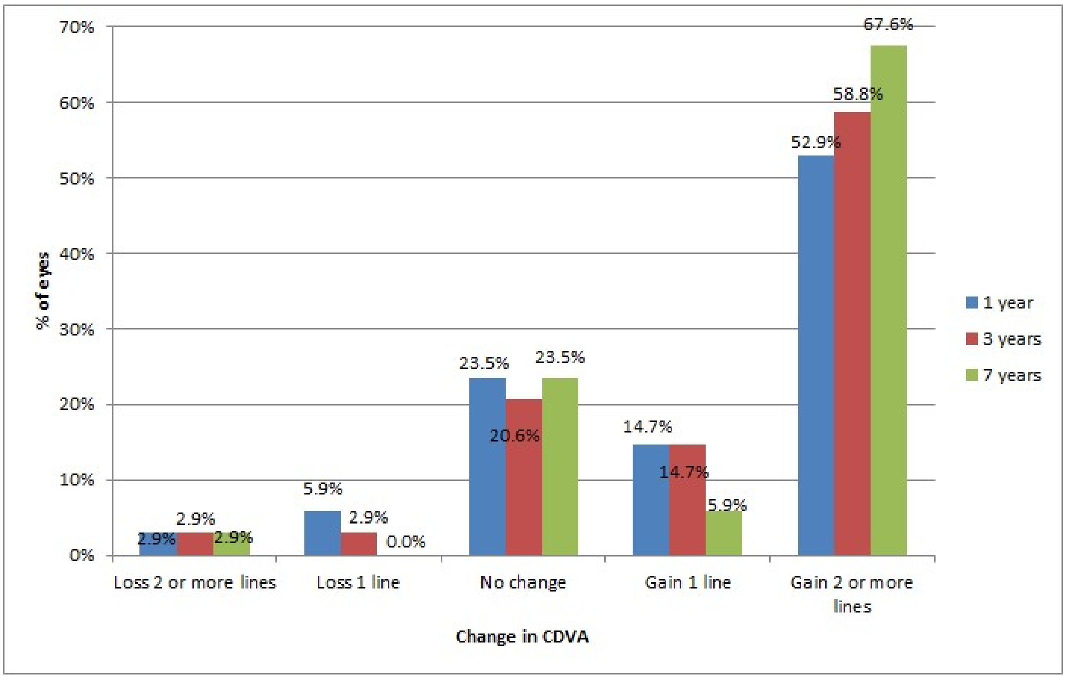

Figure 2.- Changes in keratometric readings during the whole follow-up: flattest keratometric reading (K1, blue line), steepest keratometric reading (K2, red line), and maximum keratometry (KMAX, green line).

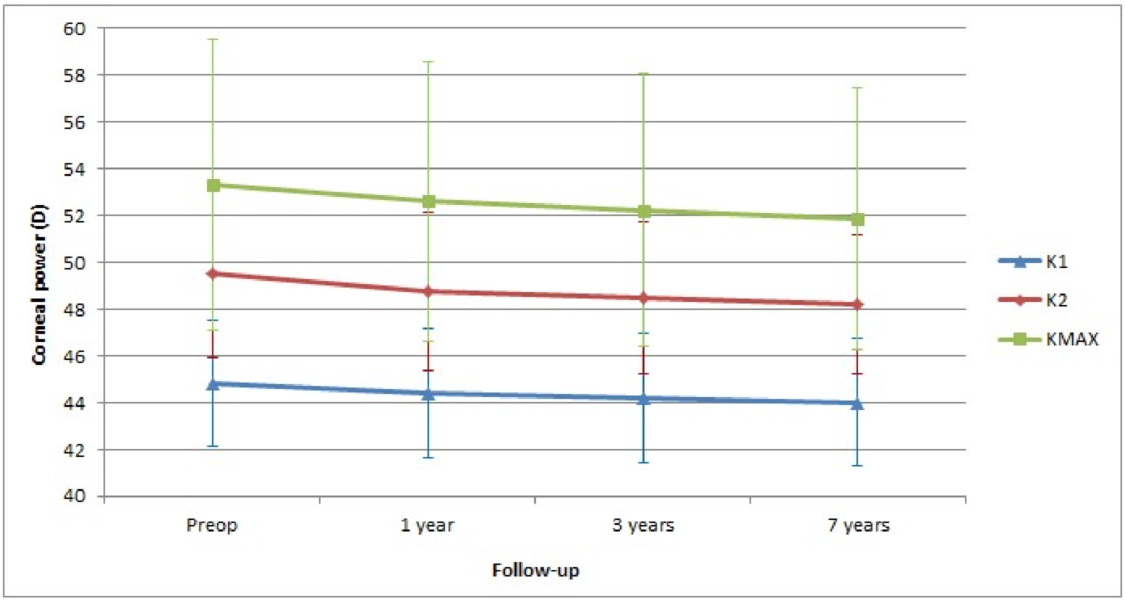

Figure 3.- Changes in the X and Y Cartesian coordinates of the points of minimum corneal thickness (MCT), maximum anterior elevation (MAE), and maximum posterior elevation (MPE).

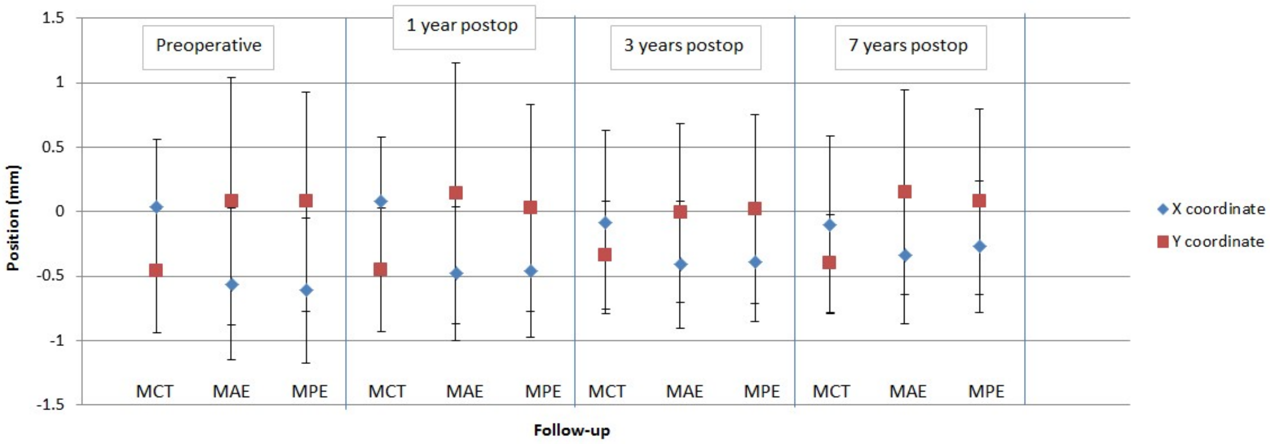

Table 1.- Summary of the preoperative and postoperative visual and refractive data in the sample evaluated.

Mean (SD) edian (Range)	Preoperative	1 year postoperative	3 years postoperative	7 years postoperative	p-value (preop-1 y)	p-value (1 y-3 y)	p-valu (3 y-7
Sphere (D)	-5.07 (4.09) -4.13 (-20.00 to 1.75)	-4.73 (3.95) -3.50 (-20.00 to 1.50)	-4.14 (3.76) -3.00 (-19.00 to 1.50)	-4.16 (3.63) -3.00 (-18.00 to 1.25)	0.006*	<0.001*	0.895
Cylinder (D)	-5.24 (1.78) -5.13 (-9.50 to -2.00)	-4.81 (1.64) -4.88 (-7.25 to -2.00)	-4.46 (1.46) -4.25 (-7.25 to -1.50)	-4.24 (1.50) -4.25 (-7.00 to -1.00)	0.005*	0.002*	0.156
Spherical quivalent (D)	-7.70 (4.15) -7.25 (-21.38 to -0.12)	-7.13 (3.98) -6.13 (-21.25 to -0.25)	-6.37 (3.75) -5.25 (-20.38 to -0.12)	-6.28 (3.59) -5.25 (-18.50 to -0.38)	0.003*	<0.001*	0.585
ogMAR CDVA	0.98 (0.36) 1.00 (0.40 to 1.70)	0.77 (0.34) 0.70 (0.15 to 2.00)	0.66 (0.32) 0.66 (0.22 to 2.00)	0.63 (0.29) 0.52 (0.15 to 1.30)	<0.001*	0.001*	0.518

* Statistically significant results.

Abbreviations: UDVA, uncorrected visual acuity; CDVA, best spectacle corrected visual acuity; SD, standard deviation.

Table 2.- Summary of the preoperative and postoperative corneal morphology data in the analysed sample.

Mean (SD) edian (Range)	Preoperative	1 year postoperative	3 years postoperative	7 years postoperative	p-value (preop-1 y)	p-value (1 y-3 y)	p-valu (3 y-7
K1 (D)	44.81 (2.71) 44.05 (37.60 to 53.20)	44.42 (2.75) 43.60 (37.20 to 53.00)	44.20 (2.74) 43.40 (37.30 to 52.70)	44.02 (2.72) 43.45 (37.10 to 52.50)	<0.001*	0.012*	0.033*
K2 (D)	49.50 (3.55) 48.70 (41.90 to 58.00)	48.77 (3.39) 47.75 (43.10 to 57.50)	48.48 (3.25) 47.60 (42.80 to 57.00)	48.24 (2.97) 47.45 (43.50 to 56.80)	0.001*	0.001*	0.041*
KMAX (D)	53.31 (6.20) 51.35 (46.20 to 72.90)	52.60 (6.00) 50.40 (45.40 to 71.80)	52.23 (5.83) 50.00 (45.40 to 70.30)	51.87 (5.62) 50.25 (44.90 to 67.10)	0.011*	0.041*	0.010*
AST (D)	4.68 (1.82) 4.50 (1.90 to 10.20)	4.38 (1.51) 4.35 (1.50 to 7.30)	4.33 (1.37) 4.50 (1.60 to 6.90)	4.24 (1.44) 4.25 (1.50 to 7.40)	0.118	0.340	0.361
MCT (µm)	471.26 (42.51) 470.50 (402 to 583)	467.06 (40.60) 467.50 (402 to 580)	466.59 (41.47) 462.50 (405 to 580)	463.47 (43.68) 458.50 (399 to 582)	<0.001*	0.936	0.112
X-coordinate MCT (mm)	0.04 (0.52) -0.15 (-0.76 to 0.95)	0.08 (0.50) 0.11 (-0.72 to 0.83)	-0.08 (0.71) -0.14 (-3.00 to 0.91)	-0.10 (0.69) -0.14 (-3.00 to 0.94)	0.351	0.040*	0.198
oordinate MCT (mm)	-0.46 (0.48) -0.51 (-1.13 to 1.15)	-0.45 (0.48) -0.46 (-1.69 to 1.43)	-0.34 (0.42) -0.34 (-0.98 to 1.36)	-0.40 (0.38) -0.43 (-0.94 to 1.22)	0.397	0.022*	0.153
CV (mm^3)	57.56 (4.00) 57.75 (49.10 to 65.90)	56.98 (4.01) 57.00 (47.20 to 65.80)	57.05 (3.90) 57.15 (48.00 to 66.00)	56.88 (3.75) 56.80 (48.20 to 65.00)	0.016*	0.914	0.646
MAE (µm)	27.88 (13.91) 25.00 (10 to 73)	27.00 (14.50) 23.50 (9 to 66)	25.65 (14.05) 22.00 (9 to 63)	25.24 (13.80) 20.50 (8 to 62)	0.162	0.002*	0.135
X-coordinate MAE (mm)	-0.56 (0.59) -0.59 (-1.35 to 1.02)	-0.48 (0.52) -0.51 (-1.35 to 0.98)	-0.41 (0.49) -0.34 (-1.20 to 0.76)	-0.34 (0.53) -0.35 (-1.00 to 0.85)	0.034*	0.078	0.181
oordinate MAE (mm)	0.08 (0.96) 0.05 (-1.64 to 1.93)	0.14 (1.01) 0.05 (-1.31 to 4.12)	-0.01 (0.69) -0.20 (-1.51 to 1.50)	0.15 (0.79) 0.02 (-1.49 to 2.24)	0.999	0.859	0.042*
MPE (µm)	53.53 (23.89) 48.50 (13 to 117)	50.85 (20.98) 49.00 (15 to 94)	49.32 (20.58) 48.50 (15 to 91)	48.06 (19.49) 48.50 (16 to 91)	0.018*	0.009*	0.034*
X-coordinate MPE (mm)	-0.61 (0.56) -0.70 (-1.35 to 0.80)	-0.46 (0.51) -0.49 (-1.28 to 0.71)	-0.39 (0.46) -0.47 (-1.10 to 0.80)	-0.27 (0.51) -0.22 (-1.19 to 0.87)	0.002*	0.099	0.085
oordinate MPE (mm)	0.08 (0.85) -0.14 (-1.71 to 1.87)	0.03 (0.80) -0.11 (-1.77 to 1.94)	0.02 (0.73) -0.02 (-1.62 to 1.90)	0.08 (0.72) 0.03 (-1.90 to 1.70)	0.688	0.789	0.090

* Statistically significant results.

Abbreviations: SD, standard deviation; K1, flattest keratometric reading; K2, steepest keratometric reading; AST, keratometric astigmatism; MCT, minimal corneal thickness; KMAX, maximum keratometry; CV, corneal volume; MAE, maximum anterior elevation; MPE, maximum posterior elevation.

Table 3.- Summary of the preoperative and postoperative anterior segment data in the analysed sample.

Mean (SD) edian (Range)	Preoperative	1 year postoperative	3 years postoperative	7 years postoperative	p-value (preop-1 y)	p-value (1 y-3 y)	p-valu (3 y-7
ASV (mm^3)	211.38 (30.78) 215.50 (129 to 262)	209.00 (32.89) 207.00 (126 to 264)	210.21 (31.75) 216.50 (125 to 260)	209.30 (21.40) 214.00 (124 to 259)	0.442	0.377	0.922
ACD (mm)	3.46 (0.25) 3.45 (2.81 to 3.85)	3.53 (0.29) 3.52 (2.91 to 4.10)	3.47 (0.26) 3.50 (2.81 to 3.88)	3.46 (0.26) 3.45 (2.80 to 3.89)	0.142	0.149	0.157

* Statistically significant results.

Abbreviations: SD, standard deviation; ASV, anterior segment volume; ACD, anterior chamber depth.