· Clinical Research ·

Corneal surface changes after stromal lenticule addition keratoplasty combined with cross-linking for severe keratoconus

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Abstract

● **AIM:** To investigate the response of the anterior and posterior corneal surface in femtosecond laser-assisted convex stromal lenticule addition keratoplasty (SLAK) combined with cross-linking (CXL) for treating keratoconus at the first 3mo of follow-up.

● **METHODS:** In this prospective observational study, 20 eyes of 20 keratoconus patients who underwent SLAK combined with CXL were included. The morphological indices in keratometry and elevation data were recorded from the Sirius at baseline and 1 and 3mo postoperatively. The mean values of maximum keratometry (K_{max}), flat keratometry (K_1), and steep keratometry (K_2) at the central, 3-mm, 5-mm, and 7-mm areas were measured from the curvature map. The changes in anterior and posterior corneal elevation under the best-fit sphere (BFS) radius at seven points horizontally of the center, 3-mm, 5-mm, and 7-mm area from the center at both nasal (N) and temporal (T) side were measured from elevation map.

● **RESULTS:** For the front corneal curvature, K_1, and K_2 at 3-mm, 5-mm, and 7-mm of the anterior corneal surface increased significantly 1mo postoperatively (all P<0.05) and remained unchanged until 3mo (P>0.05). For the back corneal curvature, K_1 and K_2 along the 3-mm back meridian significantly decreased after month 1 (P=0.002, 0.077, respectively). Posterior K_2-readings along the 5-mm and 7-mm did not change after surgery (P>0.05). Anterior BFS decreased 1mo (P<0.001) postoperatively but remained unchanged until 3mo after SLAK (P>0.05). There was no change in posterior BFS before and after the surgery (P>0.05). Anterior elevation at N5, N3, central, and T5 points and posterior elevation at central and T7 points shifted backward 1mo postoperatively (all P<0.05) and remained stable until 3mo (P>0.05).

● **CONCLUSION:** The myopic SLAK combined with CXL is an economical alternative for stabilizing the corneal surface in severe keraoconus. "Pseudoprogression" occurs in the early phase postoperatively, but it is not an indicator of keratoconus progression.

● **KEYWORDS:** small incision lenticule extraction; lenticule; addition; cross-linking; keratoconus

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INTRODUCTION

Keratoconus (KC) is a bilateral ectatic eye disease characterized by corneal stromal thinning and weakening. It turns out that there are various degrees of distortion at the corneal surface as KC progresses. At an early stage, when only posterior elevation is present without alteration of the anterior surface values, we consider this as asymptomatic KC. We refer to it as KC suspect when the posterior values are out of normal range without reaching abnormality. In this case, KC indices, Belin/ambrósio enhanced ectasia Display-D (BAD-D; Pentacam) value, and corneal biomechanics help diagnose correctly[1-2]. At a higher stage, changes in the anterior surface values are also apparent; in that case, there is visual impairment, and maybe clinical signs are already evident[3-5].

The detection of subtle changes in KC corneas remains a challenge. Ocular Response Analyzer (ORA, Reichert Ophthalmic Instruments Inc. Buffalo, NY, USA) or Corvis ST (Oculus, Wetzlar, Germany) is the devices to assess corneal biomechanics clinically[6]. However, corneal surface changes sometimes come first before they can be detected by clinical biomechanical investigation[7]. Therefore, researchers may also observe the corneal surface changes, such as keratometric and elevation values, to evaluate the corneal stability in KC[8]. Combined with cross-linking (CXL) is effective in halting the progression of KC[9]. As CXL was first introduced, it was contraindicated for corneas with the thinnest pachymetry <400 μm because of possible damage to the endothelium. To reduce this risk, researchers have used several algorithms and techniques can be performed to treat thinner corneas, such as the "sub400 protocol" (ultraviolet irradiation performed at 3 mW/cm^2) or the use of hypotonic riboflavin drops[10-11]. Studies have confirmed that the progression rate was higher in KC patients with thin corneas (<430 μm)[12-13]. Long-term follow-up studies after CXL in progressive cases have shown improvement of anterior corneal values, stabilization of pachymetry values and better visual acuity[14-15]. Nevertheless, maximum keratometric value (K_{max})>58 D may be associated with failure of primary CXL[16]. In some cases, for patients with more advanced KC with thin corneas, traditional corneal transplantation may be required[17]. Despite its high success rates, drawbacks such as graft failure or rejection should be considered. Insufficient corneal grafts from the eye bank may also be a dilemma for surgical treatments[18].

Thanks to the small incision lenticule extraction (SMILE) technique, surgeons take considerable interest in the re-implantation of the extracted lenticules because they have more options in reusing the potential tissue to treat patients with aphakia, hypermetropia, KC, and presbyopia[19]. More recently, some surgeons have considered stromal lenticule addition keratoplasty (SLAK) combined with CXL for advanced KC with thin ultra-thin corneas as an alternative to keratoplasty, and their results were promising[20]. However, the results were mainly initial visual and refraction outcomes[21-23]. In this study, we aimed to stop the progression and increase the corneal thickness in severe KC through this surgical technique. To our knowledge, no other studies have investigated the corneal surface changes after SLAK combined with CXL to confirm its stabilization effect. Hence, we are motivated to observe the response of the corneal surface changes using this new surgical approach with advanced KC.

PARTICIPANTS AND METHODS

Ethical Approval The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Xi'an No.1 Hospital's Ethics Committee (ethical approval number: 202109). After the risks and benefits were explained, the patients agreed to participate in this study, and written informed consent for study participation was obtained from them before the surgery.

Twenty eyes of 20 patients (6 female and 14 male) aged 15 to 37y with KC were selected and recruited for the study from May 2021 to June 2022 by a single surgeon (Wei W) at the Department of Laser Vision Center, Xi'an No.1 Hospital, Shaanxi Province, China. All patients had poor visual acuity and were intolerant to contact lenses. The surgery was an alternative, less invasive profile than corneal transplantation, and the tissue donors were easier to find.

Inclusion and Exclusion Criteria For recipients, the inclusion criteria were: 1) KC with progression evidence waiting for corneal transplantation. Progression was defined as the following changes within 1y[24]: increase in maximum anterior sagittal curvature (K_{max}) by >1.0 D and/or decrease in minimum corneal thickness by ≥5%; 2) thinnest corneal thickness less than 400 μm, mean keratometry: 48.00 D or greater, corrected distance visual acuity (CDVA): worse than 20/50; 3) An intolerance to rigid gas permeable contact lenses (RGPCLs); 4) Unwillingness to corneal transplantation. For donors, the inclusion criteria were: 1) Spherical equivalent (SE) -2.00 to -8.00 D with a cylinder of no more than -1.00 D; 2) CDVA of better than 20/20; 3) no infection with hepatitis B virus (HBV), HIV, hepatitis C virus (HCV). We excluded individuals with active inflammatory eye diseases, glaucoma, previous ocular surgery, significant corneal scarring, or other corneal ectasia diseases. Carcinoma, neurodegenerative diseases, and pregnant and breastfeeding patients were also excluded from the study.

Examinations and Data Collection Baseline clinical examination included evaluation of uncorrected visual acuity (UCVA), CDVA, slit-lamp biomicroscopy, intraocular pressure, corneal topography with the Sirius tomography system (CSO, Costruzione Strumenti Oftalmici, Florence, Italy) was used to obtain the anterior and posterior corneal surface of both curvature and elevation data.

Considering the possibility that the eyelids would cover the elevation map in a perpendicular direction, only data in the horizontal meridian were recorded[25]. Topographic data along the horizontal meridian was collected over a 7-mm corneal diameter in the center (C) of corneal topography, 3-mm, 5-mm, and 7-mm in the nasal corneal (N3, N5, N7), and the temporal corneal (T3, T5, T7) using the elevation map. Topographic data were obtained manually for each location (Figure 1). The best fit sphere (BFS) radius over the central 9.0 mm zone was calculated for each cornea automatically by Sirius. We also obtained the keratometric (curvature) indices as follows: the point of K_{max} of the front corneal surface; K_1 and K_2 of the anterior and posterior corneal surface at 3-, 5-, and 7-mm circles. All these parameters were examined before surgery, 1mo, and 3mo after surgery.

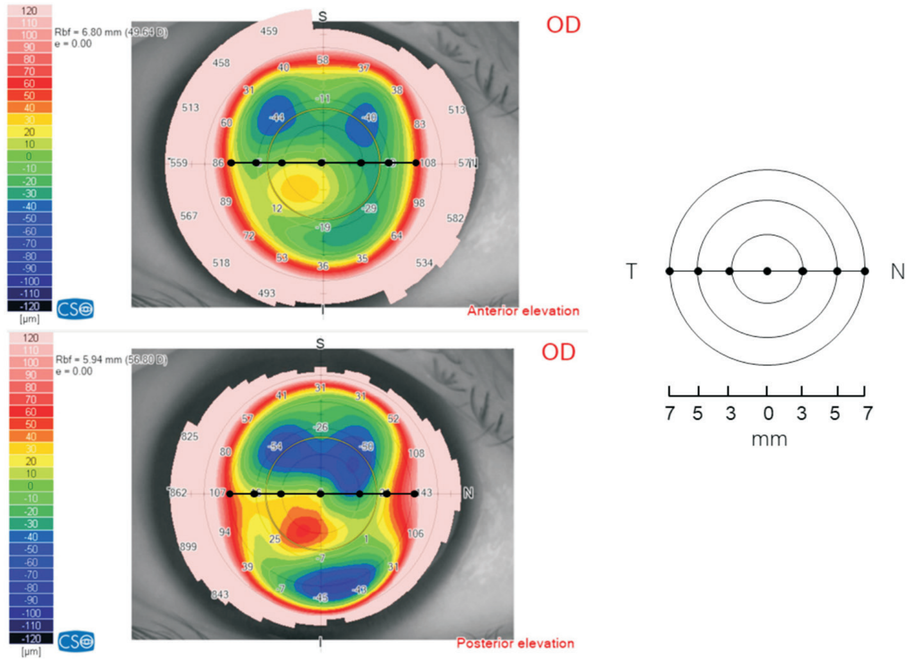

Figure 1 Anterior and posterior elevation map demonstrating 7 points along the horizontal meridians in the central 7-mm area used for calculating the change in anterior and posterior corneal elevation before and after SLAK SLAK: Stromal lenticule addition keratoplasty.

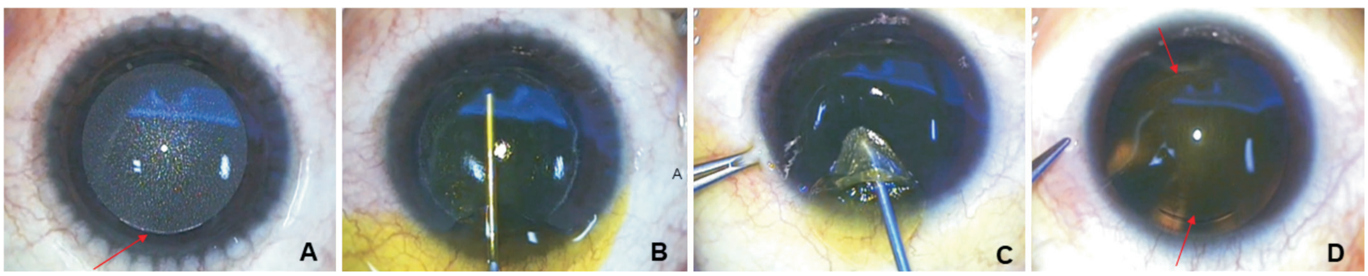

Figure 2 Surgical procedure of stromal lenticule addition keratoplasty under the dilated pupil A: A 4-mm superior incision was created by a FLEx procedure (red arrow); B: The pocket was dissected, followed by injection of 0.25% VibexXtra (Avedro) dye into the interface for 10min; C: The positive meniscus-shaped lenticule was soaked in riboflavin for 10min and implanted into the pocket; D: Transillumination highlights the edge of the implanted lenticule, which confirms the centered position (red arrow).

Surgical Technique Eligible myopic patients as donors were scheduled on the same day for treatment. One experienced surgeon (Wei W) performed all surgeries under topical anesthesia.

The ReLEx procedure was first performed on donor patients using the Visumax femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) with a pulse repetition rate of 500 kHz, 130 nJ energy. The cap diameter was 7.0 to 7.8 mm, and the cap thickness was 120 to 130-μm with a 2-mm incision at 120 degrees. The lenticule diameter was 6.0 to 6.8 mm, and the lenticule thickness was 77 to 129 μm. Before implantation, the myopic lenticule was extracted and preserved in the balanced salt solution.

Each patient had a dilated pupil before surgery to check the edge of the lenticule after lenticule implantation. The FLEx procedure was then performed on recipient patients using the same Visumax femtosecond laser. We created a stromal pocket with a diameter of 7.0 to 7.8 mm (larger than the optical zone of the donor lenticule) and a cap thickness of 110 to 200 μm from the anterior corneal surface. The flap hinge was set to 300 degrees to get a superior 4-mm incision. The procedure is shown in Figure 2. The pocket was dissected using a blunt spatula. Next, the surgeon injected 0.1% riboflavin solution (VibexXtra; Avedro, MA, USA) into the interface for 10min. The preserved lenticule was also soaked in riboflavin. The lenticule was washed with balanced salt solution (BSS) and gently inserted into the pocket through the 4-mm incision. The surgeon checked the lenticule position by the dilatated pupil margin and flattened it from the corneal surface using the blunt spatula. The eye was then exposed to UV-A radiation using the Avedro CXL system (Avedro) at 30 mW/cm^2 for 4min. Finally, a bandage lens (AcuVue Oasys, Johnson & Johnson, Inc., New Brunswick, NJ, USA) was placed on the cornea.

Postoperative Topical Medication Regimens Each patient was instructed to instill topical antibiotics (0.5% levofloxacin; Santen Pharmaceutical Co., Ltd., Japan) 4 times per day for seven days, steroids (fluorometholone 0.1%; Santen Pharmaceutical Co., Ltd.) 6 times per day with gradually reduced frequencies and artificial tears 4 times per day for 1mo.

Statistical Analysis All the statistical data were analyzed using IBM SPSS Version 22.0 (IBM Corp., Armonk, NY, USA). Normal distribution was tested using the Shapiro-Wilk test. The data was normally distributed. Changes in both anterior and posterior corneal surfaces over time were assessed by a parametric one-way repeated measure analysis of variance test, and the Bonferroni test was used for post-hoc analysis. In all analyses, the results are expressed as the mean±standard deviation (SD) or the 95% confidence intervals (95%CI), and a $P<0.05$ was considered statistically significant.

RESULTS

Twenty eyes of 20 patients (6 female and 14 male) aged 15 to 37y were treated with SLAK combined with CXL. The preoperative data of recipient patients and details of lenticules implanted are shown in Table 1. There was no adverse event, such as persistent haze or graft rejection.

Table 1 Preoperative demographic data of patients with SLAK

Characteristics	Value
Recipients	
Age (y)	23.50±5.09
Sex (male:female)	14:6
Eye treated (right:left)	12:8
CDVA, logMAR	1.24±0.38
UDVA, logMAR	0.58±0.34
Sphere (D)[a]	-11.94±7.43
Cylinder (D)[a]	-6.42±4.34
IOP (mm Hg)[b]	8.50±2.70
HVID (mm)	11.59±0.47
TCT (μm)	369.40±27.83
K_{max} (D)	69.05±10.32
K_1 (D)	52.60±5.80
K_2 (D)	58.03±6.16
K_{avg} (D)	55.14±5.78
Donors	
Lenticule diameter (mm)	6.63±0.20
Lenticule thickness (μm)	103.00±15.81
Lenticule spherical diopters (D)	-4.66±1.34
Lenticule cylindrical diopters (D)	-0.19±0.24

SD: Standard deviation; D: Diopters; UCVA: Uncorrected distance visual acuity; CDVA: Corrected distance visual acuity; IOP: Intraocular pressure; HVID: Horizontal visible iris diameter; TCT: Thinnest corneal thickness; K_{max}: Maximum keratometry; K_1: Flat keratometry; K_2: Steep keratometry; K_{avg}: Average keratometry; [a]n=11, and 1 patient's refraction was undetectable; [b]n=16, and 4 patients' IOP was undetectable. SLAK: Stromal lenticule addition keratoplasty.

Changes in Keratometry Table 2 illustrates the overall changes in anterior and posterior curvature values detected by Sirius. For the front corneal surface, K_1 and K_2 at 3-mm, 5-mm, and 7-mm of the anterior corneal surface were increased significantly 1mo postoperatively (all $P<0.05$). However, these values exhibited no significant changes after month 1 (all $P>0.05$). K_{max} also increased after month 1, but there was no statistical significance until 3mo postoperatively (P=0.032). For the back corneal surface, both posterior K_1 and K_2 keratometry along the 3-mm back meridian decreased after month 1 compared to preoperative values (P=0.005, 0.230, respectively). Although posterior K_1 and K_2 along the 3-mm increased 3mo postoperatively compared to month 1, it revealed generalized flattening than preoperatively (P=0.049, 0.037, respectively). Posterior K_1 along 5-mm decreased significantly after month 1 postoperatively (P=0.04). However, this change was insignificant at 3mo compared with baseline ($P>0.05$). There were no significant changes in posterior K_2 along 5-mm and posterior K_1 and K_2 keratometry along 7-mm meridians before and after SLAK (all $P>0.05$).

Changes in Corneal Elevation Figure 3 presents anterior and posterior BFS radius changes before and after SLAK combined with CXL. Anterior BFS decreased by 0.33 mm 1mo after SLAK, from 6.52 to 6.19 mm ($P<0.001$), but remained stable until 3mo postoperatively ($P>0.05$). There were no significant differences in posterior BFS before and after surgery ($P>0.05$). Table 3 shows the changes in anterior and posterior elevation. For elevation on the front corneal surface at the nasal side, changes on 7-mm did not significantly change before and after surgery ($P>0.05$). However, changes at N5 and N3 showed a backward shift between preoperatively and 1mo postoperatively ($P<0.001$, P=0.196, respectively). Post hoc analysis showed no significant changes in N5 and N3 between 1mo and 3mo after surgery (all $P>0.05$). For anterior elevation at the central cornea, there was a statistically significant difference in the backward displacement at 1mo after surgery compared with that before surgery ($P<0.05$), but Bonferroni post hoc analysis showed no significant change between 1mo and 3mo after surgery ($P>0.05$). For elevation on the front corneal surface at the temporal side, changes on 3-mm and 7-mm did not significantly change before and after surgery (all $P>0.05$). Changes on 5-mm showed a significant backward shift 1mo after the surgery (P=0.003), but no significant difference was found between 1mo and 3mo after surgery ($P>0.05$). For elevation on the back corneal surface, the backward shift was only found significantly on central and T7 points after surgery at 1mo postoperatively (P=0.038, <0.001, respectively), and Post hoc analysis showed no significant change between 1mo and 3mo after surgery ($P>0.05$). Besides, there were no statistical significances on N7, N5, N3, T3, and T5 points between preoperatively and 1mo and 3mo postoperatively (all $P>0.05$).

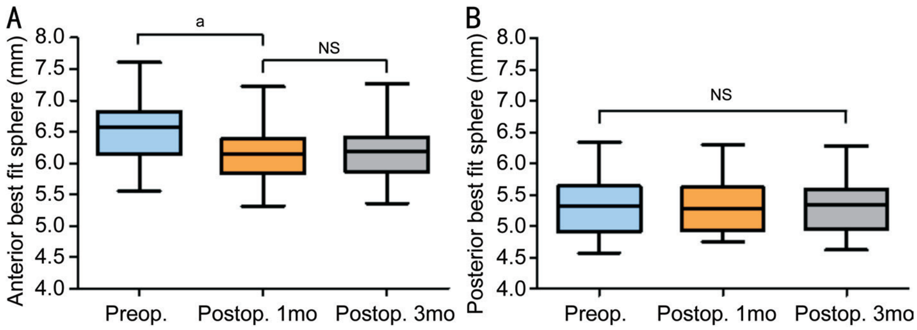

Figure 3 The variation in the anterior (A) and posterior (B) best-fit sphere (BFS) radius [a]$P<0.05$.

Table 2 Preoperative and postoperative values of curvature data for SLAK

Parameters	Preoperative	1mo postoperative	3mo postoperative	P^a
Anterior curvature				
K_{max}	64.22 to 73.88	65.95 to 79.38	66.62 to 78.62[d]	0.011
K_1 (3 mm)	51.57 to 58.22	55.07 to 61.57[d]	55.46 to 62.10[d]	<0.001
K_1 (5 mm)	50.10 to 55.54	53.67 to 59.08[d]	53.83 to 59.35[d]	<0.001
K_1 (7 mm)	48.56 to 52.76	51.46 to 55.52[d]	51.52 to 55.74[d]	<0.001
K_2 (3 mm)	58.04 to 66.02	60.81 to 69.43[d]	60.30 to 68.28[d]	0.001
K_2(5 mm)	55.38 to 61.29	58.58 to 64.91[d]	57.99 to 64.17[d]	<0.001
K_2 (7 mm)	52.71 to 57.25	55.34 to 59.92[d]	54.89 to 59.41[d]	<0.001
Posterior curvature				
K_1 (3 mm)	-9.34 to -7.98	-8.71 to -7.31[d]	-8.94 to -7.81[d]	0.016
K_1 (5 mm)	-8.39 to -7.48	-8.11 to -7.15[d]	-8.27 to -7.44	0.024
K_1 (7 mm)	-7.68 to -7.01	-7.57 to -6.93	-7.68 to -7.09	0.379
K_2 (3 mm)	-10.81 to -9.30	-10.24 to -8.75	-10.28 to -8.94[d]	0.012
K_2 (5 mm)	-8.39 to -7.48	-9.24 to -8.22	-9.16 to -8.24	0.059
K_2 (7 mm)	-8.33 to -7.66	-8.39 to -7.70	-8.24 to -7.64	0.344

Results are expressed as 95%CI; [d]Significant difference when compared with baseline ($P<0.05$); [a]Significant difference at different time points after surgery; $P<0.05$ were considered significant; K_{max}: Maximum keratometry; K_1: Flat keratometry; K_2: Steep keratometry; SLAK: Stromal lenticule addition keratoplasty.

Table 3 Preoperative and postoperative values of elevation data for SLAK

Parameters	Preoperative	1mo postoperative	3mo postoperative	P^a
Anterior elevation				
N7	33.43 to 66.47	32.18 to 66.13	29.07 to 59.73	0.190
N5	-32.55 to -8.75	-50.36 to -23.94[d]	-52.07 to -23.03[d]	<0.001
N3	-29.92 to -9.48	-38.88 to -18.42[d]	-40.93 to -20.97[d]	0.006
C	6.61 to 10.99	7.71 to 12.89[d]	7.95 to 12.46[d]	0.004
T3	4.12 to 19.08	3.25 to 21.15	0.59 to 19.41	0.488
T5	-3.45 to 14.45	-13.77 to 8.07	-15.42 to 5.62[d]	0.003
T7	36.40 to 67.40	28.43 to 73.07	31.40 to 71.00	0.875
Posterior elevation				
N7	66.63 to 143.57	62.45 to 114.55	53.64 to 110.26	0.194
N5	-62.58 to -14.92	-73.34 to -14.66	-75.90 to -33.80	0.067
N3	-76.12 to -28.98	-79.56 to -27.74	-85.42 to -41.18	0.312
C	14.09 to 22.21	8.77 to 17.53[d]	12.16 to 19.25[b]	0.002
T3	-12.67 to 10.97	-1.99 to 24.89	-10.98 to 19.78	0.451
T5	-25.34 to 2.14	-15.35 to 15.35	-28.70 to -3.00	0.474
T7	87.26 to 140.14	47.05 to 116.25[d]	50.61 to 109.79[d]	<0.001

Results are expressed as 95%CI; [d]Significant difference when compared with baseline ($P<0.05$); [b]Significant difference when compared with 1mo postoperatively ($P<0.05$); [a]Significant difference at different time points after surgery; $P<0.05$ were considered significant; C: At the central cornea; N3, N5, N7, at 3, 5, 7 mm in the central area in the nasal cornea; T3, T5, T7, at 3, 5, 7 mm in the central area in the temporal cornea. SLAK: Stromal lenticule addition keratoplasty.

DISCUSSION

CXL has been proven to be safe and effective in halting the KC progression by improving the corneal biomechanical strength[26]. However, this technique is principally avoided in thin corneas (<400 μm) as the risk of damaging the corneal endothelium is high; corneal transplantation, such as deep anterior lamellar keratoplasty, or even penetrating keratoplasty in cases of severe scarring and thinning is the traditional treatment for advanced KC[9]. In recent years, some surgeons have tried to re-use stromal lenticules obtained either from corneal grafts or refractive surgeries. Various lenticule implantations with CXL have been desirable for increasing corneal volume and regularizing corneal curvature in patients with advanced KC[20,27-28]. The procedure has been shown to result in increased corneal volume, stabilization of the cornea, and modification of the corneal shape. Our study suggests that after SLAK combined with CXL, the posterior corneal surface had a backward shift trend, indicating that this novel technique may have a stabilizing effect on the posterior corneal surface in KC patients.

In general, literature has mentioned three different shapes of lenticules: donut-shaped lenticule (*e.g.*, myopic SMILE lenticule punched at its center)[20], concave-shaped lenticule (*e.g.*, hyperopic SMILE lenticule)[29], and convex-shaped lenticule (*e.g.*, myopic SMILE lenticule)[27-28]. Based on a previous study, the concave-shaped lenticule addition seemed to produce a more significant impact on K_{mean} and SE in advanced KC patients[21]. Donut-shaped lenticule may have a greater effect on flattening keratometry[20]. In principle, patients would benefit the most if the lenticule implantation could be customized according to their corneal cone morphology. Doroodgar *et al*[22] reported their clinical results using customized corneal stromal donor lenticules obtained from myopic SMILE. They customized the lenticules in a necklace or necklace-with-ring shape depending on the corneal morphology of the recipient's eyes. Patients gained significantly improved CDVA (from 0.70 to 0.49 logMAR) and decreased keratometry (from 54.68±2.77 to 51.95±2.21 diopters). Nevertheless, it should be pointed out that in China, doctors hardly have access to hyperopic SMILE-derived lenticules. On the other hand, the tremendous number of myopic patients for SMILE correction makes it the easiest way to get these convex-shaped lenticules for implantation in KC patients. A recent study has proved that fresh myopic intrastromal lenticular implantation is a safe, economical, and reliable technique that leads to increased corneal thickness, improved visual acuity, and the regeneration of healthy keratocytes and tenocyte-like cells that are involved in stromal regeneration[28]. In our study, although convex-shaped lenticule addition induces steeping anterior corneal surface, it is a feasible technique to stabilize the cornea in patients with advanced KC in the early phase.

Sirius topography showed high predictive accuracy in the detection of KC[30]. Changes in the anterior and posterior radius of curvature of the 3-mm zone centered on the thinnest point are important in evaluating the KC progression[5]. Xanthopoulou *et al*[31] evaluated the effectiveness of epithelium-off (epi-off) accelerated corneal cross-linking (A-CXL, 9 mW/cm^2, 10min) in adult patients, and they found that the anterior steep, flat and maximal keratometry increased significantly 6wk after the surgery. However, the posterior corneal keratometry readings did not change significantly until >2y after A-CXL. They named this phenomenon "pseudoprogression". In this article, the K_{max}, anterior K_1, and K_2 increased after SLAK combined with CXL but remained unchanged from 1mo to 3mo. These results are similar to those of the above study. In comparison, the posterior surface in terms of K_1 and K_2 at 5-mm and 7-mm showed no significant changes after the surgery. More importantly, posterior K_1 and K_2 at 3-mm showed a flattening trend after SLAK. As KC progresses, the central steepening is associated with peripheral flattening, which is consistent with a central increase in surface area and a peripheral relative reduction[32]. We suggest that convex-shaped lenticule addition combined with CXL would induce "pseudoprogression" in a double way in a short time postoperatively, while it was the lenticule addition that mainly affected the central posterior corneal surface. Zhao *et al*[33] reported the clinical results from a case of KC patients with a thin cornea (356 μm). What was different was that the myopic lenticule was transplanted directly onto a central location in the recipient's eye, and CXL was performed 1mo after lenticule addition. They also found an increasing but stable trend in keratometry. These findings are important, for they can help doctors to consider RGPCLs fitting for KC patients to get better visual quality 1mo after the surgery instead of waiting for at least 3mo postoperatively as usual. Another proposed option to achieve good refractive outcomes is a CXL combined with photorefractive keratectomy or phototherapeutic keratectomy[34]. Gupta *et al*[35] compared the variation in the best-fit sphere radius (BFSR) of curvature in stable and progressive KC. In the progressive group, there were no significant differences in anterior and posterior BFSR, while they were not found to be statistically significant in the stable group. As the ectasia progresses, the steepening of the cornea will cause the BFSR to have a progressively smaller radius of curvature. In our study, the anterior BFS decreased after SLAK. However, it remained stable from 1mo to 3mo. We suggest that the convex-shaped lenticule addition may mainly cause anterior corneal surface changes in the 3-mm zone. There were no significant differences in posterior BFS over time, indicating that although

SLAK can change the posterior surface, it may have very little influence on corneal stability.

A recent study considered that anterior and posterior elevations were effective indicators for KC diagnosis[36]. It is crucial to measure front and back corneal elevations to prevent corneal ectasia following refractive surgery[37]. Therefore, evaluating the movement of the anterior and posterior corneal surface will be meaningful when examining the effect of stromal thickening on the change in the corneal mechanics after SLAK. Previous studies have reported a forward shift in the posterior corneal surface after refractive surgeries such as PRK, LASIK or SMILE, or CXL for KC[34,38-40], but little is known after SLAK combined with or without CXL. Although progression determinants for KC before CXL have been established, less is known about the corneal morphological changes after SLAK combined with CXL. Theoretically, with a lenticule being implanted in the interface of the cornea, this technique would induce changes in both the anterior and posterior corneal surfaces. However, in our study, our results indicated that the morphological changes occurred mainly in the front corneal surface related to keratometry and elevation values; the posterior elevation consistently remained stable, even had a slight backward shift trend from 1mo to 3mo than that preoperatively. It was hard to explain why only some points had the backward shift trend while some did not. For the front corneal surface, it seemed the central and peri-central parts changed significantly, while for the back corneal surface, we did not find a similar rule. We assume that the small sample size and the location of myopic lenticule may be the reasons.

Our study aimed to observe the response of the corneal surface changes using SLAK combined with CXL. The major limitations of our study include the small sample size and the short follow-up time. We need a longer follow-up period and more sensitive biomechanical parameters to evaluate its efficacy in halting the progression of KC. Another limitation is the myopic shape of the lenticule obtained from the donor patient, which may increase the corneal power after surgery. In the future, studies on customized lenticule implantation will be necessary to confirm the long-term benefits of this surgical technique. Other limitations included the differences in the thickness of the lenticules extracted from donors. Also, the astigmatic correction is low and performed only in limited donor eyes. Notwithstanding the limitations mentioned above, this study does suggest that convex-shaped stromal lenticule addition keratoplasty combined with CXL has the potential to stabilize corneal morphology in KC. It could open a new path to treat severe KC, reducing the need for conventional keratoplasties.

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