Contact Lens & Anterior Eye 38 (2015) 334–338

Contents lists available at ScienceDirect

Contact Lens & Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Short-term and long-term effects of small incision lenticule extraction (SMILE) on corneal endothelial cells

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ARTICLE INFO

Article history:
Received 27 October 2014
Received in revised form 23 February 2015
Accepted 28 March 2015

Keywords:
Small incision lenticule extraction
Corneal endothelium
Femtosecond laser

ABSTRACT

Purpose: Small incision lenticule extraction (SMILE) is being used increasingly as a novel approach to correct refractive errors with femtosecond laser. The study was aimed to investigate the corneal endothelial changes 1 day (short term) and 1 year (long term) after SMILE procedure.
Methods: In this prospective study, a total of 56 eyes of 30 patients with myopia ranging from −3.25 to −8.25 diopters (D) and cylinder up to −3.50 D were treated by SMILE. Postoperative uncorrected distance visual acuity (UDVA) and complications were assessed. Endothelial cell density (ECD), the coefficient of variation (CV), and the percentage of hexagonal cells were measured using a noncontact specular microscope preoperatively and at 1 day and 1 year postoperatively. The estimated residual stromal thickness (RST) of each patient was recorded.
Results: The median UDVA improved significantly from 1.00 log MAR preoperatively to −0.10 log MAR both at 1 day and 1 year ($p < 0.001$). No eyes developed corneal edema or other complications during the follow-up period. There were no significant changes in the ECD, CV or the percentage of hexagonal cells at any visit point (all $p > 0.05$). The mean estimated RST was 355.1 ± 32.2 μm (range 290–429 μm). Endothelial cell changes in terms of ECD, CV or the percentage of hexagonal cells were not correlated with the estimated RST ($p > 0.05$).
Conclusions: SMILE yielded improvement in visual acuity and no adverse effects to corneal endothelial cells were found. However, further studies with a lower preoperative ECD and deeper lenticule extraction are needed to conduct.

1. Introduction

The corneal endothelium, known as a tissue incapable of proliferation in vivo, is of vital importance in maintaining the health and clarity of the cornea [1]. Severe corneal endothelial damage may lead to the onset of corneal edema or corneal decompensation. Several anterior segment procedures, such as cataract surgery and Descemet stripping automated endothelial keratoplasty (DSAEK), have been reported to lower endothelial cell density (ECD). Advancements in ophthalmology allow many manual steps of surgical procedures to be replaced with a femtosecond laser. Studies provided evidence that femtosecond-assisted cataract surgery and DSAEK can cause similar or less endothelial cell loss compared with conventional surgery [2–4].

Recently, an alternative application of femtosecond laser in ophthalmology is small incision lenticule extraction (SMILE). SMILE is a procedure used to correct myopia and myopic astigmatism, only utilizing a femtosecond laser to make an intrastromal lenticule, after which the lenticule is extracted through a small incision. Promising clinical results have been reported [5–8]. However, to the best of our knowledge, the effect of SMILE on corneal endothelial cells has not been investigated. There are some concerns that should be considered. Firstly, additional thickness of 10–15 μm is added to the base of the whole lenticule for manipulation purposes. As a result, the dissection plane in the cornea is closer to corneal endothelium in SMILE than in femtosecond-assisted laser in situ keratomileusis (LASIK). Moreover, eyes undergoing SMILE have to experience almost twice the duration of suction compared with the eyes that underwent femtosecond-assisted LASIK, which may cause a disturbance to corneal endothelium. Lastly, most patients are young adults who have to stand the stress

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http://dx.doi.org/10.1016/j.clae.2015.03.011
1367-0484/

to corneal endothelium throughout their lives, and SMILE is an elective surgery. Thus, patients should be informed whether they are at risk for endothelial damage after SMILE.

The purpose of this study was to prospectively investigate corneal endothelial changes with respect to ECD, the coefficient of variation (CV) and the percentage of hexagonal cells after SMILE. Furthermore, whether estimated residual stromal thickness (RST) can predict endothelial cell changes after SMILE was also discussed.

2. Methods

2.1. Subjects

In this prospective study, 30 patients (56 eyes) were treated at Tianjin Eye Hospital, Tianjin Medical University, China, from 2011 to 2012. The study was conducted with the approval from the Ethics Committee of Tianjin Eye Hospital. Informed consent in accordance with the tenets of the Declaration of Helsinki was obtained from each patient after a thorough discussion of the benefits and known risks of the procedure.

All patients were at least 18 years of age, had a stable refraction change less than 0.50 diopters (D) for the previous 2 years, and a corrected distance visual acuity (CDVA) of 20/25 or better (0.1 log MAR or better). The use of soft contact lens and rigid contact lens had to be discontinued for at least 2 weeks and 3 weeks, respectively, prior to surgery. Preoperatively, patients had a complete ophthalmologic examination including uncorrected distance visual acuity (UDVA), CDVA, manifest and cycloplegic refractions, intraocular pressure (IOP), topography, endothelial cell analysis, slit-lamp microscopy, and dilated indirect funduscopy.

Exclusion criteria were active anterior segment disease, prior ocular trauma or surgery, an IOP greater than 21 mm Hg, diagnosed autoimmune disease, systemic connective tissue disease or atopic syndrome, and corneal topographic findings suspicious for keratoconus.

2.2. Surgical technique

The same experienced surgeon performed all surgeries using the VisuMax femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) system with a 500 kHz repetition rate. All surgeries were performed under topical anesthesia using 3 drops of oxybuprocaine hydrochloride 0.4% (Benoxil, Santen, Osaka, Japan) installed 3 min before surgery.

An S-type curved interface cone was used for each eye. The patient was asked to stare at the blinking light when the eye came close to the contact glass. After perfect centration and suction, the lenticule was created by following four steps: the posterior surface of the lenticule (with spiral-in pattern) was made, side cut of the lenticule was performed, the anterior surface of the lenticule (with spiral-out pattern) was created, and side cut of the incision was made. Once the laser sequence was finished, the suction switched off automatically. The surgeon separated the lenticule from the cornea with a lenticule dissector under the microscope and extracted the lenticule from within the cornea through the small incision. Topical ofloxacin 0.3% (Tarivid, Santen, Osaka, Japan) combined with ketorolac tromethamine 0.5% ophthalmic solution (Acular, Allergan, Irvine, Calif.) was applied immediately after surgery.

All lenticules were created using an expert pattern with the single small incision located in the superior position, a side-cut incision angle of 90°, and an incision width of 3.0–5.0 mm. In all cases, the predicted cap thickness was 110 μm and the diameter of the optical zone was 6.0 mm. The 360° side cut of the lenticule was made with angle of 90°, which was vertical to the anterior surface of the lenticule. The minimum thickness of the lenticule for manipulation purposes was set at 15 μm. The femtosecond laser energy used during all procedures was 115 nJ. The track spacing and spot spacing were between 2.0 and 3.0 μm. At the end of surgery, the estimated RST of each patient was recorded.

After surgery, topical ofloxacin 0.3% (Tarivid) was applied 4 times per day for 3 days, and fluorometholone 0.1% (Flumetholon, Santen) was used 4 times daily with a taper over 2 weeks.

2.3. Endothelial measurements

The corneal endothelial cells were assessed using a non-contact specular microscope (SP-3000P, Topcon, Tokyo, Japan) before, 1 day and 1 year after SMILE. All examinations were performed by the same technician and with the same equipment. All images were subjected to a fully automated analysis with analysis software (IMAGEnet 2000, Topcon). To achieve acceptable reliability in measurement of endothelial cell indices, images with at least 75 cells were selected at the time of measurement [9]. The parameters used for analysis included endothelial cell density (ECD), the coefficient of variation (CV) of the cell area (standard deviation divided by the mean), and the percentage of hexagonal cells. The postoperative ECD was calculated with the following formula according to previous reports [10,11]: $ECD_t = [1 + (t_2 \times K_2/n_c)]/[1 + (t_1 \times K_1/n_c)]^2 \times ECD_m$, where ECD_t and ECD_m refer to the true value and the measured value of postoperative ECD, respectively, t_1 and t_2 are the central corneal thickness (CCT) preoperatively and postoperatively, K_1 and K_2 are the keratometry (K) of the anterior surface of cornea before and after surgery, and the refractive index of cornea is $n_c = 1.376$. CCT and K values used for postoperative ECD modification were provided by topographic measurements performed with a Scheimpflug imaging system (Pentacam, Oculus, Wetzlar, Germany).

2.4. Statistical analysis

Statistical analysis was performed with SPSS 13.0 software (SPSS Inc, Chicago, Ill.). The normality was confirmed first with the Shapiro–Wilk test. Repeated-measurements analysis of variance was used to compare the changes in endothelial cell parameters over time after performing a Mauchly's test of sphericity. Greenhouse–Geisser correction factor was applied if the data did not meet the sphericity assumption. The differences between two time points were assessed using the paired t test or the Wilcoxon signed-rank test. Correlations between parameters were determined using the Pearson or Spearman correlation coefficient. Statistical significance was considered at $p < 0.05$.

3. Results

The study enrolled 56 eyes of 30 patients (11 men, 19 women). The mean age of the patients was 26.4 ± 5.7 years (range 18–40 years). The preoperative characteristics of the subjects are detailed in Table 1.

Table 1
Preoperative patient characteristics.

Parameters	Mean ± SD	Range
Sphere (D)	−5.0 ± 1.2	−3.25 to −8.25
Cylinder (D)	−0.9 ± 0.9	0.00 to −3.50
MRSE (D)	−5.5 ± 1.1	−3.50 to −8.25
Mean K	43.7 ± 1.1	41.8–46.3
Preoperative CCT (μm)	557.3 ± 24.6	515–614
Estimated RST (μm)	355.1 ± 32.2	290–429

MRSE = manifest refraction spherical equivalent; K = keratometry; CCT = central corneal thickness; RST = residual stromal thickness.