• Clinical Research •

Visual outcomes after three different surgical procedures for correction of refractive error in patients with thin corneas

Hye Seong Hwang[1], Hyun Jeong Lee[2], Seong Jun Lee[3], Jae-Hyung Kim[4]

[1]Department of Ophthalmology, Chungbuk National University, Cheongju, Chunbguk 28644, Republic of Korea
[2]Korean Minjok Leadership Academy, Hoengseong, Gangwon 25268, Republic of Korea
[3]Nuri Eye Clinic, Daejeon 35234, Republic of Korea
[4]Seoul Daabom Eye Center, Cheoungju, Chungbuk 28644, Republic of Korea
Correspondence to: Jae-Hyung Kim. Seoul Daabom Eye Center, Cheoungju, Chungbuk 28644, Republic of Korea. jkim@daabom.com
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Abstract

● **AIM:** To investigate and compare the visual and refractive outcomes of small incision lenticule extraction (SMILE), laser assisted sub-epithelial keratomileusis (LASEK), and LASEK combined with corneal collagen cross-linking (LASEK-CXL) surgery in patients with less than 500 μm of central corneal thickness (CCT).

● **METHODS:** The retrospective medical records review was conducted on the patients with CCT less than 500 μm treated with SMILE, LASEK, and LASEK-CXL. There was a total of 172 eyes, 76 eyes were in the SMILE group, 53 eyes in the LASEK group, and 43 eyes in the LASEK-CXL group. Uncorrected distance visual acuity (UDVA), spherical equivalent refraction (SE), and corneal haze were followed up in the three groups for 12mo.

● **RESULTS:** At 12mo postoperatively, there were no statistically significant differences in UDVA and in the absolute value of SE between the three groups. The predictability within ±0.50 D in the SMILE group (85.5%) was significantly higher than in both the LASEK group (64.2%, *P*<0.01) and the LASEK-CXL group (69.8%, *P*=0.04). The efficacy index and safety index were not significantly different among the three groups. Corneal haze at 12mo postoperatively was higher in the LASEK-CXL group (27.9%) than in the SMILE group (2.6%, *P*<0.01) and in the LASEK group (7.5%, *P*<0.01).

● **CONCLUSION:** In patients with CCT less than 500 μm, SMILE, LASEK, and LASEK-CXL appear to be effective for myopic correction. Among them, SMILE surgery shows the highest predictability.

● **KEYWORDS:** small incision lenticule extraction; thin cornea; laser assisted sub-epithelial keratomileusis; collagen-cross linking; visual acuity; myopia

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INTRODUCTION

Laser-assisted *in situ* keratomileusis (LASIK) is effective for the correction of myopia and has excellent refractive correction ability[1]. However, there is a risk of ectasia in patients with thin corneas because of insufficient residual cornea after surgery[2-3]. Therefore, if the central corneal thickness (CCT) is less than 490 to 460 μm, it is a relative contraindication of LASIK[4-5].

Prior to performing corneal refractive surgery in thin corneas, the main concern is not the corneal thickness itself, but rather changes of postoperative corneal biomechanics. However, little is known about which refractive surgery is more adequate for insufficient corneal thickness. Laser-assisted sub-epithelial keratectomy (LASEK) is a widely used treatment for patients who are unable to undergo LASIK[6]. Femtosecond laser small-incision lenticule extraction (SMILE) is another option for thin corneas. It has less biochemical impact than surface ablation or LASIK[7-8]. LASEK with prophylactic collagen cross-linking (LASEK-CXL) is another options for eyes with thin residual stroma, which increases the biochemical stability of the cornea[9]. It is difficult to determine what type of refractive surgery to perform in patients with thin corneas. Therefore, we aimed to investigate and compare the predictability, efficacy and complications of SMILE, LASEK, and LASEK-CXL in patients with less than 500 μm of CCT.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the Institutional Review Board of Chungbuk National University Hospital and followed the tenets of the Declaration of Helsinki.

This retrospective medical record reviewing research involved no more than minimal risk to the subjects. Therefore, the IRB gave exemption of the requirement for obtaining informed consent.

Study Population Retrospective review was conducted on the patients who received LASEK, SMILE, or LASEK-CXL at the Nuri Eye Ophthalmology Clinic, Daejeon, South Korea between November 2012 and September 2016.

Inclusion criteria included: 1) 18 years of age or older; 2) no other previous ocular surgery; 3) no present or past ocular pathology; 4) CCT thinner than 500 μm; 5) minimum corneal thickness of 460 μm with minimum estimated residual stromal bed (RSB; except cap) of 250 μm after SMILE, or of 320 μm after LASEK.

Exclusion criteria included: 1) the presence of residual, recurrent, or active ocular disease such as uveitis, retinal disorder, severe dry eye, or significant cataracts; 2) patients with topographic evidence of forme fruste keratoconus; 3) patients with a history of ocular surgery or systemic collagen vascular disease.

The ectasia risk factor score was also calculated based on the system proposed by Randleman, which took topographic pattern, age, CCT, RSB thickness, and spherical equivalent refraction (SE) into consideration[10]. The additional option of collagen cross-linking (CXL) was offered to patients with a higher ectasia risk score.

Surgical Procedures The type of surgery was determined according to the preference of the patient who satisfied the inclusion criteria. Optic zone was changed based on clinical parameters, including manifest refraction, pachymetry, expected RSB and pupil size. All surgical procedures were performed by a single experienced surgeon (Lee SJ). Before the procedure, patients underwent topical anesthesia, standard sterile draping, and speculum insertion.

SMILE was performed using a VisuMax® femtosecond laser (Carl Zeiss Meditec AG, Jena, Germany) with a repetition rate of 500 kHz and set to be from 110 to 140 nJ pulse energy and more than 6.0 mm lenticule diameter. Following a previously published surgical procedure[11], 2.0 mm of single side cut was made in the superior position. After the cutting procedure, the lenticule was dissected and manually removed through a side cut.

LASEK was performed by excimer laser ablation with a Mel-90 excimer laser (Carl Zeiss Meditec AG, Jena, Germany) using the aspheric aberration-free profiles, 250 Hz FLEXIQUENCE function and Triple-A Advanced Ablation Algorithm after the central 9.0 mm epithelium was removed using a surgical brush (Hyperopic Amoils Epithelial Scrubber, Innovative Excimer Solutions, Inc.). LASEK was also performed in an optical zone greater than 6.0 mm, and finished with mitomycin-C (MMC) 0.02% application for 15s, after which the MMC was copiously washed out of the eye.

LASEK-CXL was performed with the same protocol as LASEK. No adjustment was made to the excimer laser treatment nomogram to account for CXL, which was performed immediately following stromal ablation. For the CXL, the stromal bed was coated with Vibex Xtra (Avedro, Inc., Waltham, MA, USA) consisting of 0.25% riboflavin (saline, isotonic solution), soaked for 90s, and thoroughly irrigated with a balanced salt solution. After stromal soaking, a UVA fluence of 30 mW/cm^2 was applied for 90s (total energy, 2.7 J/cm^2) using the KXL® CXL system (Avedro, Inc., Waltham, MA, USA).

To compensate for possible torsional movements with the patient supine on the surgical bed, all of the eyes in the three groups were marked preoperatively along the horizontal meridian at the limbus at 3 and 9 o'clock with the patient seated at the slitlamp.

After small incision lenticule extraction, the postoperative regimen included topical levofloxacin (Levocle®, Hanlim, Seoul, South Korea), given 4 times daily for 1wk, and topical loteprednol (Lotemax®, Bausch & Lomb, Tampa, FL, USA), given 4 times a day for a week and the dosage was gradually reduced over 1mo.

After LASEK and LASEK-CXL, a bandage contact lens (Acuve Oasys, Johnson & Johnson Vision Care, Inc., USA) was applied to the cornea for 7d until epithelial healing was complete and then topical levofloxacin applied 4 times daily for 1wk, and topical loteprednol applied 4 times a day for 1wk and then changed to fluormetholone 0.1%, it was applied 4 times a day for 1mo and the dosage was gradually reduced over 3mo.

Preoperative and Postoperative Assessments Before surgery and at 1, 3, 6, and 12mo postoperatively, all patients had a detailed ophthalmologic examination that included evaluation of logMAR uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA), manifest refraction, slit lamp examination (Takagi SM-90N), intraocular pressure measurement (noncontact tonometer, NT-530, NCT Nidek Co., Ltd. Japan), pupil size (Colvard, Oasis Medical), Scheimpflug-based corneal topography (Pentacam, Oculus, GmbH), and indirect fundoscopy.

Corneal wavefront aberrations were measured using the Keratron Scout (Optikon 2000 SpA). Optical errors centered on the line-of-sight, representing the wavefront aberration, were recorded as Zernike polynomials and as the coefficients in the Optical Society of America standards[12]. The errors were analyzed for a 6.0 mm diameter. Changes in corneal wavefront aberration were determined using the mean values and preoperative to postoperative differences in the 16 higher-order aberration (HOA) modes of the Zernike expansion to the 7^{th} order.

Table 1 The characteristics and preoperative data of patients

Characteristics	SMILE (*n*=76)	LASEK (*n*=53)	LASEK-CXL (*n*=43)	*P*
Age (y)	29.09±6.58	27.26±6.19	30.16±8.15	0.11
Male:female	26:44	14:28	11:30	0.43
SE	-5.30±1.92	-5.06±1.30	-5.73±1.75	0.16
CDVA (logMAR)	0.01±0.04	0.01±0.02	0.01±0.03	0.81
Astigmatism (D)	1.10±0.69	1.35±1.08	1.49±0.90	0.05
CCT (μm)	491.51±7.07	488.32±11.10	473.21±15.70	<0.01
ECD (cells/mm^2)	2852.07±314.38	2894.43±258.38	2855.28±345.89	0.72
Scotopic pupil diameter (mm)	7.19±0.89	7.23±0.69	7.34±0.74	0.62
Optic zone (mm)	6.44±0.29	6.52±0.27	6.20±0.41	<0.01
Total ablation zone (mm)	7.44±0.27	8.00±0.31	7.58±0.33	<0.01
Expected ablation depth (μm)	100.26±19.55	84.00±17.57	81.70±17.70	<0.01
PTA (%)	30.57±3.95	27.43±3.44	27.80±3.38	<0.01

SMILE: Small incision lenticule extraction; LASEK: Laser assisted sub-epithelial keratomileusis; LASEK-CXL: LASEK combined with corneal collagen crosslinking; SE: Spherical equivalent; CDVA: Corrected distance visual acuity; CCT: Central corneal thickness; ECD: Endothelial cell density; PTA: Percentage of tissue altered.

Corneal haze grade was evaluated using slit-lamp bimicroscopy based on Fantes grading[13]. The CCT was measured with an ultrasound pachymeter (Pocket-II, Quantel Medical, Paris, France) by similarly experienced technicians. After five consecutive measurements were taken, minimum value was recorded. Corneal endothelial cell density (ECD) was analyzed by specular microscopy (SP3000P, Topcon Corp, Tokyo, Japan).

The percentage of tissue altered (PTA), which is known as a predictor of postoperative iatrogenc keatectasia, was calculated by dividing the flap thickness (μm) plus ablation depth (μm) by the CCT (μm) in the LASIK[14]. Since SMILE and LASEK use flapless technique, we calculated the PTA by dividing the expected ablation depth plus expected mean central epithelial thickness (50 μm) by the CCT in the three groups[15]. The efficacy index was calculated by dividing postoperative 12mo UDVA by preoperative CDVA. The safety index was calculated by dividing postoperative 12mo CDVA by preoperative CDVA. Predictability represents the proportion of postoperative SE within 0.5 or 1.0 diopters (D). These indices were calculated using data measured at 12mo postoperatively.

Statistical Analysis SPSS version 22.0 software (SPSS, Inc., Chicago, IL, USA) was used to perform the statistical analysis and $P<0.05$ was considered statistically significant. Means for continuous variables were analyzed using one-way ANOVA test and Bonferroni post-hoc test was utilized when ANOVA results had a $P<0.05$. Differences in proportions between groups were tested using Chi-square test adjusted by Bonferroni correction. The statistical program G*Power 3.1.2 (Franz Faul, University Kiel, Germany) was used to ascertain which sample size was sufficient over an ANOVA. A total sample size of $n=43$ was found to be sufficient for the power (1-β) of 0.95, effect size 0.51, actual power 0.95.

RESULTS

A total of 172 eyes were included. Totally 76 eyes were in the SMILE group, 53 eyes in the LASEK group, and 43 eyes in the LASEK-CXL group. Patient demographics and preoperative data are presented in Table 1. There were no significant differences in age, sex, SE, astigmatism, ECD, scotopic pupil diameter or CDVA among the 3 groups. The LASEK-CXL group had a lower CCT than both the SMILE and LASEK groups, but there were no significant differences between the SMILE and LASEK groups. The optic zone was smaller in the LASEK-CXL group than in the other two groups, and the diameter of the total ablation zone was in the order of LASEK, LASEK-CXL and SMILE groups. The expected ablation depth in the SMILE group was thicker than the other two groups. Also, the PTA in the SMILE group (30.57%) was higher than the other two groups.

Postoperative Visual Outcomes Table 2 shows that the SMILE group had a lower SE (0.39±0.37 D) than the LASEK group (0.58±0.47 D) at 12mo postoperatively ($P=0.04$, Bonferroni post-hoc test), but there were no statistically significant differences between the SMILE and LASEK-CXL groups, or the LASEK and LASEK-CXL groups. Also, the examinations for astigmatism showed that there were no significant differences between the three groups at 12mo postoperatively.

The UDVA and the best CDVA at 12mo postoperatively are shown in Figure 1A and 1B. All three groups exhibited similar visual acuity results. In the SMILE group, 89.5% of eyes had a postoperative UDVA of 20/25 or better and 98.7% had a postoperative CDVA of 20/40 or better. In the LASEK group, 90.6% had a postoperative UDVA of 20/25 or better and 100% had a postoperative CDVA of 20/40 or better. In the LASEK-

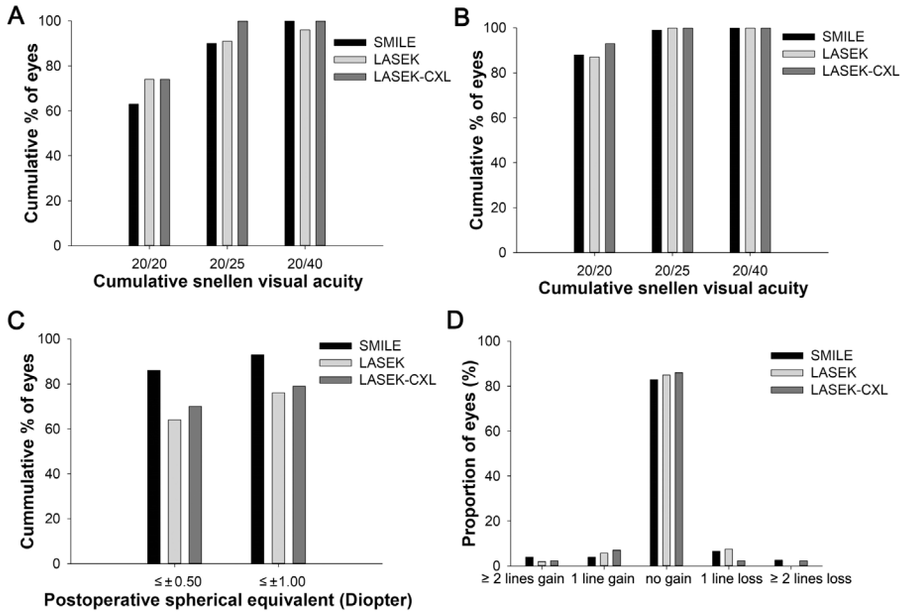

Figure 1 Postoperative distance visual acuity in the three (SMILE, LASEK, and LASEK-CXL) groups at 12mo postoperatively A: Uncorrected visual acuity; B: Best corrected visual acuity; C: Postoperative SE in the three groups 12mo postoperatively; D: Difference between preoperative and postoperative best corrected visual acuity.

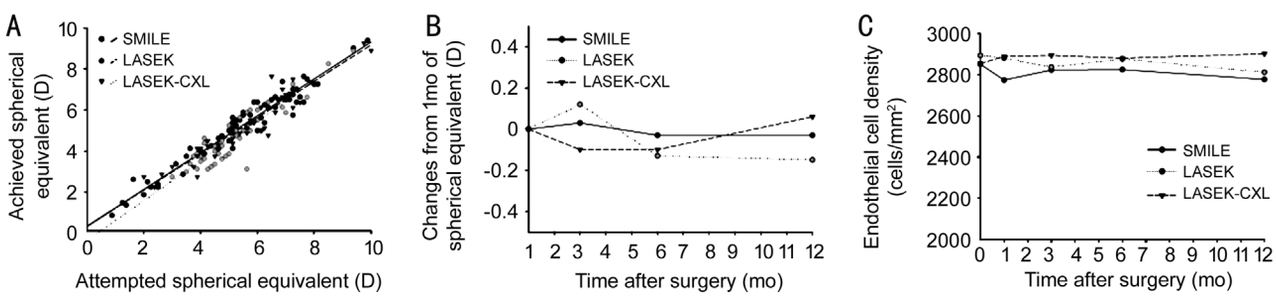

Figure 2 Postoperative spherical equivalent and endothelial cell density in the three (SMILE, LASEK, and LASEK-CXL) groups for 12mo postoperatively A: The correlation between the attempted correction and achieved correction measured at 12mo postoperatively in the SMILE, LASEK and LASEK-CXL groups; B: Changes from 1mo of manifested SE for the three groups, expressed in diopters, up to 12mo postoperatively; C: Postoperative ECD in the three groups 12mo postoperatively.

CXL group, 100% had a postoperative UDVA of 20/25 or better.

The predictability results at 12mo postoperatively were presented in Figure 1C. The predictability within ±0.50 D in the SMILE group (85.5%) was significantly higher than in the LASEK group (64.2%, $P<0.01$) and in the LASEK-CXL group (69.8%, $P=0.04$). Also, the predictability within ±1.00 D in the SMILE group (93.4%) was significantly higher than in the LASEK group (75.5%, $P<0.01$) and in the LASEK-CXL group (79.1%, $P=0.02$). Figure 2A shows the correlation between the attempted correction and achieved correction measured at 12mo postoperatively using a scatter plot. The scatter plot demonstrated that achieved SE at postoperatively 12mo were well correlated with attempted SE in the SMILE, LASEK, and LASEK-CXL groups, respectively. Figure 2B shows the change in SE after surgery. Changes in SEQ from 1 to 3mo were +0.03±0.40 D, +0.12±0.76 D, and -0.10±0.52 D in the SMILE, LASEK, and LASEK-CXL groups, respectively.

Table 2 Postoperative refractive outcomes (the averages of absolute value of SE)

Follow-up	SMILE (n=76)	LASEK (n=53)	LASEK-CXL (n=43)	P
1mo				
SE	0.39±0.32	0.74±0.67	0.63±0.41	<0.01
Cyl	0.38±0.29	0.75±0.79	0.64±0.42	<0.01
3mo				
SE	0.28±0.33	0.41±0.43	0.58±0.37	<0.01
Cyl	0.31±0.33	0.37±0.48	0.52±0.33	0.02
6mo				
SE	0.38±0.38	0.55±0.63	0.61±0.47	0.03
Cyl	0.39±0.36	0.42±0.53	0.40±0.35	0.86
12mo				
SE	0.39±0.37	0.58±0.47	0.53±0.42	0.03
Cyl	0.44±0.35	0.38±0.51	0.37±0.30	0.55

SMILE: Small incision lenticule extraction; LASEK: Laser assisted sub-epithelial keratomileusis; LASEK-CXL: LASEK combined with corneal collagen crosslinking. SE: Spherical equivalent; Cyl: Cylinder.

Table 3 Corneal HOA at preoperative and 12mo postoperatively

Items	Preoperative				12mo postoperatively			
	SMILE (*n*=57)	LASEK (*n*=15)	LASEK-CXL (*n*=17)	*P*	SMILE (*n*=76)	LASEK (*n*=53)	LASEK-CXL (*n*=43)	*P*
HOA-RMS	0.43±0.14	0.52±0.24	0.48±0.12	0.14	0.63±0.20	0.80±0.30	0.83±0.23	<0.01*
Total 3rd order	0.32±0.16	0.32±0.12	0.33±0.14	0.97	0.42±0.17	0.47±0.29	0.46±0.18	0.37
Coma	0.25±0.13	0.27±0.12	0.31±0.13	0.31	0.35±0.18	0.40±0.26	0.42±0.15	0.12
Trefoil	0.16±0.10	0.15±0.09	0.14±0.09	0.71	0.20±0.11	0.21±0.15	0.15±0.12	0.05
Total 4th order	0.26±0.08	0.31±0.11	0.29±0.07	0.12	0.37±0.15	0.53±0.23	0.58±0.22	<0.01*
Spherical aberration	0.23±0.09	0.29±0.11	0.26±0.09	0.11	0.33±0.16	0.48±0.20	0.53±0.19	<0.01*
Secondary astigmatism	0.07±0.05	0.08±0.04	0.08±0.05	0.63	0.13±0.07	0.16±0.14	0.15±0.09	0.34
Quadra foil	0.06±0.04	0.08±0.04	0.09±0.04	0.90	0.07±0.04	0.09±0.10	0.08±0.04	0.08

SMILE: Small incision lenticule extraction; LASEK: Laser assisted sub-epithelial keratomileusis; LASEK-CXL: LASEK combined with corneal collagen crosslinking; HOA-RMS: Higher-order aberration root mean square.

Changes in SE from 1 to 6mo were -0.03±0.41 D, -0.13±0.73 D, and -0.10±0.48 D in the SMILE, LASEK, and LASEK-CXL groups, respectively. Changes in SE from 1 to 12mo were -0.03±0.42 D, -0.15±1.05 D, and +0.06±0.72 D in the SMILE, LASEK, and LASEK-CXL groups, respectively. The LASEK group had the highest SE change, but there were no significant differences between three groups.

In the comparison of preoperative CDVA with CDVA at 12mo postoperatively, the proportions of CDVA loss were 9.2%, 7.5% and 4.7% in the SMILE, LASEK, and LASEK-CXL groups, respectively (Figure 1D) and there were no significant differences between the three groups (P=0.67). The efficacy index was 0.95±0.15, 0.95±0.17, and 0.99±0.09 in the SMILE, LASEK, and LASEK-CXL groups, respectively and there were no significant differences among the three groups (P=0.29). The safety index was 1.01±0.10, 1.00±0.06, and 1.01±0.08 in the SMILE, LASEK, and LASEK-CXL groups, respectively and there were no significant differences among the three groups (P=0.93).

Complications Figure 2C shows that postoperative ECD did not decrease during the 12mo follow up period. The incidence of corneal haze at 12mo postoperatively was higher in the LASEK-CXL group (27.9%) than in the SMILE group (2.6%, P<0.01) and the LASEK group (7.5%, P<0.01). Postoperative ectasia did not occur in the SMILE and LASEK-CXL groups in 12mo, but occurred in 1 case (1.9%) of the LASEK group.

This is a case of iatrogenic corneal ectasia in a 21-year-old man following LASEK. The preoperative refractive error was -3.00 Dsph/-3.50 Dcyl ×180° in the right eye, the CDVA was 20/20 in the right eye. The preoperative corneal topography was normal, with a minimum corneal thickness of 499 μm in the right eye. The expected ablation depth in the right eye was 94 μm. The immediate postoperative course was uneventful, with an UDVA of 20/20 in the right eye at the 1-month examination. This was maintained for 6mo. Nine months after LASEK, the patient presented with early signs of ectasia in the right eye on corneal topography, which had worsened in at the 12-month examination. At 12mo after LASEK, the manifest refraction was +0.25 Dsph/-2.75 Dcyl ×95° in the right eye, correcting to 20/25. The cornea was clear on slit lamp examination. Scheimpflug-based corneal topography was performed and difference maps (preoperative and postoperative) were evaluated. There was an obvious increase in the inferior steepening on the sagittal maps in right eyes (maximum K, 50.1 D) associated with asymmetric bowtie pattern with skewed axes.

The preoperative HOA results were not different in the three groups. Also, HOA at postoperative 12mo showed similar results in the three groups. However, higher-order aberration root mean square (HOA-RMS), total 4th order and spherical aberration in the SMILE group were lower than in the LASEK-CXL and LASEK groups, but there were no differences between the LASEK and the LASEK-CXL groups (Table 3).

DISCUSSION

In this study, we investigated and compared the visual and refractive outcomes of SMILE, LASEK, and LASEK-CXL in patients with less than 500 μm of CCT. At 12mo postoperatively, the predictability within ±0.50 D in the SMILE group (85.5%) was significantly higher than in both the LASEK group (64.2%, P<0.01) and the LASEK-CXL group (69.8%, P=0.04). The efficacy index and safety index were not significantly different among the three groups.

One previous study showed good safety and efficacy at 10y of follow-up when photorefractive keratectomy (PRK) and LASEK were performed in patients with CCT less than 500 μm, and showed stable visual and refractive results[16]. Another previous study reported the results of LASEK in patients with less than 500 μm of CCT[6]. In that study, at 3mo after LASEK, 95.8% had UDVA of 20/40 or better, and 77.1% had UDVA of 20/20 or better. These results were similar to those of the three

groups in our study. Also, that study reported that 75% of the eyes had manifested SE within ±0.50 D, and 96% were within ±1.00 D. However, in our study, predictability within ±1.00 D in the LASEK group (75.5%) and LASEK-CXL group (79.1%) were significantly lower than in the SMILE group (93.4%). This suggests that SMILE may be relatively more predictive than the other two procedures.

Myopic regression rate after LASIK is known to be 5% to 27%[17]. Prophylactic CXL has been introduced as a way to prevent myopic regression[18-21]. In our study, the SE changes were similar in the LASEK-CXL and SMILE groups, and largest in the LASEK group between 1 and 12mo postoperatively, but there was no statistical difference among the three groups. This may be related to the relatively small number of participants in the study.

Although the incidence of postoperative ectasia is an extremely rare occurrence, corneal ectasia is one of the most serious complications after refractive surgery. Corneal ectasia may have very poor visual prognosis, is very difficult to manage, and serious cases may require penetrating keratoplasty[22]. It is known that flap creation and tissue removal during corneal ablation reduce the biomechanical properties of the cornea[23-24]. Recently, the PTA has been introduced to predict iatrogenic corneal ectasia that may occur after LASIK, and the risk may increase if it exceeds 40%[14-15]. Because SMILE or LASEK use the flapless technique, the PTA values were calculated as the expected mean central epithelial thickness (50 μm) plus expected ablation depth divided by the CCT. In this study, the SMILE group had an average PTA of 31%, the LASEK group 27%, and the LASEK-CXL group 28%. Theoretically, SMILE surgery is thought to have little effect on the biomechanical properties of the cornea because it uses a flapless technique and tissue subtraction[25]. Also, Kanellopoulos[18] reported that 43 cases of prophylactic CXL in high myopia patients did not develop any corneal ectasia during the 3.5y follow-up period. In our study, postoperative ectasia did not occur in the SMILE and LASEK-CXL groups and occurred in 1 case (2.38%) of the LASEK group.

Among the three procedures performed in this study, the possibility of endothelial cell damage is relatively high in CXL. It was known that endothelial cell damage may occur due to exposure of free radicals during CXL process[26]. However, according to a multicenter clinical trial, there was no change in endothelial count at 1y after CXL[27]. Also, several studies have shown that when 0.02% MMC was used in corneal surface excimer laser ablation, there was no corneal endothelial cell loss during the 3mo to 5y follow up period[28]. In our study, postoperative ECD did not decrease during the 12mo follow up period in all 3 groups.

There has been no consensus as to which refractory surgery has a lower risk of corneal haze. In our study, corneal haze at 12mo postoperatively was higher in the LASEK-CXL group than in the SMILE and LASEK groups. Haze after CXL is known to be caused by back scattered and reflected light reducing corneal transparency[29]. In a previous study, more than 90% of eyes had the clinical appearance of stromal haze on slit-lamp examination after CXL[30]. The occurrence of haze peaks at 1mo and decreases gradually, and it is known to become clear after 6mo. However, in most cases, treatment is not necessary, and in some cases, low dosage steroid medication was used[31].

HOAs are an important part of the quality of vision. There is an increase in HOAs after refractive surgery, especially spherical aberrations are known to have a significant effect on night vision disturbance[32]. Yu *et al*[33] reported that the SMILE group had fewer HOAs, including spherical aberration, than the LASEK group at 3mo postoperatively in a study of mild to moderate myopia. In our study of cornea thickness less than 500 μm, HOAs at postoperative 12mo showed similar results in three groups. However, HOA-RMS, total 4th order and spherical aberration in the SMILE group were lower than in the LASEK and LASEK-CXL groups, but there were no differences between the LASEK and LASEK-CXL groups. The influence of wound healing on HOA had been nicely shown in an experimental cat model[34]. The same authors also showed that the loss of laser efficiency is a main culprit for the induction of spherical aberrations after corneal excimer laser surgery[35]. Postoperative wound healing responses and inflammatory infiltrations may be milder in SMILE surgery, and this may explain lower HOA inductions[36-37].

The strength of our study is that it is likely the first study of the visual outcome and prognosis of SMILE surgery for thin corneal thickness less than 500 μm. However, our present study also had some notable limitations that were inherent to its retrospective nature and the LASEK-CXL group had a lower CCT than the SMILE group and LASEK group. Also, the relatively small sample size and relatively short follow-up period of 12mo are limitations of this study. Therefore, a large-scale prospective design and long term follow-up period study will be needed.

In conclusion, SMILE, LASEK, and LASEK-CXL surgery appear to be effective for myopic correction in patients with thin corneas. However, SMILE provided significantly better refractive predictability than LASEK and was marginally better than LASEK-CXL which was marginally better than LASEK. Also, the SMILE group had fewer postoperative complications and less induction of some HOA compared with the LASEK and LASEK-CXL groups.

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