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The outcomes of first-generation (visumax 500) and second-generation (Visumax 800) keratorefractive lenticule extraction surgeries for astigmatism

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To evaluate the efficiency, predictability, and residual astigmatism between first- and second-generation keratorefractive lenticule extraction (KLEx) surgeries in a prominent astigmatism population. A retrospective cohort study was conducted, and individuals who underwent first- and second-generation KLEx surgeries were enrolled. A total of 31 and 35 eyes were categorized into first and second KLEx groups, respectively. Visual acuity, refraction, topographic parameters, and surgical indices were recorded. Independent t tests were used to compare the postoperative uncorrected distance visual acuity (UDVA), spherical equivalent (SE), and residual astigmatism between the two groups. The difference in UDVA was not significant three months after KLEx surgery ($P = 0.509$), and the SEs three months after surgery also presented similar values between the two groups ($P = 0.552$). The first KLEx group demonstrated greater residual astigmatism than did the second KLEx group throughout the three-month follow-up period (all $P < 0.05$). The values of surgically induced astigmatism (SIA), difference vector (DV), magnitude of error (ME) and correction index (CoI) were significantly better in the second KLEx group via vector analysis (all $P < 0.05$). Old age, high steep keratometry (K), high topographic cylinder, large angle kappa, and a small optic zone were correlated with greater residual astigmatism in the first KLEx group (all $P < 0.05$), whereas only a small optic zone was significantly correlated with greater residual astigmatism in the second KLEx group ($P = 0.047$). The second-generation KLEx is correlated with a lower risk of residual astigmatism.

Keywords Keratorefractive lenticule extraction, Visumax 800, SMILE pro, Uncorrected distance visual acuity, Astigmatism

Abbreviations

UDVA	Uncorrected distance visual acuity
KLEx	Keratorefractive lenticule extraction
D	Diopter
CDVA	Corrected distance visual acuity

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CCT	Central corneal thickness
K	Keratometry
RST	Residual stromal thickness
TIA	Target-induced astigmatism
SIA	Surgically induced astigmatism
DV	Difference vector
ME	Magnitude of error
AE	Angle of error
CoI	Correction index
aOR	Adjusted odds ratio
CI	95% confidence interval
N	Number
SD	Standard deviation

Keratorefractive surgeries have been applied to correct refractive errors such as myopia, hyperopia, and astigmatism for a long period of time[1,2]. Laser in situ keratomileusis and photorefractive keratectomy have been utilized for more than 10 years, and the visual outcomes of these two surgeries are acceptable[2]. Approximately 90% of individuals receive laser in situ keratomileusis, and 70% of individuals receive photorefractive keratectomy, which results in a postoperative uncorrected distance visual acuity (UDVA) of 20/20[3,4]. Nevertheless, postoperative complications such as significant corneal nerve damage, ocular pain, and postoperative dry eye disease have been reported in these two types of keratorefractive surgeries[5].

Keratorefractive lenticule extraction (KLEx), previously referred to as small-incision lenticule extraction[6], is a keratorefractive surgery that first became available in 2010 in which a corneal lenticule created by a femtosecond laser is removed from the corneal stroma[7–9]. Compared with laser in situ keratomileusis and photorefractive keratectomy, KLEx has the advantages of a small incision, which results in less postoperative dry eye disease[10,11]. In terms of surgical outcomes, first-generation KLEx is similar to both laser in situ keratomileusis and photorefractive keratectomy according to previous studies[12–15]. In addition, postoperative astigmatism and higher-order aberrations are similar between first-generation KLEx surgery and laser in situ keratomileusis, even though the wavefront-guided technique is not accessible in first-generation KLEx surgery[16,17].

In 2023, the second generation of KLEx surgery was made available by the same company that produced the first generation of KLEx surgery[18]. Compared with first-generation KLEx surgery, second-generation KLEx has the advantages of faster laser discharge velocity and an eye-tracking system[19,20]. Nevertheless, few studies have evaluated astigmatism correction between first- and second-generation KLEx surgeries in astigmatism populations. Because of the eye-tracking system in the second-generation KLEx device, the postoperative outcomes between the two surgeries in a prominent astigmatism population may differ.

Consequently, the purpose of this study was to survey visual and refractive outcomes between first- and second-generation KLEx surgeries in a prominent astigmatism population. Moreover, subgroup analysis according to the degree of astigmatism was conducted.

Materials and methods

Ethics declaration

All the maneuvers in this study obeyed the Declaration of Helsinki in 1964 and its late amendments. Furthermore, this study was approved by the Institutional Review Board of National Changhua University of Education (project code: NCUEREC-110-081). The essentiality of written informed consent was discarded by the Institutional Review Board because of the retrospective nature of this study and because we analyzed data from only existing medical records.

Individual selection

This retrospective cohort study was performed at the Nobel Eye Institute, which has more than 10 branches in the northern, central, and southern Taiwan areas. Individuals were enrolled if they (1) were aged 20 to 55 years, (2) presented cycloplegic sphere power greater than − 1.00 diopter (D) but lower than − 10.00 D for the first-generation KLEx surgery and lower than − 9.00 D for the second-generation KLEx surgery, (3) had cycloplegic cylinder power greater than − 1.5 D, (4) received first- or second-generation KLEx surgeries at the Nobel Eye Institute, and (5) were followed-up at any Nobel Eye Institute branch after KLEx surgery for more than three months. The rationale for the age criteria is that 20–55 years is an age interval in which the cornea does not grow prominently and cataracts do not develop frequently in Taiwanese individuals according to our clinical experience. The patients received first-generation KLEx surgery or second-generation KLEx surgery according to their choice after detailed consultation with ophthalmologists. If a patient underwent KLEx surgery with monovision (planning residual myopia) but the absolute myopia degree was higher than the inclusion criteria, the patient was excluded from this study. On the other hand, the following exclusion criteria were adopted to exclude individuals with poor preoperative status: (1) a corrected distance visual acuity (CDVA) worse than 20/40, (2) preexisting severe corneal or retinal diseases such as central corneal opacity, proliferative diabetic retinopathy, keratoconus, macula-off retinal detachment, and central retinal venous occlusion, (3) uncontrolled glaucoma or uveitis, (4) refraction alteration of more than 0.50 D in the last year, and (5) pregnancy status or breastfeeding in the last three months. We decided the eye to be enrolled in this study by drawing lots. After the selection of suitable cases according to the inclusion and exclusion criteria (the surgery type was decided by the patients after discussion with a physician), a total of 31 and 35 eyes were categorized into the first KLEx group and second KLEx group, respectively.

Surgical details

All the first-generation and second-generation KLEx surgeries in this study were performed by two experienced refractive specialists (C.-Y.L. and C.-K.C.). The first- and second-generation KLEx surgeries were performed via a first-generation femtosecond laser device (Visuamax 500, Carl Zeiss, Göschwitzer Str., Jena, Germany) and a second-generation femtosecond laser device (Visuamax 800, Carl Zeiss, Göschwitzer Str., Jena, Germany), respectively. For the first-generation KLEx surgery, the optic zone was set from 5.5 to 6.9 mm in accordance with the ablation depth and pupil size, and the corneal incision was set as 3.0 mm at 105 degrees. The energy setting of the first-generation KLEx surgery was 26, while the spot and track distances were 4.40 µm, 1.70 µm, 4.40 µm, and 1.70 µm for the lenticule interface, lenticule side cut, cap interface, and cap side cut/small incision, respectively. After the angle kappa was defined by a microscope with topography and the coaxial sighted corneal light reflex method, the whole cornea was fixed in a suction ring. After the femtosecond laser strike, a specific spatula was used to separate the upper and lower interfaces of the corneal lenticule, and then, the corneal lenticule was dragged out by forceps. With respect to the second-generation KLEx surgery, the surgical steps are generally identical to those of the first-generation KLEx surgery, except the angle kappa was presented by the software in Visumax 800, which is based on data obtained from optical biometry (IOL Master 700, Carl Zeiss, Göschwitzer Str., Jena, Germany). The energy setting of the second-generation KLEx surgery was 23, while the spot and track distances were 3.10 µm, 1.50 µm, 3.10 µm, and 1.50 µm for the lenticule interface, lenticule side cut, cap interface, and cap side cut/small incision, respectively. After the KLEx surgery, levofloxacin eye drops and prednisolone eye drops were applied for approximately one week and then changed to sulfamethoxazole and fluorometholone eye drops for another three weeks. Artificial tear was applied for at least two months after the KLEx surgery.

Ophthalmic examination

All the individuals who received KLEx surgery received identical ophthalmic exams in any branch of the Nobel Eye Institute. The preoperative examinations involved refraction CDVA, cycloplegic sphere power and cylinder power via an autorefractor (KR-8900, Topcon, Itabashi-ku, Tokyo, Japan), steep and flat keratometry (K), central corneal thickness (CCT) at the apex and thinnest parts, corneal astigmatism, angle kappa and pupil diameter via a topographic machine (TMS-5, Tomey Corporation, Nagoya, Aichi, Japan), and another angle kappa value via a biometry machine (IOL Master 700, Carl Zeiss, Göschwitzer Str., Jena, Germany). The postoperative examinations included UDVA and sphere and cylinder powers via manifest refraction. Postoperative examinations were performed via devices identical to those used for preoperative examinations. Surgical parameters, including the side-cut depth, cap thickness, optic zone, residual stromal thickness (RST), and lenticule thickness, were also obtained. The data before KLEx surgery, one day after KLEx surgery, one week after KLEx surgery, one month after KLEx surgery, and three months after KLEx surgery were collected. The spherical equivalent (SE) was determined as the sphere power plus half of the cylinder power in this study, and the angle kappa value for the second-generation KLEx surgery was defined as the average value of angle kappa from the topographic device and biometry machine.

Statistical analysis

SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analysis described in this study. The statistical power of the current study was 0.71, with an alpha value of 0.05 and a medium effect size, which was generated via G∗power version 3.1.9.2 (Heinrich Heine Universität at Düsseldorf, Germany). This served as the rationale for determining the number of eyes included in this study. The Shapiro–Wilk test was used to investigate the normality of the two study populations, and a normal distribution was obtained ($P > 0.05$). A descriptive analysis was performed to compare the age, sex, refraction status, topographic data, and surgical data between the two groups, and an independent t test was used to examine the differences in these factors between the two groups. Independent t tests were also used to assess the efficiency (i.e., UDVA), predictability (i.e., SE), and residual cylinder powers between the first KLEx group and the second KLEx group in the postoperative period. Vector analysis was performed according to the Alpins method of astigmatism analysis, and the data of cylinder power in the two groups three months postoperatively were included in the vector analysis. The vector analysis indexes including target-induced astigmatism (TIA), surgically induced astigmatism (SIA), difference vector (DV), magnitude of error (ME), angle of error (AE) and correction index (CoI) between the two groups were compared via independent t test. The TIA, SIA and DV were exhibited as arithmetic mean. With respect to the risk factors for high residual astigmatism (greater than −1.00 D three months postoperatively), the generalized estimate equation was used to examine the preoperative parameters mentioned earlier, and the adjusted odds ratio (aOR) with 95% confidence interval (CI) of each factor for greater residual astigmatism in the two groups was determined. A P value < 0.05 was designated as statistically significant, and a P value lower than 0.001 was designated as $P < 0.001$ in this study.

Results

The baseline features of the study population are illustrated in Table 1. The mean ages were 32.38 ± 7.73 and 33.37 ± 8.47 years in the first and second KLEx groups, respectively, which were not significantly different ($P = 0.625$). The sex and laterality distributions were also similar between the first and second KLEx groups (both $P > 0.05$). With respect to the preoperative parameters, nearly all the parameters were similar between the two groups (all $P > 0.05$), except that the first KLEx group had a higher steep K than the second KLEx group did (45.40 ± 1.76 versus 44.51 ± 1.51, $P = 0.030$) (Table 1).

One day after the KLEx surgery, the UDVA was significantly greater in the first KLEx group than in the second KLEx group ($P = 0.012$), whereas the difference in UDVA was not significant three months after the KLEx surgery ($P = 0.509$) (Table 2). The SE one day postoperatively was greater in the second KLEx group than in the first KLEx group ($P = 0.011$), whereas the SE three months postoperatively was similar between the two

Feature	First KLEx group (*N*: 31)	Second KLEx group (*N*: 35)	*P*
Age (mean ± SD)	32.38 ± 7.73	33.37 ± 8.47	0.625
Sex (male: female)	13:18	12:23	0.614
Laterality (right: left)	15:16	16:19	0.828
Disease			0.126
Hypertension	0	2	
Diabetes mellitus	0	2	
Heart disease	2	1	
Other	0	3	
CDVA (LogMAR)	0.01 ± 0.05	0.00 ± 0.02	0.280
Manifest refraction			
Sphere	− 4.90 ± 2.51	− 5.64 ± 2.25	0.212
Cylinder	− 1.77 ± 0.97	− 1.85 ± 1.12	0.771
SE	− 5.79 ± 2.72	− 6.57 ± 2.49	0.230
Cycloplegic refraction			
Sphere	− 4.75 ± 2.55	− 5.47 ± 2.19	0.221
Cylinder	− 1.79 ± 1.16	− 2.04 ± 0.96	0.352
SE	− 5.80 ± 2.60	− 6.56 ± 2.43	0.190
Topography			
Steep K	45.40 ± 1.76	44.51 ± 1.51	0.030*
Flat K	43.10 ± 1.52	42.44 ± 1.51	0.083
Cylinder power	2.31 ± 0.55	2.07 ± 0.54	0.089
CCT at apex	553.39 ± 24.36	557.60 ± 30.09	0.538
CCT at thinnest	547.74 ± 24.75	551.37 ± 29.72	0.597
CCT difference	5.65 ± 2.17	6.23 ± 4.68	0.524
Angle kappa	0.17 ± 0.09	0.18 ± 0.09	0.455
Pupil diameter	3.89 ± 0.68	3.78 ± 0.68	0.513
Schirmer test	14.00 ± 7.67	15.01 ± 6.64	0.567
Optic zone	6.48 ± 0.21	6.56 ± 0.35	0.263
Side-cut depth	15.81 ± 5.34	15.00 ± 5.29	0.540
Cap diameter	7.50 ± 0.23	7.45 ± 0.24	0.375
Cap thickness	113.06 ± 8.43	111.57 ± 8.29	0.472
RST	310.35 ± 29.76	307.23 ± 28.25	0.663
Lenticule thickness	128.68 ± 33.14	138.97 ± 32.33	0.207

Table 1. The baseline features of the study population. CDVA: corrected distance visual acuity, CCT: central corneal thickness, KLEx: keratorefractive lenticule extraction, N: number, RST: residual stromal thickness, SD: standard deviation, SE: spherical equivalent.

groups ($P = 0.552$) (Table 2). The degree of residual astigmatism one day after surgery was similar between the two groups ($P = 0.346$), while the first KLEx group demonstrated greater residual astigmatism than did the second KLEx group throughout the three-month follow-up period (all $P < 0.05$) (Table 2). The six standard graphs for reporting keratorefractive surgery for both the first KLEx group and the second KLEx group are presented in Fig. 1.

In the vector analysis, the second KLEx group demonstrated a significantly higher SIA, significantly lower DV, significantly lower ME and significantly higher CoI compared to the first KLEx group (all $P < 0.05$) (Table 3). On the other side, the TIA and AE values were similar between the two groups (both $P > 0.05$) (Table 3). Concerning risk factor of residual astigmatism, old age, high steep K, high topographic cylinder, large angle kappa, and a small optic zone correlated with greater residual astigmatism in the first KLEx group (all $P < 0.05$). On the other hand, only a small optic zone significantly correlated with greater residual astigmatism in the second KLEx group ($P = 0.047$) (Table 4).

Discussion

In this study, the UDVA and SE of the first- and second-generation KLEx surgeries were similar three months after surgery. On the other hand, residual astigmatism three months postoperatively was significantly greater in the first KLEx group than in the second KLEx group and the later showed a better astigmatic correction according to the vector analysis. In addition, a small optic zone was associated with greater residual astigmatism in both groups, whereas advanced age and several corneal parameters were associated with greater residual astigmatism in the first KLEx group.

Outcome	First KLEx group (*N*: 31)	Second KLEx group (*N*: 35)	*P*
UDVA (mean ± SD)			
1 day	0.06 ± 0.08	0.14 ± 0.16	0.012*
1 week	0.04 ± 0.06	0.07 ± 0.08	0.053
1 month	0.03 ± 0.06	0.03 ± 0.06	0.790
3 months	0.03 ± 0.06	0.02 ± 0.06	0.509
SE (mean ± SD)			
1 day	−0.21 ± 0.55	-0.57 ± 0.58	0.011*
1 week	−0.57 ± 0.59	−0.66 ± 0.64	0.532
1 month	−0.53 ± 0.70	−0.61 ± 0.61	0.643
3 months	−0.61 ± 0.51	−0.66 ± 0.51	0.552
Cylinder (mean ± SD)			
1 day	−0.65 ± 0.46	−0.54 ± 0.47	0.346
1 week	−0.77 ± 0.42	−0.50 ± 0.52	0.027*
1 month	−0.77 ± 0.38	−0.55 ± 0.39	0.026*
3 months	−0.80 ± 0.39	−0.50 ± 0.41	0.018*

Table 2. Postoperative visual and refractive conditions between the two groups. KLEx: keratorefractive lenticule extraction, N: number, SD: standard deviation, SE: spherical equivalent, UDVA: uncorrected distance visual acuity. *Denotes a significant difference between groups.

The three-month postoperative UDVA and SE were comparable between the first-generation KLEx surgery and the second-generation KLEx surgery in this study. According to previous studies, more than 90% of patients reach a UDVA of 20/20 in both the first-generation KLEx surgery and the second-generation KLEx surgery three months postoperatively[7,19]. Nevertheless, few studies have compared the postoperative UDVA between first-generation KLEx surgery and second-generation KLEx surgery in the same population with prominent astigmatism. To our knowledge, the findings of this study provide preliminary evidence of the similar efficiency of first-generation KLEx surgery and second-generation KLEx surgery in a population with prominent astigmatism. The initial features were generally identical between the first KLEx group and second KLEx group of this study; thus, the homogeneity of our population might be sufficient. Regarding the UDVA between the two groups at different time points, the second KLEx group demonstrated lower UDVA one day postoperatively compared to the first KLEx group. A possible explanation is that second-generation KLEx surgery results in a higher laser frequency and more laser spots than first-generation KLEx surgery does[19,20]; thus, short-term corneal edema may be more severe in second-generation KLEx surgery, which alters the UDVA. Specifically, the maximum laser repetition frequencies are 0.5 MHz and 2 MHz in the first- and second-generation KLEx surgeries, respectively. Additionally, the maximum total laser scanning are 23 s and 10 s in the first- and second-generation KLEx surgeries, respectively. Both of these indices indicate that a greater intensity of the laser was emitted in the second-generation KLEx surgery. Nevertheless, the UDVA difference three months postoperatively was slightly greater in the second KLEx group (0.01 LogMAR), and the percentage of individuals who reached a UDVA of 20/20 or better was also slightly greater in the second KLEx group. The above two results may imply that the efficiency of first- and second-generation KLEx surgeries is identical with longer follow-up intervals. Two individuals in the second KLEx group were diagnosed with diabetes mellitus, which might be a contraindication for refractive surgery. However, the two patients presented good glycated hemoglobin levels (< 6.0 mg/dL) during the past 6 months, and no diabetic retinopathy was found. Thus, the KLEx surgery was arranged. Three months after second-generation KLEx surgery, the mean UDVA and SE of the two eyes of the two patients were 20/20 and − 0.625 D, respectively. Accordingly, refractive conditions may not be altered by diabetes mellitus in these two patients.

With respect to the refraction between the two groups, the SEs were lower in the first KLEx group than in the second KLEx group one day postoperatively, whereas the other postoperative SE values between the two groups were statistically identical. The postoperative SE of the first-generation KLEx surgery was approximately − 0.10 to -0.20 D[21], and the postoperative SE in the high-astigmatism population receiving first-generation KLEx surgery ranged from − 1.63 D to + 1.38 D[21]. In addition, approximately 85% of individuals scheduled for second-generation KLEx surgery demonstrated an SE within ± 0.50 D after three months of follow-up[19]. The results of this study indicated that the predictability of first- and second-generation KLEx surgeries with respect to the SE is similar. On the other hand, the degree of postoperative residual astigmatism was significantly lower in the second KLEx group than in the first KLEx group since one week postoperatively, and the astigmatic correction was better in the second KLEx group according to the vector analysis. Few studies have reported differences in postoperative residual astigmatism between first- and second-generation KLEx surgeries in prominent astigmatism populations. The mean postoperative residual astigmatism value was approximately − 0.50 D in the second KLEx group, which is similar to the results of a previous study evaluating the general population[22–24], and the mean postoperative residual astigmatism in the first KLEx group was numerically greater. This difference may be due to the eye-tracking system used in second-generation KLEx surgery[19,20]. Although automated cyclotorsion compensation is not available in second-generation KLEx surgery, unlike in wavefront-guided laser

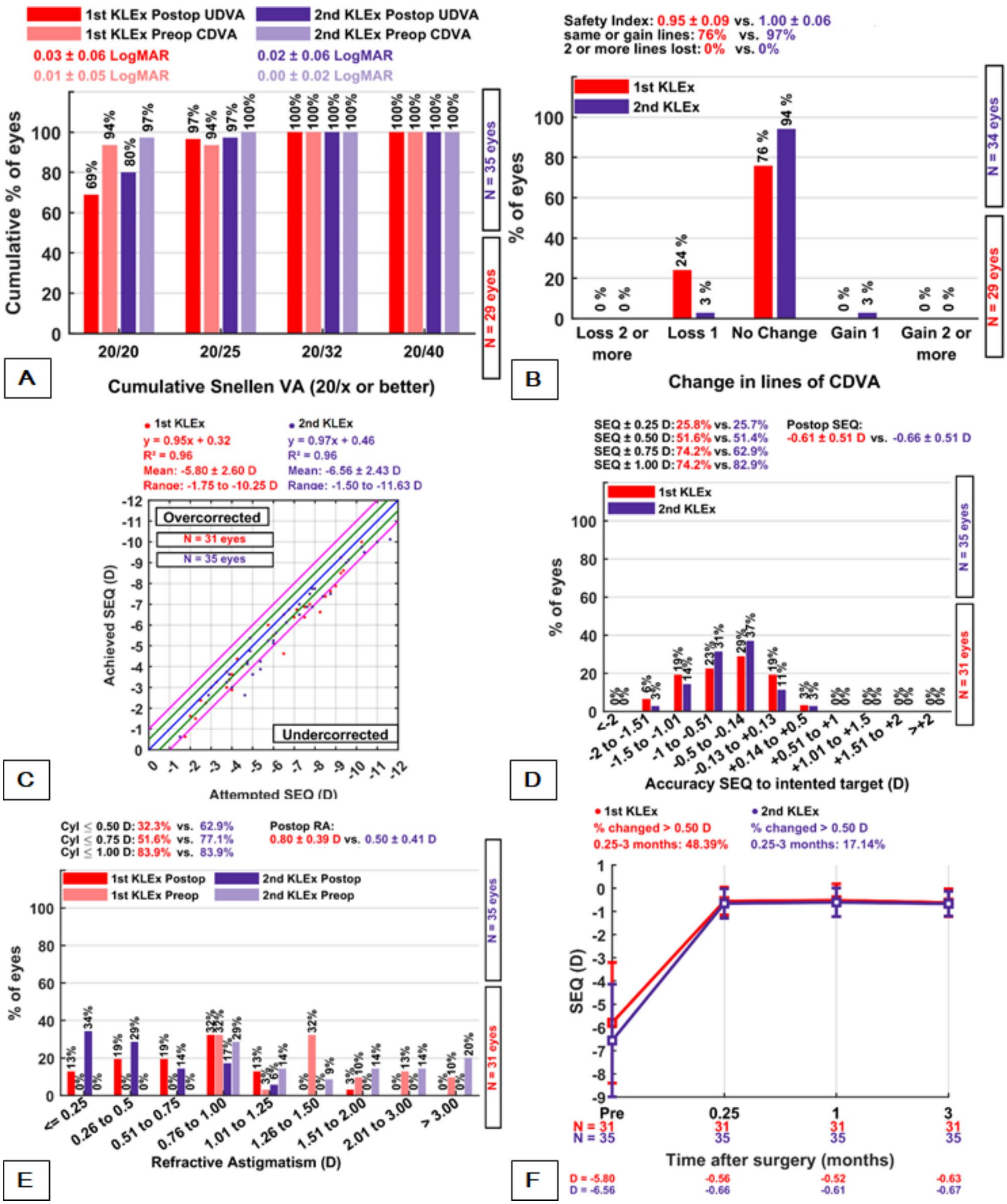

Fig. 1. Six standard graphs for reporting keratorefractive surgery. (**A**) Postoperative uncorrected distance visual acuity versus preoperative corrected distance visual acuity. (**B**) Change in corrected distance visual acuity after surgery. (**C**) Attempted spherical equivalent versus achieved spherical equivalent. (**D**) Accuracy of postoperative spherical equivalent refraction. (**E**) Postoperative astigmatism versus preoperative astigmatism. (**F**) Stability of the spherical equivalent refraction over the follow-up period. CDVA: corrected distance visual acuity; KLEx: keratorefractive lenticule extraction; SE: spherical equivalent; UDVA: uncorrected distance visual acuity.

Parameter	First KLEx group (*N*: 31)	Second KLEx group (*N*: 35)	*P*
TIA	1.61 ± 0.95	1.84 ± 0.88	0.312
SIA	0.94 ± 0.97	1.47 ± 0.86	0.024*
DV	1.39 ± 0.47	0.76 ± 0.29	< 0.001*
ME	−0.67 ± 0.45	−0.37 ± 0.31	0.004*
AE	5.36 ± 24.89	2.65 ± 11.63	0.582
CoI	0.65 ± 0.22	0.83 ± 0.16	0.001*

Table 3. The vector analysis of astigmatism between the two groups. AE: angle of error, CoI: correction index, DV: difference vector, KLEx: keratorefractive lenticule extraction, ME: magnitude of error, N: number, SIA: surgically induced astigmatism, TIA: target-induced astigmatism. *Denotes a significant difference between groups.

Factor	aOR	95% CI		*P*
		Lower	Upper	
First KLEx				
Age	1.013	1.005	1.021	0.002*
Sex	1.035	0.894	1.198	0.649
CDVA	0.417	0.060	2.911	0.378
Cycloplegic cylinder	0.982	0.942	1.023	0.378
Steep K	3.010	2.031	4.096	0.020*
Flat K	1.010	0.095	1.476	0.119
Topographic cylinder	2.011	1.057	3.518	0.022*
CCT at apex	1.002	0.985	1.020	0.808
CCT at thinnest	0.993	0.976	1.011	0.461
CCT difference	1.007	0.968	1.121	0.945
Angle kappa	1.567	1.256	2.257	0.003*
Optic zone	0.217	0.084	0.874	0.028*
Second KLEx				
Age	0.998	0.985	1.012	0.798
Sex	0.904	0.716	1.142	0.397
CDVA	2.749	0.428	7.653	0.286
Cycloplegic cylinder	1.032	0.981	1.086	0.218
Steep K	1.108	0.007	2.058	0.522
Flat K	2.545	0.009	5.880	0.537
Topographic cylinder	1.710	0.012	2.454	0.495
CCT at apex	0.978	0.956	1.000	0.051
CCT at thinnest	1.022	0.998	1.046	0.068
CCT difference	1.001	0.994	1.017	0.964
Angle kappa	0.885	0.260	3.009	0.845
Optic zone	0.617	0.107	0.956	0.047*

Table 4. Risk factors for greater residual astigmatism in the two groups. aOR: adjusted odds ratio, CDVA: corrected distance visual acuity, CCT: central corneal thickness, CI: confidence interval, K: keratometry, KLEx: keratorefractive lenticule extraction. *Denotes a correlation to high residual astigmatism.

in situ keratomileusis[25], the function of angle kappa registration and the reference line for cyclotorsion may help reduce postoperative residual astigmatism. The percentage of SE within ± 1.00 D was also numerically greater in the second KLEx group than in the first KLEx group, which may be attributed to the reduced postoperative astigmatism in the second KLEx group.

With respect to the risk factors associated with greater residual astigmatism in the first- and second-generation KLEx groups, a small optic zone was associated with greater residual astigmatism in both the first-generation KLEx and second-generation KLEx surgeries. In a previous study, a small optic zone was correlated with greater residual myopia and astigmatism in the first-generation KLEx surgery[26,27]. In addition, a small optic zone is related to a greater degree of myopic regression in laser in situ keratomileusis[28]. Our results are consistent with previous findings and may indicate that a small optic zone and the related greater degree of corneal tissue removal correlate with greater postoperative refractive variation in all refractive surgeries, regardless of preoperative astigmatism. On the other hand, old age, high steep K, high topographic cylinder, and large angle kappa were associated with greater postoperative residual astigmatism in the first KLEx group but not in the second KLEx group. The refraction stability in an older population that received refraction surgery was worse with a greater chance of retreatment[29], and high steep K and high topographic cylinder were associated with greater postoperative astigmatism regression in a previous study[30]. In addition, a large angle kappa may make centration more difficult, thus influencing postoperative residual astigmatism in the first-generation KLEx surgery, especially for a prominent astigmatism population[23]. In comparison, postoperative residual astigmatism was significantly lower in the second KLEx group, and the degree of astigmatism was not affected by most risk factors in the first KLEx group. This phenomenon may further illustrate the benefit of the eye-tracking system of the second-generation KLEx surgery for high-astigmatism management.

There are several limitations in this study. First, the retrospective design and absence of randomization in this study retarded the homogeneity of our study population, although no significant difference was observed in most of the preoperative parameters between the first and second KLEx groups. In addition, the total case numbers of this study were relatively inadequate in that only 66 eyes were included in the analysis, which may have led to significant statistical bias. Moreover, two surgeons performed the first- and second-generation KLEx surgeries, and the surgical technique used by the two surgeons may have affected the results despite the same surgical protocol being used for all the individuals. Finally, all the individuals included in this study were Han Taiwanese, and the external validity of this study may be diminished.

In conclusion, the efficiency and predictability of first- and second-generation KLEx surgeries in a prominent astigmatism population were largely similar, whereas second-generation KLEx surgery was associated with significantly lower postoperative astigmatism and better astigmatic correction. Furthermore, residual astigmatism in the first-generation KLEx surgery correlated with several corneal parameters, whereas residual astigmatism in the second-generation KLEx surgery was affected only by a small optic zone. Consequently, second-generation KLEx surgery could be recommended for those with high baseline astigmatism to reduce postoperative residual astigmatism. Further large-scale prospective studies investigating astigmatism regression in high-astigmatism populations receiving second-generation KLEx surgery are needed.

Data availability

The data used in the current study is available from the corresponding author upon reasonable request.

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References

1. Ganesh, S., Brar, S. & Arra, R. R. Refractive lenticule extraction small incision lenticule extraction: a new refractive surgery paradigm. *Indian J. Ophthalmol.* **66**, 10–19. https://doi.org/10.4103/ijo.IJO_761_17 (2018).
2. Ang, M. et al. Refractive surgery beyond 2020. *Eye (Lond).* **35**, 362–382. https://doi.org/10.1038/s41433-020-1096-5 (2021).
3. Padmanabhan, P., Mrochen, M., Basuthkar, S., Viswanathan, D. & Joseph, R. Wavefront-guided versus wavefront-optimized laser in situ keratomileusis: contralateral comparative study. *J. Cataract Refract. Surg.* **34**, 389–397. https://doi.org/10.1016/j.jcrs.2007.10.028 (2008).
4. Abdel-Radi, M., Shehata, M., Mostafa, M. M. & Aly, M. O. M. Transepithelial photorefractive keratectomy: a prospective randomized comparative study between the two-step and the single-step techniques. *Eye (Lond).* **37**, 1545–1552. https://doi.org/10.1038/s41433-022-02174-4 (2023).
5. Chang, J. Y., Lin, P. Y., Hsu, C. C. & Liu, C. J. Comparison of clinical outcomes of LASIK, Trans-PRK, and SMILE for correction of myopia. *J. Chin. Med. Assoc.* **85**, 145–151. https://doi.org/10.1097/jcma.0000000000000674 (2022).
6. Dupps, W. J. Jr., Randleman, J. B., Kohnen, T., Srinivasan, S. & Werner, L. Scientific nomenclature for Keratorefractive Lenticule extraction (KLEx) procedures: a joint Editorial Statement. *J. Refract. Surg.* **39**, 726–727. https://doi.org/10.3928/1081597x-20231010-0 (2023).
7. Reinstein, D. Z., Carp, G. I., Archer, T. J., Vida, R. S. & Yammouni, R. Large Population outcomes of Small Incision Lenticule extraction in Young myopic patients. *J. Refract. Surg.* **38**, 488–496. https://doi.org/10.3928/1081597x-20220623-01 (2022).
8. Reinstein, D. Z. et al. Objective and subjective quality of Vision after SMILE for high myopia and astigmatism. *J. Refract. Surg.* **38**, 404–413. https://doi.org/10.3928/1081597x-20220516-03 (2022).
9. Jabbarvand, M. et al. Vector analysis of moderate to high myopic astigmatism after small-incision lenticule extraction (SMILE): 12-month follow-up. *Eur. J. Ophthalmol.* **32**, 3312–3320. https://doi.org/10.1177/11206721221080821 (2022).
10. Lee, J. K., Chuck, R. S. & Park, C. Y. Femtosecond laser refractive surgery: small-incision lenticule extraction vs. femtosecond laser-assisted LASIK. *Curr. Opin. Ophthalmol.* **26**, 260–264. https://doi.org/10.1097/icu.0000000000000158 (2015).
11. Alió, D., Barrio, J. L., Vargas, V., Al-Shymali, O. & Alió, J. L. Small incision lenticule extraction (SMILE) in the correction of myopic astigmatism: outcomes and limitations - an update. *Eye Vis. (Lond).* **4**, 26. https://doi.org/10.1186/s40662-017-0091-9 (2017).
12. Zhong, Y., Li, M., Han, T., Fu, D. & Zhou, X. Four-year outcomes of small incision lenticule extraction (SMILE) to correct high myopic astigmatism. *Br. J. Ophthalmol.* **105**, 27–31. https://doi.org/10.1136/bjophthalmol-2019-315619 (2021).
13. Zhang, Y., Shen, Q., Jia, Y., Zhou, D. & Zhou, J. Clinical outcomes of SMILE and FS-LASIK used to treat myopia: a Meta-analysis. *J. Refract. Surg.* **32**, 256–265. https://doi.org/10.3928/1081597x-20151111-06 (2016).
14. Song, J. et al. Small incision Lenticule extraction (SMILE) Versus Laser assisted stromal in situ keratomileusis (LASIK) for Astigmatism corrections: a systematic review and Meta-analysis. *Am. J. Ophthalmol.* **247**, 181–199. https://doi.org/10.1016/j.ajo.2022.11.013 (2023).
15. Hashemi, H., Asgari, S., Khabazkhoob, M. & Heidari, Z. Vector analysis of astigmatism correction after PRK, FS-LASIK, and SMILE for myopic astigmatism. *Int. Ophthalmol.* **43**, 3999–4009. https://doi.org/10.1007/s10792-023-02804-0 (2023).
16. Zhao, X. et al. Comparison of Wavefront-guided Femtosecond LASIK and optimized SMILE for correction of moderate-to-high astigmatism. *J. Refract. Surg.* **37**, 166–173. https://doi.org/10.3928/1081597x-20201230-01 (2021).
17. Tian, H., Gao, W., Xu, C. & Wang, Y. Clinical outcomes and higher order aberrations of wavefront-guided LASIK versus SMILE for correction of myopia: a systemic review and meta-analysis. *Acta Ophthalmol.* **101**, 606–618. https://doi.org/10.1111/aos.15638 (2023).
18. Saad, A. et al. Refractive outcomes of small lenticule extraction (SMILE) Pro® with a 2 MHz femtosecond laser. *Int. Ophthalmol.* **44**, 52. https://doi.org/10.1007/s10792-024-02915-2 (2024).

19. Reinstein, D. Z., Archer, T. J., Potter, J. G., Gupta, R. & Wiltfang, R. Refractive and visual outcomes of SMILE for compound myopic astigmatism with the VISUMAX 800. *J. Refract. Surg.* **39**, 294–301. https://doi.org/10.3928/1081597x-20230301-02 (2023).
20. Brar, S., Ganesh, S. & Bhargav, S. Comparison of Intraoperative Time taken for Docking, Lenticule Dissection, and overall workflow for SMILE Performed with the VisuMax 800 Versus the VisuMax 500 Femtosecond laser. *J. Refract. Surg.* **39**, 648. https://doi.org/10.3928/1081597x-20230726-03 (2023).
21. Reinstein, D. Z. et al. Small incision Lenticule extraction (SMILE) for the correction of high myopia with astigmatism. *J. Refract. Surg.* **38**, 262–271. https://doi.org/10.3928/1081597x-20220314-01 (2022).
22. Gyldenkerne, A., Hjortdal, J. & Ivarsen, A. Astigmatism prediction in small-incision lenticule extraction. *J. Cataract Refract. Surg.* **46**, 524–533. https://doi.org/10.1097/j.jcrs.0000000000000083 (2020).
23. Chow, S. S. W., Chow, L. L. W., Lee, C. Z. & Chan, T. C. Y. Astigmatism correction using SMILE. *Asia Pac. J. Ophthalmol. (Phila).* **8**, 391–396. https://doi.org/10.1097/01.APO.0000580140.74826.f5 (2019).
24. Cui, G., Di, Y., Yang, S., Chen, D. & Li, Y. Efficacy of small-incision lenticule extraction surgery in high astigmatism: a meta-analysis. *Front. Med. (Lausanne).* **9**, 1100241. https://doi.org/10.3389/fmed.2022.1100241 (2022).
25. Miraftab, M., Seyedian, M. A. & Hashemi, H. Wavefront-guided vs wavefront-optimized LASIK: a randomized clinical trial comparing contralateral eyes. *J. Refract. Surg.* **27**, 245–250. https://doi.org/10.3928/1081597x-20100812-02 (2011).
26. Liu, P. et al. Influence of optical zone on myopic correction in small incision lenticule extraction: a short-term study. *BMC Ophthalmol.* **22**, 409. https://doi.org/10.1186/s12886-022-02631-4 (2022).
27. Zou, H. et al. The effects of programmed optical zones on achieved corneal refractive power with myopic astigmatism after small incision lenticule extraction (SMILE): a vector analysis. *Int. Ophthalmol.* **43**, 2493–2501. https://doi.org/10.1007/s10792-023-02649-7 (2023).
28. Liu, M., Gao, H. & Shi, W. Factors affecting myopic regression after laser in situ keratomileusis and laser-assisted Subepithelial Keratectomy for High Myopia. *Semin Ophthalmol.* **34**, 359–364. https://doi.org/10.1080/08820538.2019.1632353 (2019).
29. Pokroy, R., Mimouni, M., Sela, T., Munzer, G. & Kaiserman, I. Myopic laser in situ keratomileusis retreatment: incidence and associations. *J. Cataract Refract. Surg.* **42**, 1408–1414. https://doi.org/10.1016/j.jcrs.2016.07.032 (2016).
30. Lee, C. Y. et al. Topographic and surgical risk factors for high postoperative residual astigmatism after small incision lenticule extraction in patients with different degrees of myopia: a retrospective cohort study. *BMC Ophthalmol.* **24**, 45. https://doi.org/10.1186/s12886-024-03296-x (2024).

Author contributions

C.-K.C. made conceptualization, I.-B.L. and C.-K.C. made methodology, H.-C.C., C.-T.H., S.-F.Y. and C.-K.C. perform data collection, C.-K.C. provided software, J.-Y.H. made formal analysis, C.-Y.L. wrote original draft, C.-K.C. review and edit the manuscript, C.-K.C. made validation, C.-K.C. made supervision, all authors approved submission.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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