

# Myopic Regression After FS-LASIK and SMILE

Meng-Yin Lin, MD, PhD,\* Hsin-Yuan Tan, MD, PhD,† and Chao-Kai Chang, MD, PhD‡§

**Purpose:** To compare the degree of myopic regression after myopia correction with either femtosecond laser-assisted in situ keratomileusis (FS-LASIK) or small-incision lenticule extraction (SMILE) over 18 months.

**Methods:** Patients undergoing FS-LASIK or SMILE surgery for myopia correction were retrospectively recruited. The propensity scores were used to match patients by age and preoperative manifest spherical equivalent (SEQ) from these 2 groups. Myopic regression was analyzed using the Cox proportional hazard model.

**Results:** A total of 416 eyes of 416 patients undergoing FS-LASIK and 416 eyes of 416 patients undergoing SMILE were matched. Using 1-month SEQ as baseline, the SEQ regression values after FS-LASIK were 0D,  $-0.17 \pm 0.69D$ ,  $-0.24 \pm 0.65D$ ,  $-0.31 \pm 0.65D$ ,  $-0.32 \pm 0.63D$ , and  $-0.33 \pm 0.62D$  and the SEQ regression values after SMILE were 0D,  $-0.07 \pm 0.75D$ ,  $-0.18 \pm 0.77D$ ,  $-0.23 \pm 0.82D$ ,  $-0.21 \pm 0.77D$ , and  $-0.24 \pm 0.68D$  at 1, 3, 6, 9, 12, and 18 months, respectively. The Cox proportional hazard model showed that preoperative manifest SEQ ( $P = 0.021$ ) and designed optical zone ( $P = 0.048$ ) are significant predictors. The selected surgical procedure had no significant effect on predicting myopic regression ( $P = 0.470$ ). The cumulative survival rates of myopic regression were 54.74% and 42.10% in the FS-LASIK group and 58.66% and 43.83% in the SMILE group, at 12 and 18 months, respectively (log-rank test,  $P = 0.11$ ).

**Conclusions:** After matching based on age and preoperative manifest SEQ, we found that higher myopia and a smaller optical zone contribute significantly to the development of myopic regression after undergoing FS-LASIK or SMILE surgery at 18 months. The selected surgical procedure, however, does not affect the likelihood of myopic regression.

**Key Words:** SMILE, FS-LASIK, myopic regression, myopia

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Laser refractive surgery is a widely conducted procedure for correcting myopia. Nonetheless, postoperative myopic regression might occur and lead to dissatisfaction.<sup>1</sup> Several factors have been identified as risk factors of myopic regression after myopic refractive surgery, including preoperative spherical equivalent (SEQ),<sup>1,2</sup> age,<sup>3</sup> intraocular pressure (IOP),<sup>4,5</sup> optical zone (OZ) diameter,<sup>6</sup> and central corneal thickness (CCT).<sup>2</sup> Its development mechanism is ascribed to corneal remodeling ensuing from epithelial hyperplasia and the biomechanical alterations consequent to the removal of corneal stromal tissue.<sup>7</sup>

Since the introduction of the VisuMax femtosecond (FS) laser (Carl Zeiss Meditec, Jena, Germany) in 2007,<sup>8</sup> small-incision lenticule extraction (SMILE) has been developed as a novel refractive surgery and is gaining popularity. Unlike traditional FS laser-assisted in situ keratomileusis (FS-LASIK), which requires 2 lasers, SMILE can be performed with a single FS laser platform, making it economically advantageous.<sup>9</sup> Various studies have shown that SMILE and FS-LASIK yield comparable outcomes in terms of safety, efficacy, predictability, and stability when correcting myopia and myopic astigmatism.<sup>10,11</sup> However, SMILE offers additional benefits because of its flapless technique, resulting in better corneal integrity, reduced damage to corneal nerves, less corneal sensation loss, lower incidence of dry eyes,<sup>12</sup> and faster recovery of corneal sensitivity after surgery.<sup>11,13</sup> However, SMILE presents certain disadvantages, such as lack of iris registration, potential risks related to incomplete lenticule removal, slower visual recovery, and an additional cost of an excimer laser correction for retreatment.<sup>9</sup>

There is a paucity of research elucidating the incidence of myopic regression following SMILE.<sup>14–16</sup> The Cox proportional hazard (PH) model has been proven to be an eminent tool to evaluate myopic regression after refractive surgery<sup>2,14</sup>; hence, this study aims to utilize the Cox PH model to compare myopic regression between SMILE and FS-LASIK over an 18-month period and to assist surgeons in selecting the optimal surgical methods.

## PATIENTS AND METHODS

From January 2019 to July 2021, 1026 eyes of 516 patients undergoing FS-LASIK surgery and 1070 eyes of 538 patients undergoing SMILE surgery at Nobel Eye Institutes for myopia correction were recruited. The Joint Institutional Review Board Committee of Taipei Medical University

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approved the study protocol. The recruited patients were 21 to 53 years old. Before surgery, we provided comprehensive information to patients regarding the distinctions between these 2 refractive procedures, such as the smaller corneal opening, the flapless nature, the necessity to sacrifice more corneal thickness for equivalent myopia correction, less postoperative dry eyes, and higher cost of the SMILE procedure. Subsequently, patients made an informed decision based on these considerations. The preoperative ophthalmological examinations included uncorrected distance monocular visual acuity (VA), corrected distance monocular visual acuity (CDVA), manifest SEQ, biomicroscopy, noncontact tonometry (NIDEK, NT-530P, Japan), corneal topography (TOMEY, TMS-5, Japan), and funduscopy. Patients were excluded if they had cataract, a history of ocular disease, trauma, surgery, diabetes mellitus, or other systemic diseases known to affect the eyes. Systemic medications were allowed unless they were known to affect the cornea or anterior segment. For patients 21 to 39 years old, the target refraction was emmetropia. For patients 40 to 49 years old, a monovision strategy was used while the intended target refraction was  $-0.25$  D in the dominant eyes and  $-0.5$  D in the nondominant eyes. For patients older than 50 years, the intended postoperative refraction was  $-0.25$  D in the dominant eyes and  $-1$  D in the nondominant eyes.

## SURGICAL TECHNIQUES

### FS-LASIK Procedure

The FS-LASIK procedures were performed using an FS200 (WaveLight Alcon Surgical, Fort Worth, TX) laser platform to create flaps. The flap thickness was set to  $110\ \mu\text{m}$ , and the flap side cut angle was  $90^\circ$ . The flap diameter was  $8.5\ \text{mm}$ , with a  $50^\circ$  superior hinge in all patients. The energy and laser separation settings were as follows: side-cut pulse energy,  $0.85\ \mu\text{J}$ ; bed cut pulse energy,  $0.85\ \mu\text{J}$ ; stromal bed cut spot separation,  $8\ \mu\text{m}$ ; line separation,  $8\ \mu\text{m}$ ; side cut bed separation,  $5\ \mu\text{m}$ ; and line separation,  $3\ \mu\text{m}$ . The stromal bed was ablated with an EX-500 excimer laser (WaveLight Alcon Surgical) with either topography-guided, custom Q, or wavefront-guided modes. The most commonly designed OZ diameter was  $6.5\ \text{mm}$ . In patients with thin CCT or higher myopia correction, the OZ diameter was adjusted to  $5.5$  to  $6.20\ \text{mm}$ . After laser ablation, the corneal flap and stromal bed were rinsed with sterile balanced saline solution, and the flap was positioned back to the stromal bed.

### SMILE Procedure

SMILE was performed with a VisuMax FS laser platform (Carl Zeiss Meditec AG, Jena, Germany). The laser energy was set from  $105$  to  $135\ \text{nJ}$ . Treatment was centered on the corneal vertex. A small curved interface cone was used in all cases. The cap and lenticular spot-track distances were  $4.5\ \mu\text{m}$ , and the cap side and lenticular side spot-track distances were  $1.8\ \mu\text{m}$ . The cap thickness was designed from  $100$  to  $130\ \mu\text{m}$ , with an intended diameter of

$7.1$  to  $7.8\ \text{mm}$ . The most commonly used OZ diameter was  $6.5\ \text{mm}$ . In patients with thin CCT or higher myopia correction, the OZ diameter was adjusted to  $5.5$  to  $6.2\ \text{mm}$ . A small incision was created at  $10$  o'clock with a  $2$ - to  $4$ -mm side cut. FS laser parameters used in SMILE surgery were as follows: The laser had a repetition rate of  $500\ \text{kHz}$ . The spot-line separation was set at  $3.0\ \mu\text{m}$  for the lenticule,  $3.0\ \mu\text{m}$  for the flap, and between  $2.0\ \mu\text{m}$  for the flap side cut. The spot energy was set at  $140\ \text{nJ}$ . After the lenticule and the side cut had been created, the eye was positioned under the operating microscope, and the lenticule was gently separated through the anterior and posterior lamellar photodisruption planes with a blunt spatula. After the lenticule was completely freed from the stroma, it was extracted with forceps.

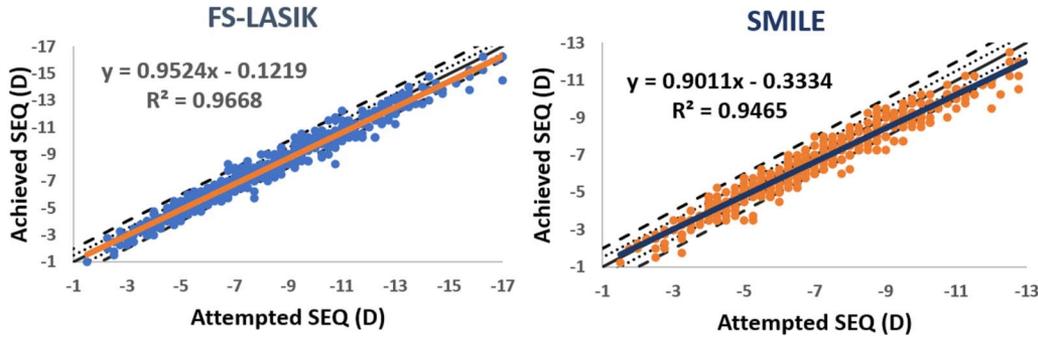
The postoperative medications after both procedures were the same. These initially consisted of Econopred Plus  $1\%$  (Novartis, Fort Worth, TX), levofloxacin  $0.5\%$  (Cravit, Santen), and preservative-free artificial tears, Optive (Allergan, Waco, TX), 4 times a day for 2 weeks and then followed by  $0.1\%$  fluorometholone and Optive (Allergan) for 1 month.

### Outcome Measures

After surgery, patients were followed at 1 day, 1 week, and 1, 3, 6, 9, 12, and 18 months. As the intended SEQ varied with patients' age, myopic regression was defined as a myopic shift greater than  $0.50$  D at 3, 6, 9, 12, or 18 months postoperatively, in which the manifest SEQ at 1 month served as the baseline SEQ. To build a predictive model for myopic regression, 1 eye from each patient undergoing bilateral refractive surgery was randomly selected. In patients who underwent refractive surgery in only 1 eye, only 1 eye was recruited. The preoperative variables included age, sex, manifest SEQ, cycloplegic SEQ (KR-8100, Topcon Corp), CCT (Sonomed 200 PC, Sonomed, Inc), preoperative central corneal curvature (mean keratometry [K], KR 8100), IOP, Schirmer test 1, ablation depth or lenticule thickness, OZ diameter, flap thickness, and flap diameter. In patients undergoing enhancement, only data before enhancement were collected. The values of flap thickness, cap thickness, lenticular thickness, flap diameter, and cap diameter were predetermined by the laser platform preoperatively, rather than measured intraoperatively. In the FS-LASIK procedure, the residual stromal thickness (RST) was calculated by subtracting the flap thickness and total ablation thickness from the preoperative CCT while in the SMILE procedure, the RST was calculated by subtracting the cap thickness and lenticule thickness from the preoperative CCT.

### Statistical Analysis

To select predictors, we searched throughout the literature for possible predictors affecting postoperative myopic regression. Pearson correlation was then used to analyze the selected predictors among our data to avoid multicollinearity. To reduce selection bias, the propensity score method was used to match age and preoperative manifest SEQ between these 2 groups. The cumulative



**FIGURE 1.** Scatterplot of the attempted versus the achieved SEQ after FS-LASIK and SMILE.

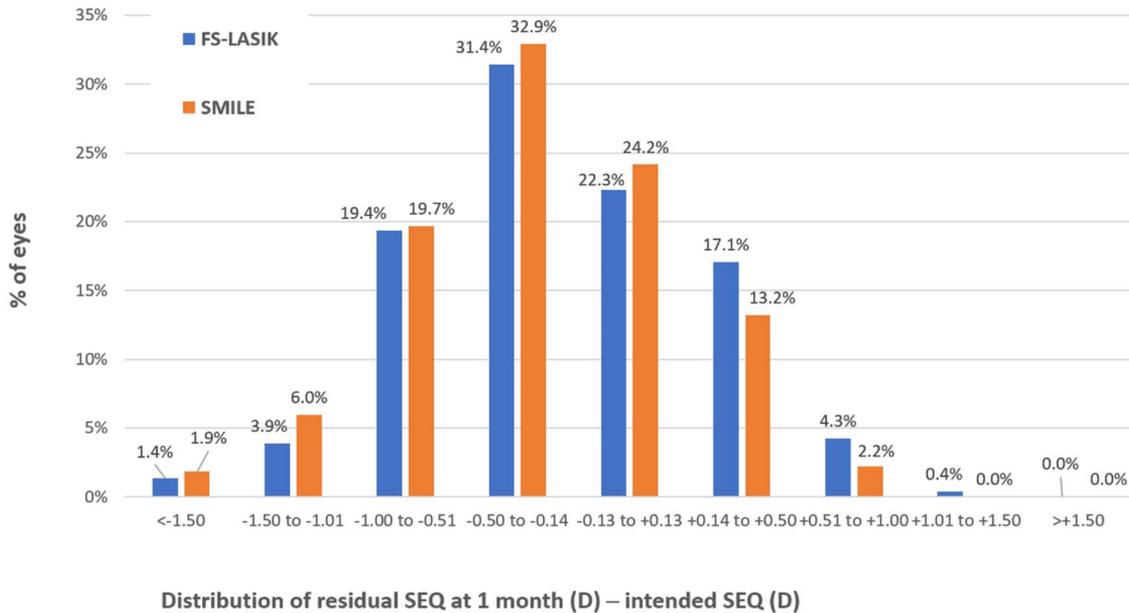
survival rate was analyzed by a log-rank test and plotted based on the Kaplan–Meier curves for the SMILE and FS-LASIK groups. The Cox PH model was then used for multivariate analysis and to examine the effect of predictors on the hazard of myopic regression. Data were analyzed using SAS 9.4 (SAS Institute, Cary, NC). Statistical significance was defined as  $P < 0.05$ . Independent-sample  $t$  tests were implemented to compare the mean  $\pm$  SD in the SMILE and FS-LASIK groups.

**RESULTS**

One eye was randomly selected to represent each patient, and consequently, 516 eyes from the FS-LASIK group and 528 eyes from the SMILE group were enrolled. At 18 months, the mean best uncorrected VA improved to  $0.02 \pm 0.06$  logMAR in the FS-LASIK group and to  $0.02 \pm 0.08$  logMAR in the

SMILE group ( $P = 0.793$ ). The CDVA was  $-0.01 \pm 0.03$  logMAR in the FS-LASIK group and  $-0.02 \pm 0.04$  logMAR in the SMILE group. Figure 1 presents a scatterplot of the attempted versus the achieved SEQ. Figure 2 illustrates the distribution of postoperative SEQ minus the intended SEQ. Eyes that were within  $\pm 0.50$  D accounted for 70.7% in FS-LASIK and 70.3% in SMILE ( $P = 0.865$ ). Eyes that were within  $\pm 1.0$  D accounted for 94.5% in FS-LASIK and 92.2% in SMILE ( $P = 0.613$ ). The enhancement rate in the FS-LASIK procedures was 4.98%; the enhancement rate in the SMILE procedures was 1.32%.

Through one-to-one matching with propensity scores based on age and manifest SEQ, we obtained a matched sample of 416 eyes in each group. The baseline characteristics of the matched sample are presented in Table 1. After matching, the preoperative age ( $P = 0.621$ ), manifest SEQ ( $P = 0.835$ ), and CCT ( $P = 0.087$ ) were not significantly



**FIGURE 2.** The distribution of postoperative SEQ minus the intended SEQ. Eyes that were within  $\pm 0.50$  D accounted for 70.7% in FS-LASIK and 70.3% in SMILE ( $P = 0.865$ ). Eyes that were within  $\pm 1.0$  D accounted for 94.5% in FS-LASIK and 92.2% in SMILE ( $P = 0.613$ ).

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different between these 2 groups. In terms of corneal parameters, the flap thickness was  $110.00 \pm 0.00 \mu\text{m}$  and  $112.84 \pm 7.87 \mu\text{m}$  ( $P < 0.001$ ); the ablation depth was  $104.82 \pm 29.64 \mu\text{m}$  and lenticular thickness was  $133.24 \pm 25.74 \mu\text{m}$  ( $P < 0.001$ ); and the RST was  $331.50 \pm 45.67 \mu\text{m}$  and  $304.40 \pm 27.55 \mu\text{m}$  ( $P < 0.001$ ) in the FS-LASIK and SMILE groups, respectively.

In terms of postoperative outcomes, when using SEQ at 1 month as the baseline, the progression of SEQ values after FS-LASIK procedures was 0 D,  $-0.17 \pm 0.69$  D,  $-0.24 \pm 0.65$  D,  $-0.31 \pm 0.65$  D,  $-0.32 \pm 0.63$  D, and  $-0.33 \pm 0.62$  D at 1, 3, 6, 9, 12, and 18 months, respectively. The SEQ values after SMILE procedures were 0 D,  $-0.07 \pm 0.75$  D,  $-0.18 \pm 0.77$  D,  $-0.23 \pm 0.82$  D,  $-0.21 \pm 0.77$  D, and  $-0.24 \pm 0.68$  D at 1, 3, 6, 9, 12, and 18 months, respectively (Fig. 3). Throughout the postoperative period, the manifest SEQ between the 2 procedures exhibited no significant difference (all  $P > 0.05$ ). At 18 months, the myopic regression between the 2 procedures remained comparable ( $P = 0.13$ ).

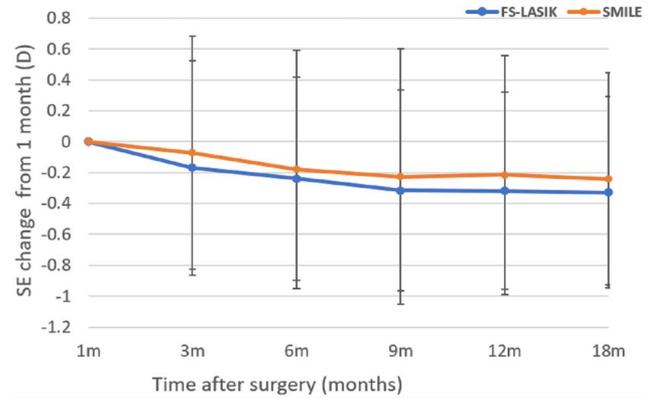


FIGURE 3. Postoperative SEQ progression, using SEQ at 1 month as baseline.

TABLE 1. Basic Characteristics of the Matched Preoperative Variables

Variables	FS-LASIK (n = 416)	SMILE (n = 416)	P
Mean age (yr)	32.42 ± 7.88	32.16 ± 7.17	0.621
Range	21–53	20–52	
Sex, n (%)			0.433
Male	164 (40.5)	175 (43.2)	
Female	241 (59.5)	230 (56.8)	
Mean manifest SEQ			
Sphere (D)	-6.78 ± 2.68	-6.76 ± 2.21	0.881
Cylinder (D)	-1.31 ± 0.88	-1.30 ± 0.89	0.819
Axis (°)	99.92 ± 73.45	100.19 ± 75.36	0.959
SEQ (D)	-7.50 ± 2.69	-7.47 ± 2.27	0.835
Range of SEQ (D)	-1.25 ~ -16.75	-1.25 ~ -12.75	
Mean cycloplegic SEQ			
Sphere (D)	-6.33 ± 2.65	-6.21 ± 2.21	0.483
Cylinder (D)	-1.33 ± 0.87	-1.29 ± 0.88	0.585
Axis (°)	104.03 ± 73.16	102.41 ± 73.82	0.759
SEQ (D)	-7.02 ± 2.66	-6.88 ± 2.31	0.415
Mean keratometry (D)	43.73 ± 1.36	43.57 ± 1.40	0.101
Flap thickness (μm)	110.00 ± 0.00	112.84 ± 7.87	<0.001
Flap diameter (mm)	8.57 ± 0.19	7.42 ± 0.29	<0.001
CCT (μm)	547.04 ± 33.96	550.86 ± 28.25	0.087
Range	423–668	479–672	
RST (μm)	331.50 ± 45.67	304.40 ± 27.55	<0.001
Range	263–487	253–446	
Total ablation depth (μm)	104.82 ± 29.64	133.24 ± 25.74	<0.001
IOP (mm Hg)	15.88 ± 2.93	15.94 ± 2.78	0.759
Schirmer test	11.98 ± 7.78	11.50 ± 7.53	0.395
Optical zone (mm)	6.46 ± 0.21	6.43 ± 0.29	0.036
Range	5.0–8.0	5.2–7.0	

The 2 groups were compared with the independent *t* test for continuous variables and  $\chi^2$  test for categorical variables.

### Kaplan–Meier Curves and Cox PH Model

The Pearson correlation analysis revealed a high correlation between CCT and RST (correlation coefficient >0.7). Considering the significant correlation between RST and postoperative biomechanics reported in previous studies, we selected RST instead of CCT as one of the variables for additional analysis.<sup>17</sup> Ultimately, the variables including surgical method, age, preoperative manifest SEQ, RST, mean K, Schirmer II results, IOP, flap thickness, and OZ were then processed using the Cox PH model and are listed in Table 2. Higher preoperative manifest SEQ ( $P = 0.021$ ) and smaller OZ ( $P = 0.048$ ) were identified as significant predictors. The surgical method, however, was insignificant ( $P = 0.470$ ). This indicates that even having been matched based on age and preoperative manifest SEQ, a higher degree of preoperative myopia still seems to be the most significant predictor of myopic regression. The cumulative survival rates at 12 and 18 months were 55.07% and 43.03%, respectively, in the FS-LASIK group and 58.29% and 43.46%, respectively, in the SMILE group (Fig. 4). Although undergoing the SMILE procedure exhibited a lower regression rate than that undergoing FS-LASIK, the difference was not statistically significant (log-rank test,  $P = 0.11$ ).

### Correlation Between OZ and Myopic Regression

In both groups, patients adopting a smaller OZ ( $\leq 6.2$  mm) had relatively higher myopia ( $-9.97$  D) and thinner CCT ( $523.99 \mu\text{m}$ ) while patients adopting a larger OZ ( $\geq 6.5$  mm) had relatively lower myopia ( $-6.91$  D,  $P < 0.001$ ) and thicker CCT ( $554.44 \mu\text{m}$ ). The differences in preoperative myopia and corneal thickness were significantly different between smaller and larger OZs (both  $P < 0.001$ ). In the group with a larger OZ, 30.46% had CCT less than  $540 \mu\text{m}$  and 12.62% had CCT less than  $520 \mu\text{m}$ , while in the group with a smaller OZ, 72.95% had CCT less than  $540 \mu\text{m}$  and 43.44% had CCT less than  $520 \mu\text{m}$ . The CCT distribution between smaller and larger OZs was significantly different (both  $P < 0.001$ ).

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**TABLE 2.** Multivariate Analysis of Myopic Regression at 18 Months in the Cox Proportional Hazard Model (N = 832)

Parameter	Regression Coefficient	P	HR	95% CI for HR	
Group (FS vs. SMILE)	0.106	0.470	1.112	0.834	1.484
Age (yr)	0.001	0.937	1.001	0.984	1.017
Schirmer (mm)	0.001	0.866	1.001	0.985	1.018
IOP (mm Hg)	-0.010	0.699	0.990	0.943	1.040
Mean K (D)	-0.032	0.499	0.968	0.882	1.063
RST (μ m)	0.001	0.783	1.001	0.996	1.006
Manifest SEQ (D)	-0.088	0.021	0.916	0.850	0.987
Optical zone (mm)	-0.538	0.048	0.584	0.332	1.027
Flap/cap thickness	-0.006	0.678	0.994	0.969	1.021

CI, confidence interval; HR, hazard ratio.

**DISCUSSION**

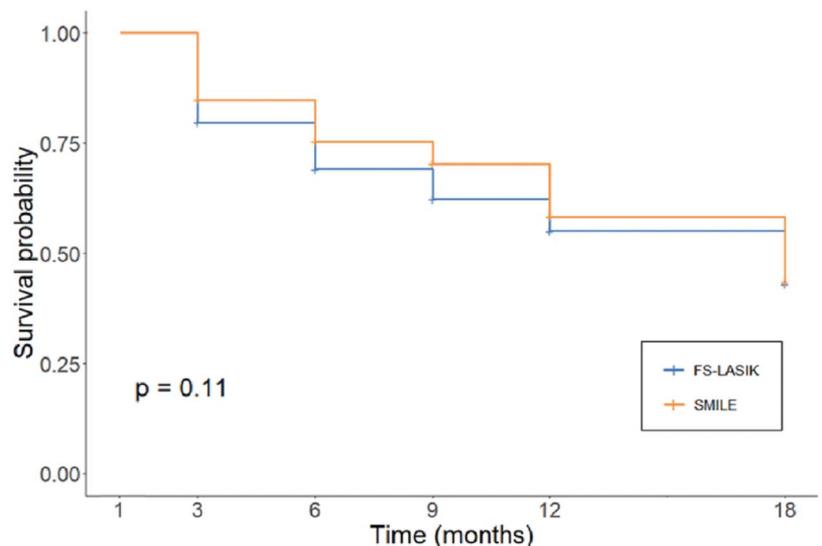
The process of myopic regression following refractive surgery involves corneal epithelial remodeling and biomechanical stability.<sup>7</sup> The contralateral eye study conducted by Kanellopoulos<sup>18</sup> and the matched eye study of Canto-Cerdan et al<sup>19</sup> examined changes in epithelial thickness and refractive power after myopia correction using SMILE and FS-LASIK techniques. Both studies demonstrate comparable epithelial thickening, which underscore the significance of postoperative biomechanical stability in the context of myopic regression.

In this study, the average flap thickness in the FS-LASIK group was 110.00 ± 0.00 μm while the average cap thickness in the SMILE group was 112.84 ± 7.87 μm. Although CCT (P = 0.087) and manifest refraction (P = 0.835) were comparable between the 2 groups, the total ablation depth was 104.82 μm in FS-LASIK and 133.24 μm in SMILE. Consequently, the RST was 331.50 ± 45.67 μm in FS-LASIK and 304.40 ± 27.55 μm in SMILE (P < 0.001). Our finding aligns with previous studies that even with the

same myopia correction, the SMILE procedure excises a significantly greater lenticular thickness than the ablation thickness in the FS-LASIK procedure.<sup>20,21</sup> Even with more corneal thickness removal and consequently a lower RST in the SMILE group, the survival rate was still comparable with that in the FS-LASIK group (P = 0.470). This might be attributed to the better preservation of the corneal anterior stroma and superior biomechanical stability in SMILE compared with flap creation in FS-LASIK, which involves the removal of a biomechanically stronger part of the cornea, including Bowman’s layer and the anterior stroma.<sup>22–24</sup>

Zhou et al<sup>25</sup> compared the survival rates of patients (-6D to -10D) undergoing FS-LASIK or 2 other refractive surgeries. In their FS-LASIK group (SEQ -7.55D, age 27.92 years), the survival rate at 12 months was 59.12% while the survival rate of the FS-LASIK group (SEQ -7.5D, age 32.42 years) at 12 months in this study was 54.74%. In another study by Zhou et al<sup>14</sup> comparing myopic regression after FS-LASIK and SMILE for mild-to-moderate myopia, they reported the cumulative survival rates at 12 months to be 88.1% in the SMILE group and 83.7% in the FS-LASIK group and a similar risk of myopic regression between SMILE and FS-LASIK. In this study, the cumulative survival rates at 12 and 18 months were 55.07% and 43.03% in the FS-LASIK group and 58.29% and 43.46% in the SMILE group, respectively. The lower survival rate in this study may be attributed to the higher preoperative SEQ and older age in this study since a higher preoperative SEQ and older age are both significant factors predisposing patients to myopic regression.<sup>2,26</sup> However, even at 18 months in this study, the survival rates between FS-LASIK and SMILE remain comparable.

Previous studies identify a smaller OZ<sup>25,27,28</sup> and a larger transition zone<sup>25</sup> as significant predictors of myopic regression. They inferred that spherical ablation was designed with a large OZ and a small transition zone for low and moderate myopia while aspherical ablation was designed with a small OZ and a large aspheric transition zone for patients



**FIGURE 4.** Kaplan–Meier curves of myopic regression comparing FS-LASIK and SMILE using the log-rank test (P = 0.11).

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with thinner corneal thickness or relatively higher myopia to save the depth of ablation.<sup>25</sup> In this study, we also deduce that a small OZ ( $\leq 6.2$  mm) contributes significantly because of its strong correlation with higher myopia. Whereas transition zone was not considered as a predictor in the current study because limited research recognizing its relevance in forecasting myopic regression. Additional studies are required to elucidate the correlation between the transition zone and myopic regression.

Moshirfar et al<sup>29</sup> reviewed the enhancement rate after SMILE and FS-LASIK procedures. They found that the enhancement rate after the SMILE procedure ranged from 1% to 4%<sup>30</sup> and the enhancement rate after LASIK usually ranged from 5% to 28%.<sup>31</sup> In this study, the enhancement rate in the FS-LASIK group was 4.98% while the enhancement rate in the SMILE group was 1.32%. No eyes lost more than 1 line of CDVA, and there were no complications related to the enhancement procedure. Factors associated with retreatment included age older than 40 years, high initial refractive errors, and high preoperative astigmatism.<sup>32</sup> The higher retreatment rate in the FS-LASIK rate may be reasoned by the older average age and higher preoperative SEQ in this study. Our result suggests that surgical enhancement could be a viable intervention for some patients experiencing myopic regression.

This study contains several advantages. First, we utilized the postoperative manifest SEQ at 1 month as baseline for comparison, which is opposed to the conventional 1 week. It has been found that SMILE exhibits slower recovery of visual and refractive status than FS-LASIK.<sup>13,33</sup> Agca et al<sup>34</sup> suggested that this discrepancy may be attributed to the higher intensity of backscattered light in SMILE during the initial 3 months after surgery, which can be linked to the behavior of extracellular matrix and activated keratocytes. Thus, we opted for the relatively stable manifest SEQ at 1 month as baseline to observe the progression of myopic regression after surgery. Second, we used propensity scores to match age and preoperative SEQ. Preoperative SEQ and age are both risk factors of retreatment after myopic LASIK.<sup>35</sup> As the progression of presbyopia is directly correlated with advancing age, we voluntarily controlled the target refraction by matching age. Third, instead of CCT, we included RST as 1 variable, as it may provide a more comprehensive representation of the biomechanical properties following surgery. Fourth, patients from the 2 groups had comparable CCTs ( $P = 0.087$ ). With comparable CCT and matched age and manifest SEQ, we can mitigate selection bias more effectively and ultimately find the inherent distinctions between these 2 surgical methods.

This study possesses some limitations as well. First, this study was conducted retrospectively, lacking the element of randomization. Second, the sample size we recruited was limited. Third, owing to the long follow-up period, censored data were inevitable. Therefore, we used the Cox PH model to process and analyze the information effectively. Fourth, the observation period lasted only 18 months. Fifth, the direct biomechanical comparison between FS-LASIK and SMILE eyes that developed regression is absent. Sixth, we did not measure the axial length after surgery. The lack of axial

length measurements over time results in a difficulty to distinguish between actual myopic regression and simple myopic progression, particularly in younger populations who may naturally become more myopic over time. Seventh, myopic regression in this study is accurately SEQ regression by its definition as preoperative myopia and SEQ are highly correlated (Pearson correlation coefficient  $>0.7$ ). Besides, the conducted literature review did not reveal astigmatism to be a frequently included variable in the regression model while many studies identified SEQ as a significant variable.<sup>2,25,36</sup> To mitigate multicollinearity, we opted for SEQ over myopia in our regression model.

In summary, this comparative study of myopic regression after either FS-LASIK or SMILE can be applied to low, moderate, and high myopia over an observation span of 18 months. By matching patients based on age and preoperative SEQ, we identified higher SEQ as the most significant factor predisposing patients to the occurrence of myopic regression following FS-LASIK or SMILE procedures. The choice of surgical procedure, however, does not exert a significant influence on the likelihood of myopic regression. For future studies, extending observation period to 24 or 36 months could probably uncover distinct regression patterns between FS-LASIK and SMILE. Comparing the biomechanical differences between these 2 surgeries is also required to comprehensively understand myopic regression postrefractive surgery.

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