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Comparison of postoperative long-term stabilities of tear film and cornea after femtosecond small incision lenticule extraction and femtosecond laser *in situ* keratomileusis.

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Abstract

Objective: To compare the effects of femtosecond Small Incision Lenticule Extraction (SMILE) and femtosecond laser *in situ* keratomileusis (LASIK) on postoperative long-term stabilities of tear film and cornea.

Methods: 115 patients with corneal refractive surgery in our hospital from August 2014 to August 2016 were selected as the subjects, and were divided into the SMILE group and FS-LASIK group according to the date of admission. The changes in noninvasive tear film Breakup Time (NI-BUT), Schirmer I test (SIt) value and posterior corneal surface height were measured and compared before and after operation between the two groups.

Results: Before operation, there were no significant differences in NI-BUT value and SIt value between the two groups (P>0.05); At 1 and 3 months after operation, the NI-BUT value and SIt value of the SMILE group were significantly higher than those of the FS-LASIK group (P<0.05); At 6 and 12 months after operation, there were no significant differences in NI-BUT value and SIt value between the two groups (P>0.05). At 1 months after operation, the NI-BUT value and SIt value of the SMILE group were significantly lower than those before operation (P<0.05); There were no significant differences between the NI-BUT value and SIt value of the SMILE group at 3, 6 and 12 months after operation and those before operation (P>0.05). At 1 and 3 months after operation, the NI-BUT value and SIt value of the FS-LASIK group were significantly lower than those before operation (P<0.05); There were no significant differences between the NI-BUT value and SIt value of the FS-LASIK group at 6 and 12 months after operation and those before operation (P>0.05).

Conclusion: There were no significant differences in the posterior corneal surface height between the femtosecond SMILE and femtosecond LASIK, but the femtosecond SMILE had obvious advantage in tear film stability, especially in recovery course at early stage after operation.

Keywords: Femtosecond laser, Excimer laser *in situ* keratomileusis, Small incision lenticule extraction, Tear film, Cornea.

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Introduction

Femtosecond laser is a kind of infrared laser with very high instantaneous power. It has been widely applied in clinical ophthalmology for very precise cutting effect and created a new field for corneal refractive surgery. After the femtosecond laser is used for making corneal flap for laser *in situ* keratomileusis (LASIK), the femtosecond LASIK is developed. The FS-LASIK with good safety and efficacy is one of the most widely used operations in clinical practice [1]. With continuous development of the femtosecond laser technology, femtosecond laser Small Incision Lenticule Extraction (SMILE) is developed and has been applied in clinical treatment gradually. The operative procedure reported for the first time in 2011 [2], has advantage in flapless microresecting [3]. It can make nerve fibers recover faster [4], and can further enhance the safety and efficacy of operation. Previous studies have shown that corneal refractive surgery may change the stabilities of tear film and corneal biomechanics because of injuries of nerve fibers and ocular surface epithelia and even can further affect long-term effects of operation [5,6]. The purpose of this study is to compare and analyse the effects of the two corneal refractive surgeries of the FS-SMILE and FS-LASIK on postoperative long-term stabilities of tear film and cornea in order to provide scientific basis for rational selection of operative procedures.

Data and Methods

General data

115 patients with corneal refractive surgery in our hospital from August 2014 to August 2016 were selected as the subjects, and were divided into two groups according to the date of admission (odd-numbered day or even-numbered day). The patients on the odd day are assigned to the SMILE group (110 eyes of 55 patients) and treated with the FS-SMILE. The patients on the even day are assigned to the FS-LASIK group (120 eyes of 60 patients) and treated with the FS-LASIK. The entry requirements of subjects are as follows: (1) Entry criteria: Annual refractive changes are less than -0.50 D, which must last for more than two years; The preoperative spherical refraction is within -6.00 D, and cylindrical refraction is -2.50 D or less; No medication histories of corticosteroids and antiglaucoma drugs which affect tear secretion and tear film stability; No wearing history of corneal contact lens or having stopped wearing them for over two weeks; (2) Exclusion criteria: Surgical contraindication; Other complicated eye diseases; With general connective tissue diseases or immune system disorder. The general data such as age and preoperative eye refraction between the two groups were comparable, and the comparison results showed no statistical differences (P>0.05). The detailed information is shown in Table 1.

Table 1. Comparison of general data before and after operation between both groups.

Group	Eye number	Age	Spherical refraction (D)	Cylindrical refraction (D)	Central corneal thickness (μm)	Intraocular tension (mmHg)
SMILE	110	27.77 ± 5.16	-5.15 ± 1.01	-0.38 ± 0.49	532.14 ± 19.52	16.02 ± 2.02
FS-LASIK	120	27.17 ± 5.50	-5.53 ± 1.08	-0.40 ± 0.61	540.08 ± 21.27	15.89 ± 2.12
t		5.398	1.239	1.418	1.388	0.527
P		0.580	0.201	0.158	0.175	0.156

Methods

Surgical methods: All the subjects were treated by the same surgeon, and the Zeiss VisuMax femtosecond laser (Germany) was used. Firstly, the patients in each group were given preoperative routine preparations and then were superficially anaesthetized with Oxybuprocaine Hydrochloride 4 g/L. In the SMILE group, the femtosecond laser double-layer scanning was performed. The corneal refractive lenticule and cap-shaped microincision were prepared by cutting. After separating free lenticule, the microincision was taken as the pathway for lenticule extraction. In the FS-LASIK group, the corneal flap with a thickness of about 110 μm was made with femtosecond laser technology, and then the ablation of corneal stroma was performed. During the surgery, the thickness of corneal cap of the SMILE group was consistent with that of corneal flap of the FS-LASIK group.

Postoperative management

The postoperative medications of patients in both groups were consistent: The levofloxacin eye drops was given 4 times daily, and its administration lasted until 1 w after operation; the fluorometholone eye drops was given 4 times daily, and its administration lasted until 1 w after operation; The sodium carboxymethylcellulose eye drops was given 4 times daily, and its administration lasted until 2 months after operation.

Test methods

At 1, 6 and 12 months before and after the surgery, the following assays were performed respectively: (1) The Breakup Time of noninvasive tear film (NI-BUT) was tested and measured three times using German Oculus ocular analyzer, and then the results of the three tests were averaged. A higher NI-BUT value indicates a better tear film stability; (2) The Schirmer I test (SIt) value was measured using filter paper of 5 mm ×35 mm, the immersion wetting length was recorded after 5 min. A higher reading indicates a better lacrimal secretion; (3) The posterior corneal surface height was measured using Pentacam anterior eye segment analysis system. The height data indicate the vertical dimension from any point on the anterior and posterior surfaces of cornea to the Best Fit Sphere (BFS).

Statistical analysis

The related data were analysed with the SPSS 19.0 software, the measurement data were expressed as mean ± standard deviation and analysed by the t test, and P value<0.05 is considered significant.

Results

Comparison of NI-BUT value at different times between both groups

Before operation, there were no significant differences in the NI-BUT value between the two groups (P>0.05); At 1 and 3 months after operation, the NI-BUT value of the SMILE group was significantly higher than that of the FS-LASIK group, and the differences were statistically significant (P<0.05); At 6 and 12 months after operation, there were no significant differences in the NI-BUT value between the two groups (P>0.05). In the SMILE group, the NI-BUT value at 1 months after operation was significantly lower than that before operation (P<0.05), and there were no statistically significant differences between the NI-BUT value at 3, 6 and 12 months after operation and

that before operation (P>0.05). In the FS-LASIK group, the NI-BUT value at 1 and 3 months after operation was significantly lower than that before operation (P<0.05), and there were no statistically significant differences between the NI-BUT value at 6 and 12 months after operation and that before operation (P>0.05). The detailed information is shown in Table 2.

Table 2. *Comparison of the NI-BUT value at different times between both groups (s).*

Group	Before operation	1 months after operation	3 months after operation	6 months after operation	12 months after operation
SMILE	10.85 ± 1.89	7.97 ± 1.10[a]	9.12 ± 1.15	9.87 ± 0.70	10.92 ± 1.11
FS-LASIK	10.54 ± 1.49	6.47 ± 1.01[a]	8.72 ± 0.90[a]	9.75 ± 0.80	10.55 ± 1.20
t	0.579	2.071	2.051	0.7	1.421
P	0.537	0.04	0.042	0.419	0.13

Note: Compared with the preoperative NI-BUT value of this group, [a]P<0.05

Comparison of the SIt value at different times between both groups

Before operation, there were no significant differences in the SIt value between the two groups (P>0.05); At 1 and 3 months after operation, the SIt value of the SMILE group was significantly higher than that of the FS-LASIK group, and the differences were statistically significant (P<0.05); At 6 and 12 months after operation, there were no significant differences in the SIt value between the two groups (P>0.05). In the SMILE group, the SIt value at 1 months after operation was significantly lower than that before operation (P<0.05), and there were no statistically significant differences between the SIt value at 3, 6 and 12 months after operation and that before operation (P>0.05). In the FS-LASIK group, the SIt value at 1 and 3 months after operation was significantly lower than that before operation (P<0.05), and there were no statistically significant differences between the SIt value at 6 and 12 months after operation and that before operation (P>0.05). The detailed information is shown in Table 3.

Table 3. *Comparison of the SIt value at different times between both groups (mm).*

Group	Before operation	1 months after operation	3 months after operation	6 months after operation	12 months after operation
SMILE	14.82 ± 1.99	11.33 ± 2.15[a]	14.03 ± 1.83	14.67 ± 1.73	14.73 ± 1.73
FS-LASIK	14.99 ± 1.84	8.98 ± 1.58[a]	10.82 ± 2.30[a]	13.07 ± 2.64	14.37 ± 1.93
t	0.562	8.63	4.115	1.899	1.223
P	0.487	<0.001	<0.001	0.094	0.278

Note: Compared with the preoperative SIt value of this group, [a]P<0.05

Comparison of posterior corneal surface height at different times between both groups

At 1, 3, 6 and 12 months before and after operation, there were no significant differences in the posterior corneal surface height between the two groups (P>0.05). The detailed information is shown in Table 4.

Table 4. *Comparison of posterior corneal surface height at different times between both groups.*

Group	Before operation	1 months after operation	3 months after operation	6 months after operation	12 months after operation
SMILE	1.46 ± 0.63	1.61 ± 0.81	1.29 ± 0.82	1.22 ± 0.78	1.18 ± 0.82
FS-LASIK	1.38 ± 0.58	1.71 ± 0.83	1.63 ± 0.79	1.51 ± 0.59	1.12 ± 0.81
t	0.61	1.515	0.72	0.566	0.723
P	0.455	0.212	0.511	0.493	0.508

Conclusion

The femtosecond laser is an infrared laser with very high instantaneous power. It works in the form of pulse, can focus into a tiny tissue space in a short time, and can separate the tissue through multiphoton ionization excitation pathway and form plasma. Under the influence of electromagnetic field of the plasma, the femtosecond laser may form laser blasting effect and make the tissue produce carbon dioxide and water microbubbles. When a large number of microbubbles are connected, a very precise cutting effect will be reached [7]. The femtosecond laser has been widely used in the field of corneal refractive surgery for very precise cutting effect [8,9]. And then, the femtosecond LASIK and femtosecond SMILE are developed successively. The two corneal refractive surgeries now have been widely used in clinical practice both at home and abroad for good safety and efficacy [10,11]. It is noteworthy that the corneal refractive surgery may to a certain extent injure nerve fibers and ocular surface epithelial tissues, and then can change the stabilities of tear film and corneal biomechanics after operation, but almost previous studies focus on the stabilities of tear film and cornea at early stage, there is a lack of concern on long-term effects [5,6]. Therefore, it is of great clinical significance to observe the effects of the femtosecond SMILE and femtosecond LASIK on postoperative long-term stabilities of tear film and cornea.

Tear film on normal ocular surface is a kind of hydrogel with multiple biological components. It has the functions of protecting, moisturizing and nourishing cornea. When there are some abnormal changes in quality, quantity or dynamics of tear, the tear film stability will be affected, and then can lead to dry eye symptoms such as dryness and burning sensation [12,13]. The results of this study showed that at 1 and 3 months after operation, the NI-BUT value and SIt value of the SMILE group were significantly higher than those in the FS-LASIK group ($P<0.05$), which indicated that the SMILE group had better tear film stability, the SMILE procedure can effectively decrease the damage for corneal nerve and the disturbance to tear film stability; In the SMILE group, the NI-BUT value and SIt value at 1 month after operation were significantly lower than those before operation ($P<0.05$), and there were no statistically significant differences between the NI-BUT value and SIt value at 3, 6 and 12 months after operation and those before operation ($P>0.05$). In the FS-LASIK group, the NI-BUT value and SIt value at 1 and 3 months after operation were significantly lower than those before operation ($P<0.05$), and there were no statistically significant differences between the NI-BUT value and SIt value at 6 and 12 months after operation and those before operation ($P>0.05$). The above-mentioned results showed that the NI-BUT value and SIt value of the SMILE group recovered faster and had recovered to the preoperative level since 3 months after operation, and had been maintained stably until 12 months after operation. However, the NI-BUT value and SIt value of the FS-LASIK group demonstrated slower recovery. At 3 months after operation, they were still lower and recovered to the preoperative level until 6 to 12 months after operation. This is mainly because the femtosecond SMILE is a kind of flapless microresecting surgery, its advantages such as small incision and light damage for corneal nerve are conducive to rapid recovery of nervous tissue. For these reasons, the NI-BUT value and SIt value of the SMILE group demonstrated faster recovery and better tear film stability [14]. On the contrary, the FS-LASIK impairs afferent sensory nerve fibers during the making of corneal flap and ablation of corneal stroma, and then weakens corneal surface perception, decreases tear clearance rate and tear film stability [15-17]. However, these injuries can also recover in a long term after operation.

Posterior corneal surface height is an important factor for corneal stability. After corneal refractive surgery, the corneal thickness will be significantly decreased, the posterior corneal surface morphology will be changed, and then the refractive regression in some patients may occur, the long-term efficacy of operation can further be affected, and even the symptoms such as keratoconus and iatrogenic corneal ectasia may be induced. Therefore, it is of great value to guarantee the stability of posterior corneal surface height for ensuring curative effect and preventing postoperative complications [18,19]. The results of this study showed that at 1, 3, 6 and 12 months before and after operation, there were no statistically significant differences in posterior corneal surface height between the two groups ($P>0.05$). This showed that there were no significant differences in posterior corneal surface heights at different times after operation between the two operative procedures. It may be because all the subjects in this study had low or medium myopia with spherical refraction of less than -6.00 D. In the treatment of this kind of low or medium myopia, the ablation depth of corneal stroma is shallow and the damage to corneal structure is light and meanwhile, the posterior corneal surface morphology is not significantly affected. These research results are consistent with those of Min et al. [20].

In conclusion, it was found in this study that there were no significant differences in the changes of posterior corneal surface height between the femtosecond SMILE and femtosecond LASIK. However, based on obvious advantages in tear film stability, especially in recovery course at 1 and 3 months after operation. Thus, the femtosecond SMILE is worthy of clinical application.

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