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Visual outcomes and visual function following SMILE for myopia and myopic anisometropia

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飞秒激光 SMILE 矫正近视及近视性屈光参差患者的视觉效果与视觉功能

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摘要

目的:评估飞秒激光小切口角膜微透镜取出术(SMILE)治疗非弱视成人近视性屈光参差的视觉结果与视觉功能。

方法:前瞻性对比队列研究。纳入 2015 年 10 月至 2016 年 1 月在中山眼科中心连续接受 SMILE 手术治疗近视或近视散光的患者。根据双眼等效球镜度差值≥1.50 D 将其分为两组:屈光参差性近视组(双眼等效球镜度差值≥1.50 D)和非屈光参差性近视组(双眼等效球镜度差值<1.50 D)。于术前及术后 1 wk、1、3、6 mo 分别测量屈光状态、裸眼与矫正远视力(UDVA 与 CDVA),以及视觉功能参数,包括融合性聚散幅度、立体视锐度和水平隐斜视。

结果:研究共纳入 49 例 98 眼,其中屈光参差组 19 例 38 眼,男 11 例,女 8 例,平均年龄 25.4±6.2 岁,非屈光参差性近视组 30 例 60 眼,男 19 例,女 11 例,平均年龄 26.8±4.6 岁。术后 6 mo,非屈光参差组的矫正视力(CDVA)显著优于屈光参差组($P=0.036$)。然而,两组的安全性和有效性指数未见显著差异。术后 6 mo,屈光参差组的融合性聚散幅度(破裂点与恢复点)下降($P=0.005$ 和 $P=0.03$),且显著低于非屈光参差组($P=0.029$ 和 $P=0.046$)。与术前及术后 1 wk 相比,两组在术后 1、3、6 mo 的远近立体视均有显著改善(均 $P<0.05$)。两组术后在远近距离的眼位偏斜量均未出现有临床意义的改变。

结论:SMILE 是矫正非弱视成人近视性屈光参差的一种可预测、有效且安全的方法。尽管融合性聚散幅度发生变化,但术后立体视功能可以得到改善。

关键词:飞秒激光小切口角膜微透镜取出术;屈光参差;立体视觉;聚散幅度

Abstract

• AIM: To evaluate visual outcomes and visual function in nonamblyopic adults with myopic anisometropia treated with small incision lenticule extraction (SMILE).

• METHODS: Prospective comparative cohort study. The consecutive patients who underwent SMILE for the treatment of myopia or myopic astigmatism at Zhongshan Ophthalmic Center (Guangzhou, China) between October 2015 and January 2016 were included. They were divided into two groups based on the bilateral difference of a spherical equivalent (SE) refraction ≥1.50 D: the anisometropic myopia group (interocular SE difference ≥1.50 D) and non-anisometropic myopia group (interocular SE difference < 1.50 D). Refractive status, uncorrected and corrected distance visual acuity (UDVA and CDVA), and visual function parameters including fusional vergence amplitude, stereoacuity and horizontal phoria were measured preoperatively and at 1 wk, 1, 3 and 6 mo after surgery.

• RESULTS: A total of 49 cases (98 eyes) were included in the study, and 19 cases (38 eyes) in the anisometropic group, including 11 males and 8 females, with a mean age of 25.4±6.2 y, and 30 cases (60 eyes) in the non-anisometropic myopia group, including 19 males and 11 females, with a mean age of 26.8±4.6 y. The CDVA of the non-anisometropia group was significantly better than that of the anisometropia group 6 mo postoperatively ($P=$

0.036). However, the safety and efficacy indexes of the two groups did not show significant differences. The fusional vergence (break point and recovery point) of the anisometropia group decreased (P=0.005 and P=0.03) and was significantly lower than that in the non-anisometropia group at 6 mo post operatively (P=0.029 and P=0.046). Both groups showed a significant improvement in distance and near stereopsis at 1, 3 and 6 mo in comparison with the preoperative baseline and 1 wk postoperatively (all P<0.05). No clinically significant change in the amount of ocular alignment in terms of distance and near deviation postoperatively in either groups.

• CONCLUSION: SMILE is a predictable, effective, and safe method for correcting myopic anisometropia in adults without amblyopia. Although the fusional vergence amplitudes changed, stereopsis can be improved after surgery.

• KEYWORDS: small incision lenticule extraction; anisometropia; stereoacuity; vergence amplitude
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INTRODUCTION

Anisometropia is an unequal refractive condition of the two eyes, which may lead to dysfunction in central fusion function, leading to binocular vision including asthenopia, binocular vision dysfunction, and in more severe cases, strabismus or amblyopia[1-2]. While spectacles and contact lenses remain the traditional treatments for anisometropia, an increasing number of people are opting for refractive surgery to correct this condition[3]. Small incision lenticule extraction (SMILE) procedure classified as a minimally invasive corneal refractive surgery suitable for patients aged 18-50 y with myopia extends from -1.00 to -10.00 diopters (D) and astigmatism ≤ -5.00 D[4-5]. Key advantages include no corneal flap creation, high biomechanical stability, lower postoperative dry eye risk and rapid visual recovery. However, postoperative complications as dry eye, keratitis and ectasia should not be underestimated[6]. This technique has been established as a safe and effective corneal refractive procedure for the treatment of myopia and myopic astigmatism because of its safety, efficacy, predictability, and fewer valuation-related complications[7-8].

While previous studies have established the predictability and accuracy of corneal refractive surgerieswhich encompasse SMILE, laser *in situ* keratomileusis (LASIK) and photorefractive keratectomy (PRK) in nonamblyopic adults with myopic anisometropia and documented the impact of anisometropia on postoperative corneal morphology and higher-order aberrations[9-11], a critical gap remains: no comprehensive study has directly compared refractive outcomes (efficacy, safety, stability) and visual function between nonamblyopic adults with versus without myopic anisometropia following SMILE. Moreover, regarding myopic anisometropia, the visual development has been completed, the impact of SMILE on visual functions such as vergence amplitude, stereoacuity, and horizontal phorias remains underexplored in the scientific literature. To address this gap, a prospective cohort study was conducted with the primary aim of comparing the refractive outcomes and visual function of SMILE among nonamblyopic adults with or without myopic anisometropia. We evaluated the following outcome measures: corrected distance visual acuity (CDVA), uncorrected distance visual acuity (UDVA) and spherical equivalent (SE) were for comparing the safety, efficacy, and predictability between nonamblyopic adults with versus without myopic anisometropia following SMILE.

PARTICIPANTS AND METHODS

Ethical Approval All participants provided written informed consent before enrollment in the study. The study protocol was approved by the Ethics Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University (No.2013MEKY036) and was conducted in accordance with the tenets of the Declaration of Helsinki. Our research was registered by the clinical trial (No.ISRCTN26161084).

This was a prospective comparative cohort study conducted at the Zhongshan Ophthalmic Center (Guangzhou, China) between October 2015 and January 2016. It included 49 consecutive patients undergoing SMILE for the correction of myopia or myopic astigmatism. The division into two groups in the current study was based on the criterion of a ≥1.50 D interocular difference in SE refraction: the anisometropic and non-anisometropic myopia groups, defined by an interocular SE difference of ≥1.50 D and <1.50 D, respectively[9].

Final enrollment included 19 patients in anisometropic myopia group and 30 patients in non-anisometropic myopia group (Table 1).

Eligible participants were aged 18 to 30 y, stable myopia with ≥1 y of follow-up and a CDVA of 20/20 or better, SE of -1.00 to -10.00 D with or without myopic astigmatism (≤-2.0 D), eligible for myopic laser refractive surgery, presenting with refractive error as the sole anterior segment anomaly. Exclusion criteria included any ocular surface disease, along with a history of corneal/intraocular surgery, ocular trauma, keratoconus, cataract, or systemic collagen, vascular, or autoimmune diseases. Moreover, participants with manifest strabismus (*e.g.*, tropia detectable without dissociation) were excluded to minimize confounding effects on the outcomes measured, particularly for tasks requiring binocular alignment. However, we did not exclude participants with latent strabismus (*e.g.*, phorias detectable only with dissociation).

Table 1 Demographic and preoperative characteristic of anisometropia and non-anisometropia groups

Parameters	Anisometropiagroup (n=19)	Non-anisometropia group (n=30)	P
Eyes(n)	38	60	
Age ($\bar{x}\pm s$, y)	25.4±6.2	26.8±4.6	0.575
Sex (male/female)	11/8	19/11	-
Binocular sphere($\bar{x}\pm s$, D)	-4.52±1.78	-4.59±1.72	0.843
Binocular range (D)	-1.75 to -9.25	-1.5 to -9.125	-
Binocular SE ($\bar{x}\pm s$, D)	-4.94±1.78	-4.84±1.70	0.788
Binocular CDVA ($\bar{x}\pm s$, LogMAR)	-0.09±0.08	-0.11±0.05	0.180
Anisometropia ($\bar{x}\pm s$, D)	2.24±0.93	0.38±0.31	0.000
Baseline alignment (distance and near)			
Orthophoria	5 (13%)	11 (18%)	
Exophoria (1-8 PD)	4 (11%)	26 (44%)	
Exophoria (>8 PD)	15 (39%)	2(3%)	
Esophoria (1-8 PD)	11 (29%)	12 (20%)	
Esophoria (>8 PD)	3(8%)	9 (15%)	

D: Diopters; SE: Spherical equivalent; PD: Prism diopters; CDVA: Corrected distance visual acuity; UDVA: Uncorrected distance visual acuity.

Patient Assessment All examinations were conducted preoperatively and at 1 wk, 1, 3, and 6 mo postoperatively. Patient evaluations comprised monocular UDVA and CDVA measured by Snellen charts, objective and manifest refraction, ocular anterior segment by slit lamp. The specific instruments employed were the Wavelight Oculyzer II (Alcon Laboratories, Inc.) for topography, the AC Master ultrasound pachymeter (Carl Zeiss Meditec AG) for corneal thickness, and the TX-20 noncontact tonometer (Canon, Inc.) for intraocular pressure measurement. The following ocular parameters were assessed to characterize visual function: divergence and convergence amplitudes (near and distance), stereoacuity (near and distance), and near and distance horizontal phorias. For both the distance and near measurements, the divergence amplitude was measured first to avoid excessive vergence values induced by convergence stimulation[12-13]. We used Risley rotary prisms to evaluate the horizontal vergence ranges. Horizontal Risley prisms were introduced before both eyes and progressively increased in power during fixation on a line of Snellen E optotypes. Equal amounts of rotatory prism were slowly added in front of each eye using both base-in and base-out prism to test fusional vergence at a constant velocity (approximately 2 Δ/s) until horizontal diplopia was first reported, which was recorded as the break value.

The examiner then reduced the prism power until the subject refused diplopic images to determine the recovery point (recovery value). For the Distance Randot Stereotest, subjects viewed the stereotest booklet (Distance Randot Stereotest, Stereo Opticals Co., Inc., range: 400-60 arcsec) at 3 m in a normally illuminated room lighting conditions (~500 lx) while wearing polarizing glasses[14-15]. For the Randot Circles Test, subjects viewed the Randot circles test (Stereo Randot Test 2 for Adults, Stereo Optical, ranged: 400-12.5 arcsec) at 40 centimeters in a normally illuminated room lighting conditions (~500 lx) while wearing polarizing glasses[16-17]. Participants who used corrective spectacles wore the polarizing glasses over their lenses. For subjects who did not see the maximum chart, the value of stereoacuity was recorded as 800 arcsec for the statistical analysis.

Heterophoria was measured using the von Graefe technique. A 6-Δ base-up prism was placed before the right eye for dissociation, while a Risley rotary prism before the left eye was used to neutralize the horizontal deviation and quantify the measurement[18]. We calculated the angle of deviation to analyze the actual change in ocular misalignment, with positive values indicating an increase and negative values a decrease in deviation, irrespective of the initial type of misalignment. Ocular alignment was categorized as follows: orthophoria (0 prism diopters, PD), small-angle heterophoria (1-8 PD), and large-angle heterophoria (>8 PD)[19].

Surgical Techniques A 500-kHz femtosecond laser platform (VisuMax 500, Carl Zeiss Meditec AG) was utilized for all surgical procedures. Parameters of femtosecond laser are listed: the spot distance and tracking spacing were both set at 4.5 mm for the lenticule, 1.8 mm for the lenticule side-cut, 4.5 mm for the cap, and 2.0 mm for the cap side-cut. The lenticule diameter was set between 6.5 and 7.5 mm in accordance with the patient's pupil size measured in the dark. Side cuts made to access the lenticule were set 90° apart at a circumferential width of 2.0 mm. The cap thickness in all patients was for 120 μm. After the lenticule was separated completely, it was extracted using lens forceps for femtosecond laser surgery (66 Vision Tech Co, Ltd., Suzhou, China) through a single 2.0-mm incision superotemporally. Postoperatively, all patients received levofloxacin eye drops (Santen Pharmaceutical Co., Ltd., Japan) administered four times daily for the first 2 weeks for prophylaxis; tobramycin/dexamethasone (TobraDex®; Alcon) four times daily during

the first week to control inflammation; and sodium hyaluronate (Ursapharm) four times daily for 1 mo for ocular surface lubrication.

Statistical Analysis Data were analyzed using SPSS (v16.0; SPSS Inc.). Normality was assessed with the Kolmogorov-Smirnov test. Based on its result, comparisons between groups at each time point were made with the paired Student's *t*-test (for normal data) or the Wilcoxon signed-rank test (for non-normal data). One-way analysis of variance (ANOVA) was employed to compare convergence and divergence amplitude at different time periods. Owing to the non-linear value of stereoacuity, the Kruskal-Wallis test was utilized for evaluating the temporal changes in distance and near stereoacuity. All stereoacuity values were recorded as log (arcsec) values and made logarithmic transformation prior to analysis. All quantitative data are presented as mean ± standard deviation. A P value of < 0.05 was considered statistically significant.

RESULTS

Demographic Data This study enrolled a cohort of 49 patients (98 eyes) and allocated to the anisometropic ($n=38$ eyes) and non-anisometropic (n = 60 eyes) myopia groups. The baseline characteristics of both groups are summarized in Table 1. In brief, two groups differed significantly in anisometropia (anisometropic: 2.24 ± 0.93 D *vs* non-anisometropic: 0.38±0.31 D; $P=0.000$). No significant differences were observed between the two groups regarding of patients' age ($P=0.575$), preoperative sphere ($P=0.843$), SE ($P=0.788$) or CDVA (0.180).

Safety and Efficacy No complications were observed intraoperatively, perioperatively, or postoperatively in either group. There was no loss of more than two lines in any of the two groups. For the anisometropia subgroup ($n=19$), 1 case (5%), 4 cases (21%), 1 case (5%) and 2 cases (11%) with ≥1-line VA reduction at 1 wk, 1, 3 and 6 mo postoperatively. For the non-anisometropia subgroup ($n=30$), 10 cases (33%), 8 cases (27%), 7 cases (23%) and 7 cases (23%) with ≥1-line VA reduction at 1 wk, 1, 3 and 6 mo postoperatively. When analyzed by eye count rather than patient count, 5 eyes (13%), 6 eyes (16%), 2 eyes (5%) and 6 eyes (16%) in the anisometropia group lost one line at 1wk, 1, 3 and 6 mo postoperatively, respectively. In the non-anisometropia group, it was 17 eyes (28%), 10 eyes (17%), 10 eyes (17%) and 12 eyes (20%) during the postoperative period (at 1 wk, 1, 3, and 6 mo; Figure 1). Whenanalyzed on a per-patient basis, UDVA and CDVA No statistically significant differences were observed between the anisometropia, an absence of statistically significant differences between the anisometropia and non-anisometropia groups throughout the 6-month follow-up period (assessed at 1 wk, 1, 3, and 6 mo postoperatively (Table 2). No statistically significant differences in the safety index (postoperative CDVA/preoperative CDVA) were found in anisometropic versus non-anisometropic groups at 1 wk (1.14 *vs* 1.07, $P=0.126$), 1 (1.13 *vs* 1.11, $P=0.807$), 3 (1.17 *vs* 1.11, $P=0.293$) and 6 mo (1.14 *vs* 1.15, $P=0.508$) after SMILE. The efficacy index (postoperative UDVA/preoperative CDVA) did not differ significantly between groups at 1 wk (1.12 *vs* 1.04, $P=0.124$), 1 (1.11 *vs* 1.08, $P=0.807$), 3 (1.17 *vs* 1.11, $P=0.293$) and 6 mo (1.12 *vs* 1.10, $P=0.909$) after SMILE.

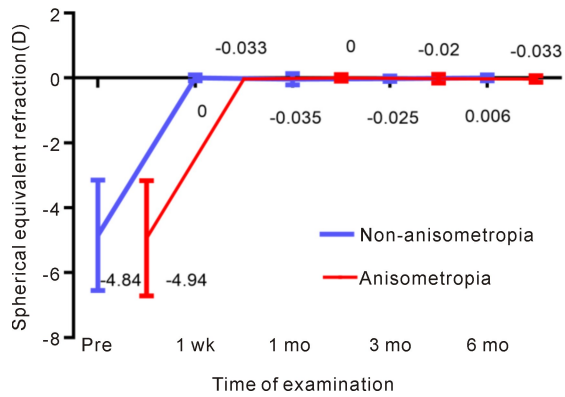

Figure 1 Mean spherical equivalent of two groups plotted as a function of time postoperatively.

Refraction, Predictability The achieved SE at postoperation was within ±0.50 D of the attempted power in all eyes. The slope and correlation coefficient between the attempted and achieved manifest SE were 1.0030 and 0.9970 for the non-anisometropia group, 0.9996 and 0.9966 for the anisometropia group (Figure 1), respectively.

The change inthe manifest SE is shown in Figure 2. No significant differences were found in the SE at 1 wk ($P=0.111$), 1 ($P=0.252$), 3 ($P=0.734$) and 6 mo ($P=0.101$) postoperatively between the two groups.

Visual Function Extraocular motility examination showed no cases of vertical deviation or decompensated phoria in either group before and after SMILE. In the anisometropia group, the positive fusional vergence near (break point and recovery point) decreased 6 mo postoperatively ($P=0.005$ and $P=0.03$, respectively; Table 3). However, the change in negative and positive fusional vergence was not statistically significant between the preoperative and postoperative follow-ups in the non-anisometropia group (Table 4). Distance negative fusional vergence parameters (break point and recovery point) in the anisometropia group showed a marked decrease compared to the non- anisometropia group 6 mo after surgery (break points of anisometropia group: 8.3±2.2 *vs* non-anisometropia group: 9.9±2.7; $P=0.029$; recovery points of anisometropia group: 4.9±2.1 *vs* non- anisometropia 6.2±2.0; $P=0.046$).

The mean of the measured nearand distance stereopsis threshold (log seconds of arc) was recorded as 1.98±0.28 and 1.75±0.33 between the anisometropia and non- anisometropia group before SMILE respectively ($P=0.024$), Significant difference was observed in stereopsis threshold at 6 mo after SMILE ($P=0.008$). Compared to the values before SMILE, there were significant improvements in the postoperative distance and near stereopsis threshold of the two groups at 3,

Table 2 Compared of UDVA and CDVA after small incision lenticule extraction between anisometropia and non-anisometropia groups ($\bar{x}\pm s$, LogMAR)

Parameters	Anisometropia group ($n=19$)	Non-anisometropia group ($n=30$)	P
CDVA			
Preoperative	−0.09±0.06	−0.11±0.05	0.491
1 wk	−0.14±0.04	−0.13±0.05	0.337
1 mo	−0.13±0.04	−0.15±0.04	0.166
3 mo	−0.15±0.04	−0.15±0.03	0.545
6 mo	−0.14±0.05	−0.16±0.03	0.113
UDVA			
Preoperative	-	-	-
1 wk	−0.14±0.05	−0.11±0.05	0.420
1 mo	−0.12±0.05	−0.12±0.07	0.566
3 mo	−0.14±0.05	−0.13±0.06	0.919
6 mo	−0.14±0.05	−0.14±0.05	0.856

CDVA: Corrected distance visual acuity; UDVA: Uncorrected distance visual acuity.

Table 3 Means and standard deviations for data recorded in anisometropia group: negative and positive fusional vergence (break and recovery points), ocular alignment $\bar{x}\pm s$

Vergence test	Pre	1 wk	1 mo	3 mo	6 mo
BI to break at 6 m	8.3±3.8	8.6±2.3	9.3±3.7	9.4±4.2	8.3±2.2
BI to recovery at 6 m	5.3±4.7	6.1±1.9	5.8±2.0	6.3±2.4	4.9±2.1
BO to break at 6 m	12.4±6.1	13.2±4.7	12.5±4.6	11.6±4.0	12.5±5.8
BO to recovery at 6 m	9.1±5.8	9.2±3.7	7.7±4.1	7.5±2.9	8.3±4.3
BI to break at 40 cm	21.5±6.9	20.2±5.1	20.8±6.2	21.3±6.0	21.3±5.6
BI to recovery at 40 cm	12.6±5.9	12.2±5.8	13.4±5.2	13.1±4.6	14.2±4.9
BO to break at 40 cm	25.9±6.6	23.2±7.3	21.4±8.5	19.4±6.9	20.3±6.8[a]
BO to recovery at 40 cm	16.4±6.9	14.2±7.5	12.5±5.4	10.9±5.9	12.2±6.5[a]
Ocular alignment at 6 m	1.09±5.17 (toward Eso)	0.66±4.93 (toward Eso)	−0.13±4.83 (toward Exo)	−1.56±3.93 (toward Exo)	−2.41±3.35 (toward Exo)
Ocular alignment at 6 m (absolute value)	3.93±3.42	4.18±2.51	3.55±3.17	3.21±2.47	2.93±2.87
Ocular alignment at 40 cm	−2.46±5.84 (toward Exo)	−3.18±4.87 (toward Exo)	−4.53±4.14 (toward Exo)	−6.19±4.41 (toward Exo)	−5.87±5.18 (toward Exo)
Ocular alignment at 40 cm (absolute value)	4.70±4.14	4.29±3.87	4.74±3.89	5.92±4.44	6.61±4.14

[a]Significantly different between the preoperative level and 6 mo postoperatively in anisometropia group ($P<0.05$). Pre: Pre-operation; BI: Base-in prism for divergence; BO: Base-out prism for convergence; Eso: Esophoria; Exo: Exophoria.

and 6 mo postoperatively (all $P<0.05$; Figure 3).

Preoperatively, for the anisometropia group (a total of 19 patients), 16 (84%) and 17 (89%) patients with asymptomatic ocular misalignment, 7 had exodeviation at distance and 12 at near fixation, while 9 had esodeviation at distance and 5 at near fixation. Additionally, small-angle heterophoria was observed in 42% of patients, and large-angle heterophoria in 18%. In the non-anisometropia group ($n=30$), asymptomatic ocular misalignment was present in 22 patients (73%) at distance and 27 (90%) at near fixation. The distribution of manifest deviations was as follows: 11 had exodeviation at distance and 17 at near; 11 had esodeviation at distance and 10 at near. Additionally, small-angle heterophoria was observed in 63% of patients, and large-angle heterophoria/heterotropia in 18%. Analysis of the direction of heterophoria shift showed that the anisometropia group exhibited a transient shift toward esophoria at 1 wk postoperatively for distance fixation, with a mean magnitude of $0.66^{\Delta}\pm4.93^{\Delta}$. This was followed by a shift toward exophoria at the subsequent time points (1, 3, and 6 mo), with mean magnitudes of $-0.13^{\Delta}\pm4.83^{\Delta}$, $-1.56^{\Delta}\pm3.93^{\Delta}$, and $-2.41^{\Delta}\pm3.35^{\Delta}$, respectively. For near fixation, a consistent shift toward exophoria was observed at all postoperative intervals (1 wk, 1, 3, and 6 mo), with mean magnitudes of $-3.18^{\Delta}\pm4.87^{\Delta}$, $-4.53^{\Delta}\pm4.14^{\Delta}$, $-6.19^{\Delta}\pm4.41^{\Delta}$, and $-5.87^{\Delta}\pm5.18^{\Delta}$, respectively (Table 3). In contrast, the non-anisometropia group showed a transient shift toward esophoria at 1 wk and 1 mo postoperatively for distance fixation, with mean magnitudes of $1.02^{\Delta}\pm4.52^{\Delta}$ and $0.65^{\Delta}\pm5.03^{\Delta}$, respectively. This was followed by a shift toward exophoria at later time points (3 and 6 mo), with mean magnitudes of $-1.6^{\Delta}\pm5.02^{\Delta}$ and $-1.88^{\Delta}\pm3.81^{\Delta}$. For near fixation, a consistent shift toward exophoria was observed at all intervals (1 wk, 1, 3, and 6 mo), with mean magnitudes of $-0.8^{\Delta}\pm5.31^{\Delta}$, $-2.90^{\Delta}\pm5.31^{\Delta}$, $-3.75^{\Delta}\pm5.40^{\Delta}$, and $-3.60^{\Delta}\pm4.97^{\Delta}$, respectively (Table 4). We found no statistically

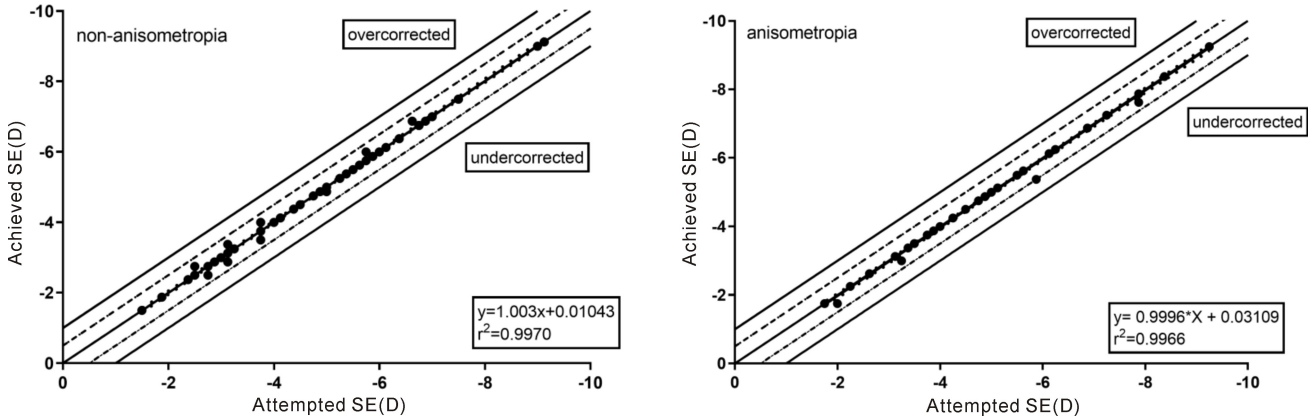

Figure 2 Predictability: attempted versus archived manifest SE corrections of two groups made 6 mo after small incision lenticule extraction SE: Spherical equivalent.

Table 4 Means and standard deviations for data recorded in non-anisometropia group: negative and positive fusional vergence (break and recovery points), ocular alignment

Vergence test	Pre	1 wk	1 mo	3 mo	6 mo
BI to break at 6 m	9.1±2.9	10.2±4.2	9.5±2.8	9.9±3.2	9.9±2.7
BI to recovery at 6 m	6.2±3.7	6.6±2.9	6.5±3.1	6.6±2.6	6.2±2.0
BO to break at 6 m	14.6±6.1	14.0±5.4	12.9±5.5	14.0±4.6	14.3±3.2
BO to recovery at 6 m	10.3±5.0	9.7±3.9	8.9±5.5	9.4±3.7	9.4±3.0
BI to break at 40 cm	21.5±5.4	19.8±5.2	21.8±3.9	21.4±4.3	21.2±3.9
BI to recovery at 40 cm	11.6±5.2	11.2±5.1	11.0±5.0	11.4±5.3	12.3±4.5
BO to break at 40 cm	24.7±8.1	24.4±7.1	23.8±7.0	23.7±6.3	23.1±6.5
BO to recovery at 40 cm	15.9±7.9	15.9±6.9	14.4±7.0	13.4±5.5	13.9±6.2
Ocular alignment at 6 m	0.8±4.69 (toward Eso)	1.02±4.52 (toward Eso)	0.65±5.03 (toward Eso)	−1.6±5.02 (toward Exo)	−1.88±3.81 (toward Exo)
Ocular alignment at 6 m (absolute value)	3.40±3.27	3.65±2.64	4.02±3.01	4.37±2.85	3.65±2.10
Ocular alignment at 40 cm	0.18±6.74 (toward Eso)	−0.80±5.13 (toward Exo)	−2.90±5.31 (toward Exo)	−3.75±5.40 (toward Exo)	−3.60±4.97 (toward Exo)
Ocular alignment at 40 cm) absolute value)	5.38±3.93	4.03±3.19	4.47±3.87	5.58±3.38	5.10±3.34

BI: Base-in prism for divergence; BO: Base-out prism for convergence; Eso: Esophoria; Exo: Exophoria.

significant differences in the mean absolute value of ocular alignment between the preoperative and postoperative visits between the two groups. Moreover, the mean absolute value of ocular alignment in terms of distance and near deviation was clinically insignificant at any time point during the entire follow-up between the two groups.

DISCUSSION

The aim of this study was to evaluate the safety, efficacy, and visual function following myopic SMILE in eyeswith or without myopic anisometropia. By analyzing the outcomes in the anisometropia and groups not exhibiting anisometropia, these findings indicate that SMILE yielded similar results in the anisometropia group *vs* to the non-anisometropia group matched on the basis of age, follow-up duration, manifest refraction spherical equivalent (MRSE), sphere, CDVA, together with surgical parameters. By analyzing on a per-patient basis, UDVA and CDVA revealed no statistically significant differences between the anisometropia and non-anisometropia groups throughout the 6-month follow-up period (assessed at 1 wk, 1, 3, and 6 mo postoperatively (Table 2). For non-anisometropic patients, the approximate maximum CDVA was reached at 3 mo, which corresponds to the known 3- to 6-month period for refractive stabilization reported in the literature[20]. For anisometropic patients, CDVA continues to change for over 6 mo (Table 2), indicating that plastic changes in the visual cortex are involved and that these changes may underlie the slow postoperative CDVA variations seen in anisometropic patients[21-22]. Similarly, CDVA of LASIK and PRK continues to change for over 24 mo in anisometropic patients[10]. These results may implicate corneal refractive surgery for anisometropia may trigger a slow-acting neural plasticity, which enhances visual performance[23-24]. Concerning efficacy, the anisometropia group demonstrated comparable final MRSE and refractive accuracy relative to the non-anisometropia group. No significant difference was found in the proportion of patients achieving a postoperative manifest SE within 0.50 D between both groups (Figure 1).

After 6 months of follow-up, overall, 100% eyes achieved a postoperative refraction within ±0.50 D of the SE of the two groups (Figure 2). Zhao *et al*[25] found 86.1% of the SMILE treated eyes were within ±0.50 D. Compared with other

refractive surgery, Vuori *et al*[10] indicated that 73% of eyes in the isometropic control group achieved a postoperative refraction within ±0.50 D of the attempted correction after PRK or LASIK. Another study also suggested the accuracy rates of their control isometropic group treated with PRK were 74%. However, in their myopic anisometropic group, accuracy rate significantly decreased[9]. We reported greater accuracy rate observed in the myopic group. The higher accuracy rates observed in our study could be explained by the milder degree of anisometropia. A threshold of 1.5 D in manifest refraction difference between eyes was used to define anisometropia and most eyes of anisometropia group having a mean interocular difference of less than 2.5 D. Moreover, previous studies only compared outcomes of more myopic anisometropic eyes. In our study, we compared both eyes of the same person in the anisometropia and non-anisometropia groups. An efficacy index of 1.12 and 1.10 and safety index of 1.14 and 1.15 were obtained in anisometropia and non-anisometropia group respectively at 6 mo after SMILE, which were in line with previously reported values[26-27]. Good visual acuity is the premise for discussing the visual quality. No significant difference was found in the efficacy and safety indices between the two groups, which is consistent with the results of a previous study[11]. In the anisometropia cohort, a sustained trend of UDVA improvement was observed throughout the follow-up period. This change was statistically significant compared to preoperative levels, yet no intergroup differences emerged when contrasted with non-anisometropia controls. While neuronal plasticity—a critical determinant of amblyopia treatment efficacy—is conventionally reserved for early childhood, emerging evidence suggests substantial plasticity persists even in the adult visual system[28-29]. Nevertheless, this study primarily aimed to evaluate the technical feasibility of refractive surgery and its impact on visual acuity in anisometropic patients, rather than to establish causal neurobiological mechanisms. Our data focused on clinical outcomes, including refractive error correction and binocular function, aligning with analogous studies prioritizing surgical metrics over neuroplasticity analysis. Additionally, the inclusion criteria mandated a CDVA of 20/20 or better, thereby explicitly excluding amblyopic cases.

In addition to the standard reporting of refractive outcomes, our studyevaluated the change in visual function including fusional vergence amplitude parameters, ocular alignment, and stereoacuity, in myopia with or without anisometropia following SMILE. Myopia is frequently associated with exodeviation, particularly convergence insufficiency type, with the mean SE significantly influencing near-angle deviation measurements[30-31]. In our study, up to 18 (38%) and 29 (59%) of the 49 myopic patients exhibited distance and near exodeviation, respectively. Despite this and the growing popularity of refractive surgery, the incidence of ocular misalignment specifically attributable to myopic surgery is poorly defined. Although 18% patients in our study with large angle heterophoria/heterotropia pre-operation, those with a history of strabismus or diplopia, prisms in glasses were excluded. We investigated the impact of myopic SMILE on exodeviation which is different with previous studies included a pre-selected population with various manifest strabismus[32-33]. In the anisometropia group, the positive fusional vergence near decreased 6 mo postoperatively (Table 3). However, there were no statistically significant differences in the negative and positive fusional vergence preoperatively and postoperatively in the non-anisometropia group (Table 4). Previous studies have reported a significant reduction in the convergence amplitude after PRK, which might exacerbated near exodeviation after surgery[34-35]. In the current study, participants in the anisometropia group had lower distance divergence amplitude than those in the non-anisometropia group after SMILE. However, the ocular alignment value remained unchanged postoperatively. Similarly, Godts *et al*[36] reported no variation in ocular alignment or visual function following surgery, even among patients with manifest deviation. We identified that SMILE for anisometropia myopia, in general, did not find to exert a significant influence on ocular alignment.

Stereoacuity, which is considered the ability to perceive depth and objects in a three-dimensional space, is the finest element of binocular vision[37]. Kirwan and O'Keefe[38] confirmed that myopia combined with anisometropia can result in diminished stereoacuity because it leads to inconsistency in the size of the binocular images despite the best correction. In the current study, we found that myopic patients with anisometropia had worse near stereoacuity than myopic patients without anisometropia preoperatively. However, no significant intergroup difference was detected was observed between both groups after SMILE. Furthermore, patients in both groups showed improved near and distance stereopsis after surgery (Figure 3). Consistent with our findings, Sarkar *et al*[39] indicated that near stereoacuity showed a significant improvement from approximately 40 to 20 seconds of arc 6 mo after SMILE. However, other studies have suggested that stereoacuity was not significantly affected by SMILE using Randot Circles and the near Frisby stereotest[40-41]. Compared with other refractive procedures, recent studies reported deterioration of stereoacuity after LASIK and PRK. Deterioration in stereoacuity could stem from several potential mechanisms, including alterations in ocular aberrations, corneal opacification, or epithelial irregularities, which warrants evaluation in future studies[42]. Kato *et al*[43] reported significant improvements in stereoacuity were observed in patients undergone implantable collamer lens implantation and explained these changes on the basis of a greater retinal magnification of images, elimination of prismatic effect of spectacles, correction of anisometropia, enhanced quality of vision in both eyes, and better near vision than distance vision preoperatively. Our primary findings show improved near and distance stereopsis after SMILE. The enhancement in stereoacuity may be attributed to improved visual acuity and reduced anisometropia , which optimize retinal image clarity

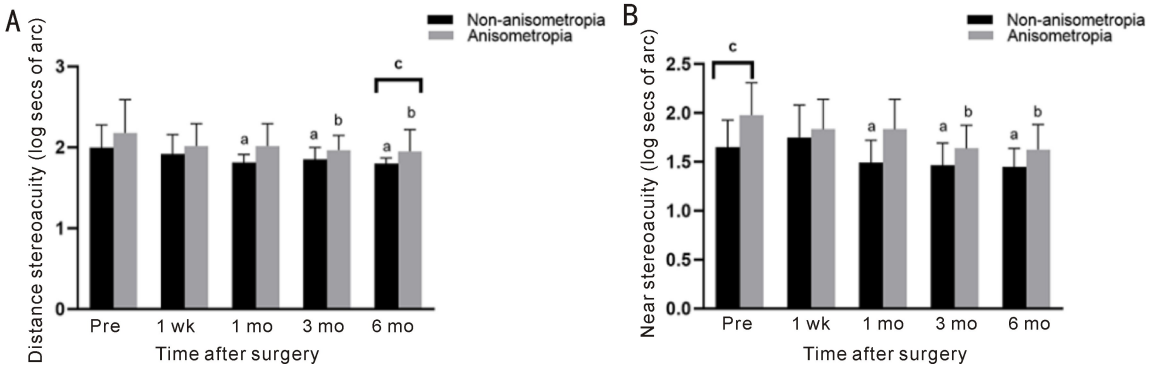

Figure 3 Level of distance (A) and near (B) stereopsis of preoperatively and each time after surgery Error bars showed the maximum or minimum. [a]Significantly different between the preoperative level and 1, 3 and 6 mo postoperatively in non-anisometropia group ($P \leqslant 0.001$); [b]Significantly different between the preoperative level and 1, 3 and 6 mo postoperatively in anisometropia group ($P \leqslant 0.001$); [c]Significantly different between two groups preoperatively ($P<0.05$).

and minimize binocular disparity. Through these mechanisms, cortical processing of binocular signals is enhanced, thereby strengthening fusion and improving stereopsis. Furthermore, compared SMILE with LASIK and PRK, better ocular surface stability and biomechanical strength, decreased higher-order aberrations and less postoperative dry eye incidence might improve binocular vision[44]. Although SMILE surgery improves retinal image clarity and induces short-term cortical stimulation, it does not enhance brain structure or function. Therefore, the full development of visual function remains dependent on extended time and accumulated visual experience. Vuori *et al*[45] reported that plastic changes may take place in the primary visual cortex from pre- to 12 mo post-refractive surgery in adult anisometropic patients. Therefore, it is valuable to investigate the potential of visual plasticity training to consolidate surgical outcomes and achieve durable visual quality restoration after SMILE.

Limitations of this pilot study mainly include its small samplesize specially in the anisometropic groups with only 38 eyes of anisometropia group. A larger cohort with a longer follow-up period may provide more evidence on whether fusional vergence amplitude, stereoacuity and horizontal phoria change after SMILE. Additionally, near point convergence, binocular accommodative facility, and accommodative convergence/accommodation ratio assessments refer to evaluate both accommodative and visual function were not originally part of our study design. Future studies should focus on accommodative and binocular dysfunctions using rigorously designed testing protocols, with the goal of establishing validated criteria for accurately diagnosing general binocular disorders.

In conclusion, myopic SMILE is effective and safe in achieving refractive and visual outcomes in eyes with anisometropia, as demonstrated in this comparative study. In adults with anisometropia, correcting the interocular refractive difference can lead to significant improvement in stereoscopic function. Although patients with myopic anisometropia should be informed that SMILE may reduce distance divergence amplitude compared to non-anisometropia controls, postoperative ocular alignment values showed no statistically significant variations. Our data also support the selection of SMILE as an established procedure for corneal stromal refractive surgeries for the correction of anisometropia.

Conflicts of Interest: Weng SB, None; Xiang DM, None; Liu T, None; Lin LM, None; Liu Q, None.

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