Influence of age on small incision lenticule extraction outcomes

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ABSTRACT

Purpose To evaluate the influence of patient's age at the time of surgery on small incision lenticule extraction (SMILE) refractive outcomes.

Methods This is a retrospective, consecutive, comparative study. We compared the refractive outcomes after myopic SMILE from two groups of patients divided by age (patients ≤35 and ≥40 years old). All eyes were evaluated preoperatively and at 1 and 6 months postoperatively. Main outcome measures were differences on efficacy, safety, predictability and astigmatic changes by vector analysis with ASSORT software between both study groups.

Results 102 matched eyes of 53 patients were included. Preoperatively, we evidenced no differences in the mean SE or astigmatism between groups. However, 6 months postoperatively we observed a significantly worse mean astigmatism (p=0.019), while not regarding SE, in the older population, with a trend towards undercorrection of the refractive cylinder in the ≥40 group. We also observed a statistically significant difference in the efficacy (0.86–1 month and 0.97–6 months in ≥40group vs 0.97–1 month and 1.07–6 months in the ≤35 group; p=0.003) and safety indexes (0.93–1 month and 1.04–6 months in ≥40 group vs 1.0–1 month and 1.11–6 months in the ≤35 group; p=0.008) at 6 months among groups.

Conclusions Post-SMILE refractive outcomes in those patients over 40 years of age, although acceptable, are not as good as those obtained in younger patients, showing a significantly lower efficacy and safety indexes, and poorer astigmatic outcomes, with a tendency towards undercorrection. We hypothesise that the increased corneal stroma stiffness in the aged group modifies the post-SMILE corneal stroma remodelling capacity, thus affecting the SMILE refractive and visual response.

INTRODUCTION

Small incision lenticule extraction (SMILE) is a flap-free intrastromal laser assisted refractive surgery procedure for the correction of myopia and myopic astigmatism that was first introduced in 2011.[1 2] In it, femtosecond laser is used to create an intrastromal lenticule that is extracted through a small corneal incision. SMILE has been reported to be an effective, safe and predictable refractive surgery solution.[3–13] Moreover, SMILE causes biomechanical changes in the cornea (by a loss of strenght), although these deleterious effect has been proven to be less after SMILE than after laser assisted in situ keratomileusis (LASIK).[14 15]

Although SMILE refractive outcomes have been extensively reported in the last few years by different authors,[3–13] only one previous study reports, independently, the SMILE outcomes in a presbyopic population.[16] Moreover, no study had focused before on comparing the SMILE outcomes between groups of different age: corneal stroma stiffness increases with age,[17] and as a consequence, corneal remodelling and biomechanical response to the lenticule extraction could differ among corneas with different underlying strength and stiffness (young vs aged corneas). In this scenario, refractive response to a SMILE procedure could differ according to the patient's age at the time of surgery.

The purpose of our study is to evaluate if patient's age at the time of surgery, and so the increased corneal stiffness over time,[17] influences the refractive outcome after SMILE for the treatment of myopia with or without myopic astigmatism.

MATERIALS AND METHODS

This is a retrospective, consecutive, comparative study. In order to evaluate the influence of patient's age on SMILE outcomes, we compared the refractive outcome of treated patients ≤35 years with the one obtained from patients ≥40 years of age. All included SMILE procedures were performed between November 2016 and September 2019 at Vissum Instituto Oftalmologico in Alicante (Spain). First 20 SMILE patients of both involved surgeons were excluded to avoid bias according to the initial learning curve and laser adjustment. Fifty-one consecutive eyes of patients ≥40 years of age were selected and subsequently matched with 51 eyes of patients ≤35 years, based on a preoperative refractive spherical equivalent (SE) difference within ±0.25 D for each pair.[18 19]

In order to avoid bias, eyes where monovision was targeted (always in the non-dominant eye) were excluded from the sphere refractive analysis. All eyes were included for the evaluation of the astigmatic outcome. Each patient signed a consent form in accordance with the Helsinki Declaration.

Inclusion criteria

Inclusion criteria was: myopia with or without mild to moderate astigmatism (≤3D of cylinder); mesopic pupil less than 7 mm; expected residual stromal bed under the cap >250 µm; preoperative central corneal thickness >490 μm and expected postoperative mean keratometry >35 D. Soft contact lenses were discontinued for at least 2

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weeks (4 weeks in case of rigid lenses) before the preoperative analysis and surgery.

Exclusion criteria

In order to obtain two well separated groups by age, patients ≤35 or ≥40 were included; patients between 36 and 39 years of age were excluded. Other exclusion criteria included: ocular comorbidities, nuclear lens sclerotic changes, irregular or suspicious topography, previous ocular surgery (except strabismus surgery) and severe amblyopia with a corrected distance visual acuity (CDVA) <20/100.

Preoperative assessment

The following tests were included: uncorrected distance visual acuity (UDVA); CDVA; manifest and cycloplegic refraction; slit-lamp biomicroscopy; intraocular pressure; ultrasonic pachimetry (OcuScan RxP, Alcon Laboratories, USA); corneal topography and 6 mm corneal aberrometry with MS-39 topographer (CSO, Italy); scotopic, low and high mesopic pupillometry with MS39 and fundus evaluation. Patients were prepared for surgery by applying 1 drop of oxybuprocaine hydrochloride and tetracaine hydrochloride. All eyes with astigmatism higher than 1D received correction of the intraoperative cyclotorsional error assisted by preoperative slit lamp manual marking at the horizontal axis as previously described.[20]

Surgical technique

All surgeries were performed by two experienced surgeons (JLAdB and JLA) using the VisuMax Femtosecond Laser System (Carl Zeiss Meditec AG, Germany) and applying an identical surgical technique and correction nomogram. The SMILE procedure was performed as previous described.[7] Briefly, in all cases lenticule diameter was between 6.5 and 7 mm, the cap thickness was set at 120 µm, the cap diameter was 7.5 mm, and only one corneal incision was performed with a length of 2,3 mm located at 140° in all right eyes and at 120° in all left eyes.

Postoperative follow-up

Patients were treated with a standard combination of tobramycin and dexamethasone (Tobradex; Alcon) eyedrops five times daily for a week, and lubricating eyedrops for at least 1 month. Postoperative examination was registered at 1 month and at 6 months for the purpose of this study. UDVA, manifest refraction with fogging, CDVA, slit-lamp biomicroscopy, corneal wavefront aberrations and topography were recorded. An experienced Good Clinical Practices certified optometrist performed all the postoperative tests.

Vector analysis of astigmatic changes

Vector analysis of astigmatic changes was performed according to the Alpins method with ASSORT software (ASSORT).[21] The following parameters were evaluated: target-induced astigmatism vector (TIA; the astigmatic change the surgery was intended to induce), surgically induced astigmatism vector (SIA; the real astigmatic change achieved by the surgery), and the difference vector (the additional astigmatic change required to meet the intended target of the initial surgery). In a perfect astigmatic correction, the TIA and SIA should have the same magnitude, so the difference vector is zero. Through these three values, the programme obtains other indices: magnitude of error (the arithmetic difference between the SIA and the TIA; positive for overcorrections and negative for undercorrections), the angle of error (the angle described by the SIA and TIA vectors), the index of success (calculated by dividing the difference vector by the TIA; the preferable value is zero), and the correction index (CI; the ratio obtained by dividing the SIA by the TIA). The preferable CI value is 1.0; values >1.0 reflect an overcorrection and values <1.0 reflect an undercorrection.

Statistical analysis

It was performed with the SPSS software package V.20.0 for Windows (SPSS). Normality of the study sample was confirmed by the Kolmogorov-Smirnov test. Nonparametric tests were needed, and the Wilcoxon signed rank test and Mann-Whitney U test were used for non-normality data. Parametric Student's t-test were used for normality data.

Differences were considered statistically significant when the p value was less than 0.05. Visual acuity was converted into logMAR scale from the decimal notation for statistical analysis. The standardised graphs and terms for refractive surgery outcomes were used.[22]

Main outcomes measures

Main outcome measures were differences on efficacy (percentage of eyes that showed equal or better UDVA compared with preoperative CDVA), safety (percentage of eyes that lost lines (Snellen) of CDVA after the primary procedure compared with preoperative CDVA), predictability (percentage of eyes within ±0.5 D and ±1.0 D of the intended correction), and astigmatic changes by vector analysis between both study groups (patients≤35 and≥40 years of age).

RESULTS

This study evaluated 51 eyes of 26 patients with ages ranging from 21 to 35 years (mean age 27.98±3.86 years) and 51 eyes of 27 patients with ages ranging from 40 to 48 years (mean age 44±2.4 years). All eyes were evaluated preoperatively, at 1 month and at 6 months postoperatively. For the analysis of the spherical outcomes, eyes that had targeted a myopic outcome for monovision were discarded (13 eyes with monovision in the group ≥40 years old).

Refractive outcomes

Table 1 shows the visual and refractive outcomes over time. In the group of patients≥40 years old, mean preoperative SE was −5.11±2.19 D and mean preoperative astigmatism was −0.77±0.74 D. In the group of ≤35 years old, mean preoperative SE was −5.27±1.75 D (p=0.776) and mean preoperative astigmatism was −1.01±0.62 D (p=0.102).

At 6 months, both groups gained lines of CDVA, but this improvement was more pronounced and statistically significant only in the young population group (p=0.05 vs p<0.001). Moreover, while the ≥40 years group did not show differences in both UDVA and CDVA between the 1-month and 6-month postoperative visits (p>0.9), the ≤35 years group visual parameters kept significantly improving between both postoperative visits (p<0001). Actually, despite CDVA being similar preoperatively among groups (p=0.555), at 6 months postoperative the young population showed significantly better CDVA than the aged population (p=0.005) (table 2). Differences in UDVA among groups were stronger at 6 months postoperative (p=0.005) than before surgery (p=0.037), in favour of the young group. However, sphere and SE outcomes were equivalent in both groups, Finally, despite the higher amount of preoperative refractive astigmatism in the young group (p=0.102), at 6 months postoperative we evidenced a statistically significant

Table 1 Visual and refractive outcomes

	Preoperative	1-month FU	6 months FU	P value		
				Pre–1M	Pre–6M	1M–6M
40 years						
UDVA, logMAR						
Mean±SD	1,53±0.44	0.00±0.10	0.00±0.09	<0.001	<0.001	0.922
Range	0.52 to 2.00	−0.08 to 0.27	−0.08 to 0.30			
CDVA, logMAR						
Mean±SD	−0.02±0.05	−0.03±0.07	−0.03±0.05	0.271	0.050	0.905
Range	−0.08 to 0.19	−0.08 to 0.19	−0.08 to 0.18			
Sphere, D						
Mean±SD	−4.68±2.14	0.14±0.34	0.12±0.32	<0.001	<0.001	0.755
Range	-9.50 to 0.75	−0.50 to 1.00	−0.50 to 1.00			
Cylinder, D						
Mean±SD	−0.77±0.74	−0.31±0.43	−0.32±0.41	<0.001	<0.001	0.721
Range	−2.75 to 0.00	−1.50 to 0.00	−1.50 to 0.00			
SE, D						
Mean±SD	−5.11±2.19	−0.01±0.32	−0.04±0.32	<0.001	<0.001	0.646
Range	-9.50 to 1.25	−0.75 to 0.62	−0.75 to 0.50			
DE, D						
Mean±SD	−5.61±2.25	−0.15±0.46	−0.20±0.43	<0.001	<0.001	0.597
Range	-10.00 to 2.00	−1.50 to 0.50	−1.25 to 0.50			
35 years						
UDVA, logMAR						
Mean±SD	1.34±0.38	0.00±0.08	−0.04±0.06	<0.001	<0.001	<0.001
Range	0.49 to 2.00	−0.08 to 0.25	−0.08 to 0.22			
CDVA, logMAR						
Mean±SD	−0.01±0.07	−0.01±0.06	−0.05±0.06	0.499	<0.001	<0.001
Range	−0.08 to 0.40	−0.08 to 0.22	−0.08 to 0.22			
Sphere, D						
Mean±SD	−4.77±1.73	0.08±0.26	0.08±0.24	<0.001	<0.001	0.942
Range	-8.00 to 1.25	−0.50 to 1.25	−0.25 to 1.00			
Cylinder, D						
Mean±SD	−1.01±0.62	−0.16±0.28	−0.13±0.26	<0.001	<0.001	0.450
Range	−2.50 to 0.00	−1.25 to 0.00	−1.00 to 0.00			
SE, D						
Mean±SD	−5.27±1.75	0.0±0.23	0.02±0.22	<0.001	<0.001	0.714
Range	-9.50 to 1.25	−0.62 to 1.00	−0.50 to 0.75			
DE, D						
Mean±SD	−5.78±2.25	−0.08±0.28	−0.05±0.28	<0.001	<0.001	0.638
Range	−10.25 to 2.25	−0.75 to 0.75	−1.00 to 0.50			

CDVA, corrected distance visual acuity; DE, defocus equivalent; FU, follow-up; SE, spherical equivalent; UCDVA, uncorrected distance visual acuity.

better resultant refractive cylinder in the young group compared with the ≥40 years group (p=0.019) (table 2).

Efficacy and safety

Efficacy index in the group of patients≥40 years was 0.86 at 1 month and 0.97 at 6 months. In the group of ≤35 years was 0.97 at 1 month and 1.07 at 6 months, existing statistically significant differences at 6 months among groups (p=0.003). In the group of patients ≥40 years, 34 eyes (89%) had a UDVA of 20/20 or better (figure 1A) and 32 eyes (84%) had a UDVA same or better than preoperative CDVA (figure 1B). In the group of patients≤35 years, 49 eyes (96%) had a UDVA of 20/20 or better (figure 2A) and 51 eyes (100%) had a UDVA same or better than preoperative CDVA (figure 2B).

Safety index in the group of patients≥40 years was 0.93 at 1 month and 1.04 at 6 months, while in the group of ≤35 years was 1.00 at 1 month and 1.11 at 6 months, existing statistically significant differences at 6 months between groups (p=0.008). In the group of patients≥40 years, the CDVA remained the same or improved in 36 eyes (95%) 6 months after surgery (figure 1C), and no eye lost two lines of CDVA. In the group of ≤35 years, 100% of eyes had the same or improved CDVA (figure 2C).

Predictability

At 6 months, in the ≥40 years group, 50% of eyes had an SE within ±0.13D and 95% within ±0.50D (figure 1E), while in the ≤35 years group, 76% of eyes had an SE within ±0.13D and 94% within ±0.50D (figure 2E). Both groups had 100% of eyes within ±1.00D of SE The scatterplot of the attempted vs the achieved SE correction at the sixth postoperative month is shown in figure 1D (≥40 years group) and figure 2D (≤35 years group).

Table 2 Comparison of visual and refractive outcomes among groups

	Preoperative			6 months FU		
	≤35 years old	≥40 years old	P value	≤35 years old	≥40 years old	P value
UDVA, logMAR						
Mean±SD	1.34±0.38	1.53±0.44	0.037	−0.04±0.06	0.00±0.09	0.005
Range	0.49 to 2.00	0.52 to 2.00		−0.08 to 0.22	−0.08 to 0.30	
CDVA, logMAR						
Mean±SD	−0.01±0.07	−0.02±0.05	0.555	−0.05±0.06	−0.03±0.05	0.005
Range	−0.08 to 0.40	−0.08 to 0.19		−0.08 to 0.22	−0.08 to 0.18	
Sphere, D						
Mean±SD	−4.77±1.73	−4.68±2.14	0.772	0.08±0.24	0.12±0.32	0.843
Range	−8.00 to 1.25	−9.50 to 0.75		−0.25 to 1.00	−0.50 to 1.00	
Cylinder,D						
Mean±SD	−1.01±0.62	−0.77±0.74	0.102	−0.13±0.26	−0.32±0.41	0.019
Range	−2.50 to 0.00	−2.75 to 0.00		−1.00 to 0.00	−1.50 to 0.00	
SE, D						
Mean±SD	−5.27±1.75	−5.11±2.19	0.776	0.02±0.22	−0.04±0.32	0.149
Range	−9.50 to 1.25	−9.50 to 1.25		−0.50 to 0.75	−0.75 to 0.50	
DE, D						
Mean±SD	−5.78±2.25	−5.61±2.25	0.687	−0.05±0.28	−0.20±0.43	0.064
Range	-10.25 to 2.25	-10.00 to 2.00		−1.00 to 0.50	−1.25 to 0.50	

CDVA, corrected distance visual acuity; DE, defocus equivalent; FU, follow-up; SE, spherical equivalent; UCDVA, uncorrected distance visual acuity.

Stability

No statistically significant differences were detected between the first and the sixth postoperative months in any of the refractive parameters in both groups (table 1). In the group of patients≥40 years, the SE changed over 0.50 D only in one eye (figure 1F), while in the group of patients≤35 years, the SE changed over 0.50 D in three eyes (figure 2F).

Astigmatism analysis

Six months after surgery, in the ≥40 years group, 38 eyes (75%) had astigmatism ≤0.50 D and 49 eyes (96%) had astigmatism ≤1.00D (figure 1G). On the other hand, in the ≤35 years group, 47 eyes (92%) had astigmatism ≤0.50 D and 51 eyes (100%) had astigmatism ≤1.00 D (figure 2G). Table 3 shows the results obtained from the astigmatic vector analysis 6 months after surgery. There was a statistically significant difference in the CI between the two study groups (p=0.009), showing a mild overcorrection tendency in patients ≤35 years and a mild undercorrection tendency in patients ≥40 years. A scatterplot of the TIA versus SIA at the sixth postoperative month as well as the difference vector graph are shown for ≥40 years group in figure 1H and online supplemental figure 1, respectively, and for ≤35 years group in figure 2H and online supplemental figure 2 respectively. Figure 1H evidences an undercorrection tendency of the SIA in patients over 40 years, while figure 2H evidences a perfect predictability of the SIA in patients younger than 35 years. Figure 1I shows that five eyes (11%) had an angle of error over 15° in the group of ≥40 years, while figure 2I shows that three eyes (6%) had an angle of error over 15° in the group of ≤35 years 6 months after surgery.

Regarding topographic cylinder, in the ≥40 years-old group it changed from −0.81±0.53 D preoperatively to −0.89±0.54 D at 6 months postoperative, while in the ≤35 years old group, it changed from −1.18±0.68D to −0.87±0.46D. Preoperatively, differences between age groups were significant (p=0.003), but they disappeared postoperatively (p=0.961).

Corneal aberrations

Online supplemental table shows comparative root mean square (RMS) values preoperatively and 6 months after surgery. Despite preoperative RMS total being worse in the young group (p=0.046), 6 months after surgery we evidence no differences between groups (p=0.401). Same pattern was observed with the RMS astigmatism, despite being worse in the young group preoperatively (p=0.033), differences lost significance postoperatively (p=0.198), with an actual tendency for worse values in aged group. No statistically significant differences were detected between groups in the rest of analysed parameters (online supplemental table 1).

DISCUSSION

To the best of our knowledge, this is the first study to compare SMILE refractive outcomes in relation with patient's age at the time of surgery: patients≥40 vs ≤35 years of age. We defined these groups in order to clearly differentiate both study groups by age, leaving close to 5 years gap in between, in order to identify any difference in the SMILE refractive and visual outcome provided by the expected older stiffer corneas.

Our ≤35 years group SMILE refractive outcomes were excellent and equivalent to those previously reported in the literature by other authors.[23–26] On the other hand, our ≥40 years group showed also overall good results, but compared with the younger population, a clear tendency for worse refractive and visual outcomes for the majority of parameters analysed in the current study. At 6 months, we found a statistically significant worse efficacy (0.97 vs 1.07; p=0.003) and safety indexes (1.04 vs 1.11; p=0.008) in the ≥40 years population, with 84% and 100% of eyes achieving at least a postoperative UDVA ≥preoperative CDVA in the ≥40 years and ≤35 years groups, respectively (figures 1B and 2B). Moreover, 5% of eyes lost one line of CDVA in the aged group (vs none in the ≤35 years group). Also, predictability was shown to be better in the younger population, with 50% of eyes within ±0.13 D of SE in the ≥40 years group

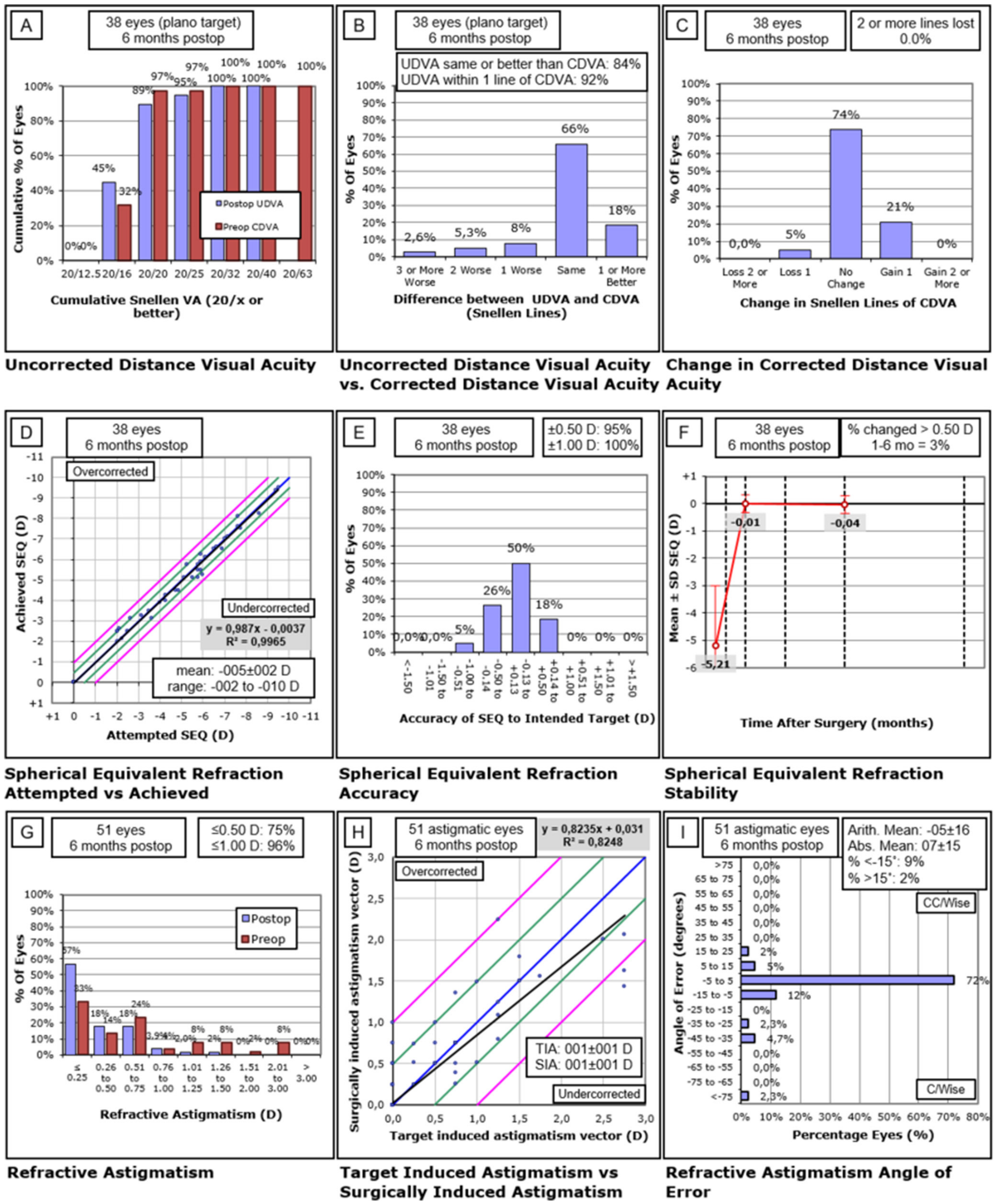

Figure 1 Group of patients older than 40 years old. (A) Comparison of 6-month postoperative uncorrected distance visual acuity (UDVA) and preoperative corrected distance visual acuity (CDVA) (efficacy). (B) Changes in lines between preoperative CDVA and postoperative UDVA 6 months after surgery (efficacy). (C) Changes in lines of CDVA 6 months after surgery (safety). (D) Intended versus achieved correction (spherical equivalent refraction) 6 months after surgery. (E) Distribution of postoperative SE (predictability) 6 months after surgery. (F) Stability of the manifest refraction over time. (G) Distribution of preoperative and postoperative astigmatism. (H) Target-induced astigmatism (TIA) versus surgically induced astigmatism (SIA) 6 months after surgery. (I) Distribution of postoperative angle of error 6 months after surgery.

at 6 months, in contrast to 76% of eyes in the ≤35 years group (figures 1E and 2E).

A relevant finding was the fact that visual parameters (UDVA and CDVA) did significantly improve between the first and the sixth postoperative months in the young population ($p<0.001$), but this further improvement didn't happen in the older population ($p>0.9$), where vision remained stable between both postop visits. Actually, total CDVA improvement was more pronounced and significantly better in the younger population. Also, UDVA showed a better improvement in the young group (tables 1 and 2). This fact could be the consequence of the more elastic and less stiff young corneas, allowing for a further stromal remodelling with time allowing for a better final visual outcome, that doesn't happen in the stiffer and more rigid older corneas.

While we could not demonstrate relevant differences in the sphere outcomes among groups, the ≥40 years group showed significantly worse astigmatic outcomes compared with the younger group, showing higher amounts of residual refractive

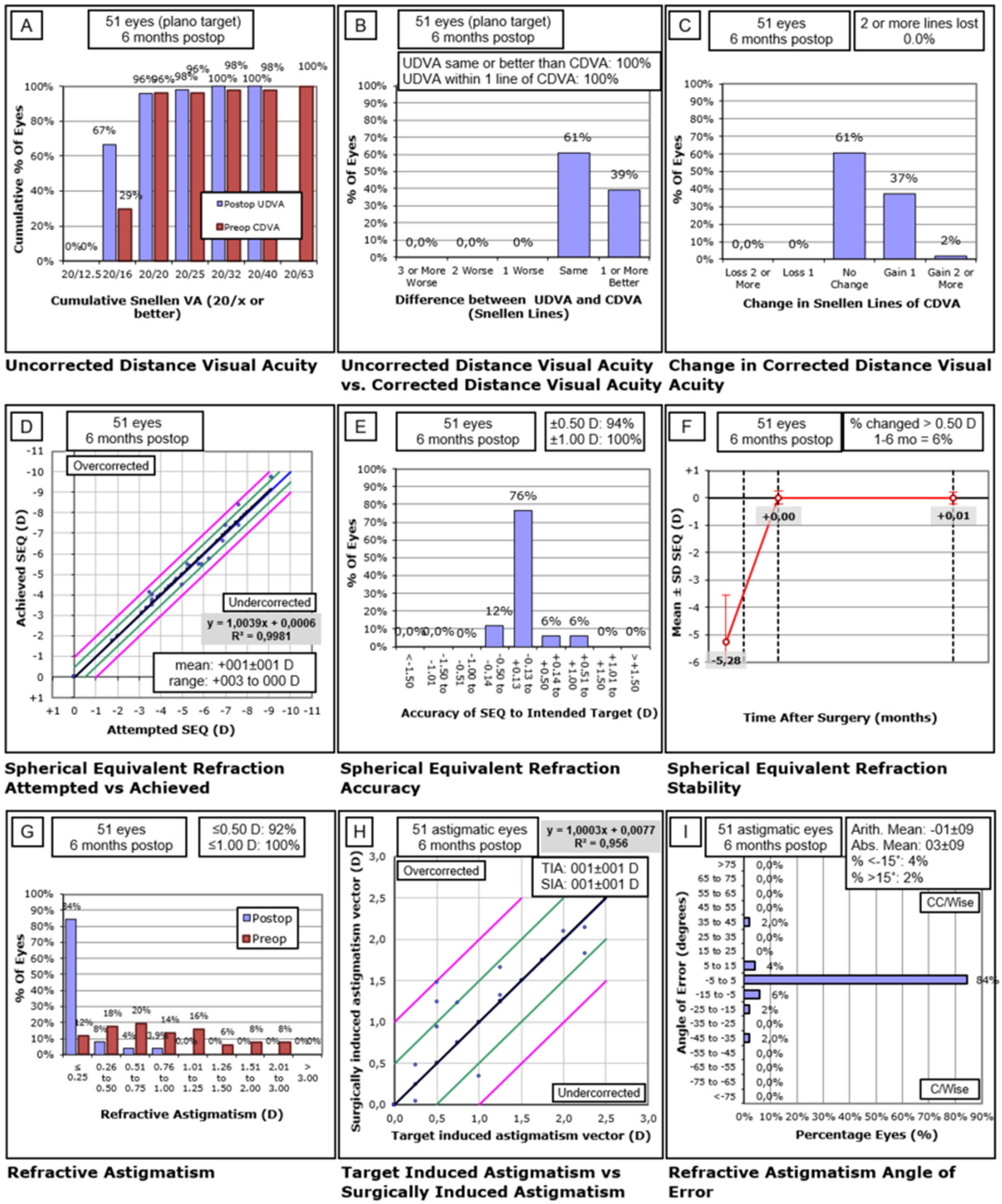

Figure 2 Group of patients younger than 35 years old. (A) Comparison of 6-month postoperative uncorrected distance visual acuity (UDVA) and preoperative corrected distance visual acuity (CDVA) (efficacy). (B) Changes in lines between preoperative CDVA and postoperative UDVA 6 months after surgery (efficacy). (C) Changes in lines of CDVA 6 months after surgery (safety). (D) Intented versus achieved correction (spherical equivalent refraction) 6 months after surgery. (E) Distribution of postoperative SE (predictability) 6 months after surgery. (F) Stability of the manifest refraction over time. (G) Distribution of preoperative and postoperative astigmatism. (H) Target-induced astigmatism (TIA) versus surgically induced astigmatism (SIA) 6 months after surgery. (I) Distribution of postoperative angle of error 6 months after surgery.

astigmatism (p=0.019) (tables 1 and 2): 75% vs 92% had astigmatism ≤0.50 D, respectively (figures 1G and 2G). Vector analysis demonstrated a tendency towards undercorrection of the refractive cylinder in those patients over 40 years of age (figure 1H). However, as seen in this figure, the relevant dispersion of the postoperative results in the aged group, with even cases of overcorrection, precluded us from extracting a reliable nomogram adjustment for the astigmatism correction in this population.

Finally, aberrometry outcomes supported the findings already observed regarding the worse astigmatic outcomes in the older population. However, we could not demonstrate any other relevant difference among the other analysed corneal aberrations.

To the best of our knowledge, there is only one previous article reporting, independently, SMILE outcomes in presbyopic patients (>45 years old).[16] However, they did not perform a comparative analysis with a younger population, and they only evaluated the SE refractive outcomes, without paying attention

Table 3 Vector analysis of refractive astigmatism outcomes at 6 months postoperative

	≤35 years old	≥40 years old	P value
TIA, D			
Mean±SD	1.01±0.62	0.77±0.74	0.021
Range	0.00 to 2.50	0.00 to 2.75	
SIA, D			
Mean±SD	1.05±0.61	0.80±0.58	0.030
Range	0.00 to 2.50	0.00 to 2.24	
DV, D			
Mean±SD	0.13±0.27	0.38±0.58	0.004
Range	0.00 to 3.49	0.00 to 3.49	
ME			
Mean±SD	0.04±0.23	0.03±0.43	0.939
Range	−0.65 to 0.98	−1.31 to 1.00	
AE (degrees)			
Mean±SD	−0.67±9.06	−4.05±15.59	0.529
Range	−42 to 40	−88 to 18	
CI			
Mean±SD	1.09±0.42	0.90±0.58	0.009
Range	0.17 to 2.96	0.00 to 2.96	
IOS			
Mean±SD	0.19±0.44	0.35±0.68	0.169
Range	0.00 to 2.00	0.00 to 3.00	

AE, angle of error; CI, correction index; DV, difference vector; IOS, Index of Success; ME, magnitude of error; SIA, surgically induced astigmatism vector; TIA, target induced astigmatism vector.

to the astigmatic results. They reported similar or even worse results than the ones we have obtained in our population over 40 years of age, with 31% of eyes within ±0.13 D of SE (50% in our group ≥40 years) and 80% of eyes within ±0.5 D (95% in our group ≥40 years). Also they reported a binocular UDVA ≥20/20 in 90% of patients (89% in our group ≥40 years regarding monocular UDVA). Thus, these authors showed equivalent results as ours that, at the same time, confirms their inferiority compared with the outcomes we have got, and the ones reported by other authors, in a younger population. To explain these findings, we hypothesise that the biomechanical response of the human corneal stroma to the lenticule extraction varies as corneal stiffness increases with age,[17] reducing stromal elasticity and remodelling capacity, modifying, as a consequence, the refractive response to the SMILE procedure. Probably, this possible lack of remodelling capacity of the stiffer older corneas is masking part of the astigmatic correction and justifying the tendency for the cylinder undercorrection. At this point, we shall remember that SMILE technique has raised some concerns regarding its accuracy for the correction of moderate to high astigmatism,[3 6 27 28] and even in myopic patients without preoperative subjective astigmatism, the presence of preoperative objective keratometric astigmatism ≥0.50 D seems to double the risk for the induction of a postoperative subjective astigmatism ≥0.50 D after SMILE.[29] Nevertheless, in our study, both refractive and topographic keratometric cylinders were actually higher in the younger group preoperatively (significant difference for the topographical cylinder), however, this group ended up with smaller values of both cylinder types compared with the older group postoperatively (significant difference for the refractive cylinder). So the worse astigmatic outcome in the older group is likely attributable to a different response to the procedure linked with age. Finally, SMILE creates larger functional optical zones (measured by topography) than LASIK for an equivalent myopic correction and despite the usual SMILE smaller programmed optical zones. This fact has been suggested to be the consequence of a different corneal biomechanical response to the SMILE procedure.[30] Considering that corneal biomechanical response to SMILE likely differs with age, as suggested in the current paper, this could influence the induced functional optical zone in relation with patient's age, and subsequently affect the astigmatic correction.

The main limitation of the current study is, in addition to the retrospective nature, its vulnerability to the paired date bias, as both patient's eyes were included when available. However, since this is the first paper dealing with this topic, we preferred to include all eyes in order to be able to increase the study sample. Nevertheless, further studies with larger samples and without this potential bias are required in order to confirm these outcomes and stablish a reliable recommendation for nomogram adjustment in such population.

In conclusion, SMILE is an efficient, safe, stable and relatively predictable refractive surgery solution for the management of myopia with or without mild to moderate astigmatism in patients over 40 years of age, however, worse refractive outcomes than those obtained in younger patients should be expected and advised, with a tendency towards astigmatic undercorrection. This difference is SMILE outcomes in relation with patient's age at the time of surgery might be connected to the expected different corneal stroma stiffness and remodelling capacity.

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Competing interests JLAdB is part of the medical advisory board of CSO.

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Provenance and peer review Not commissioned; externally peer reviewed.

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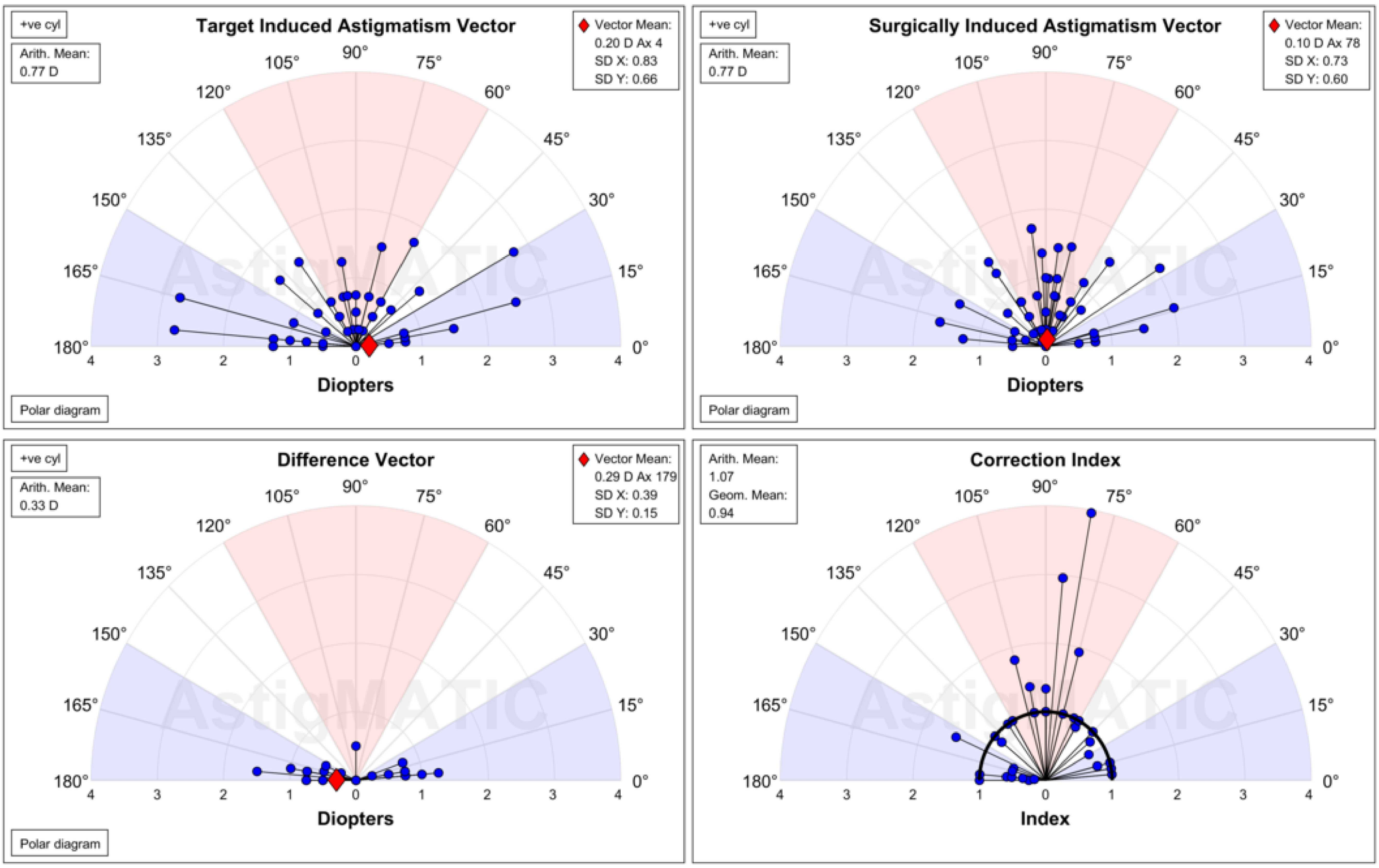
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SD Y: 0.66
Diopters
Polar diagram
Surgically Induced Astigmatism Vector
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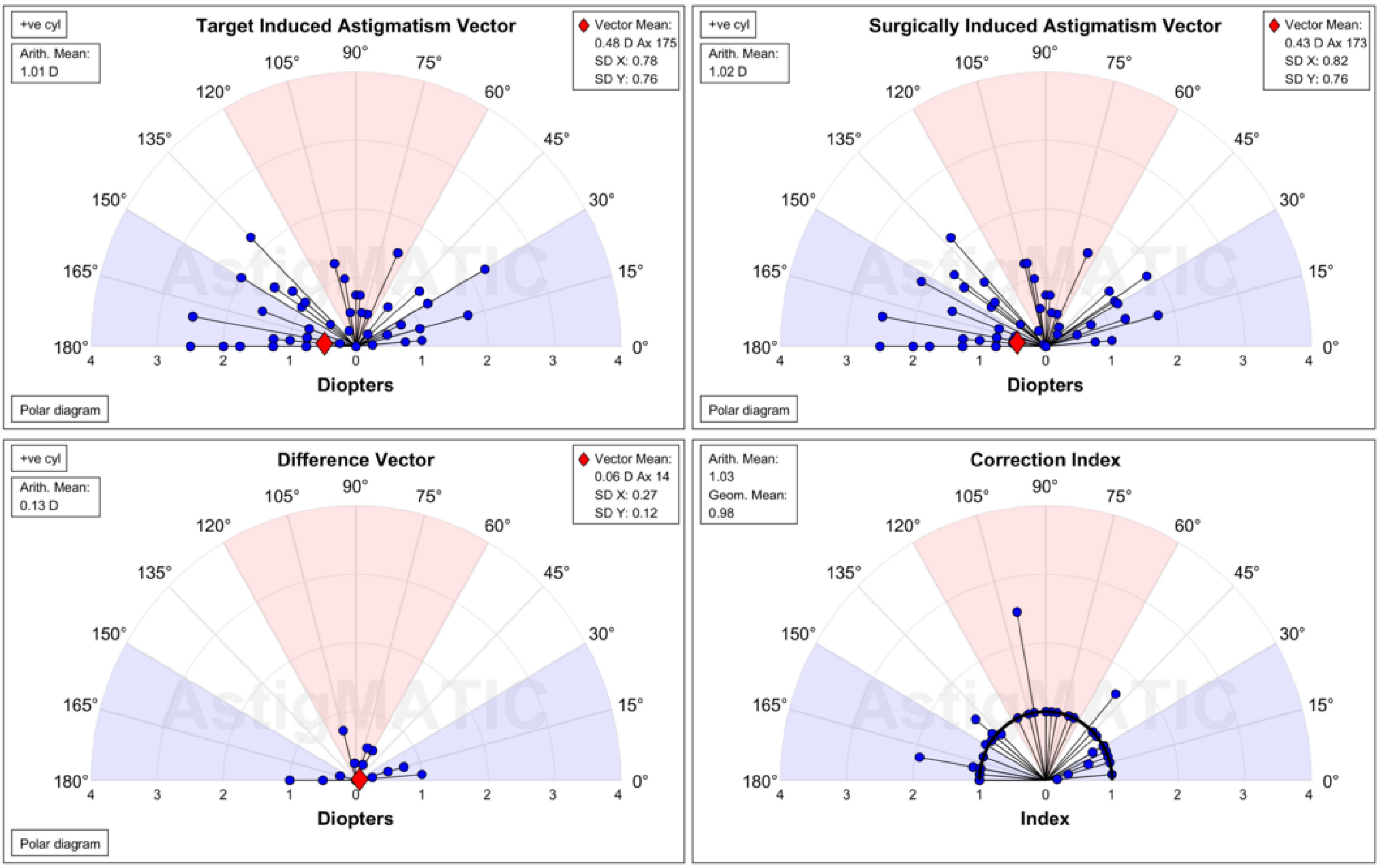
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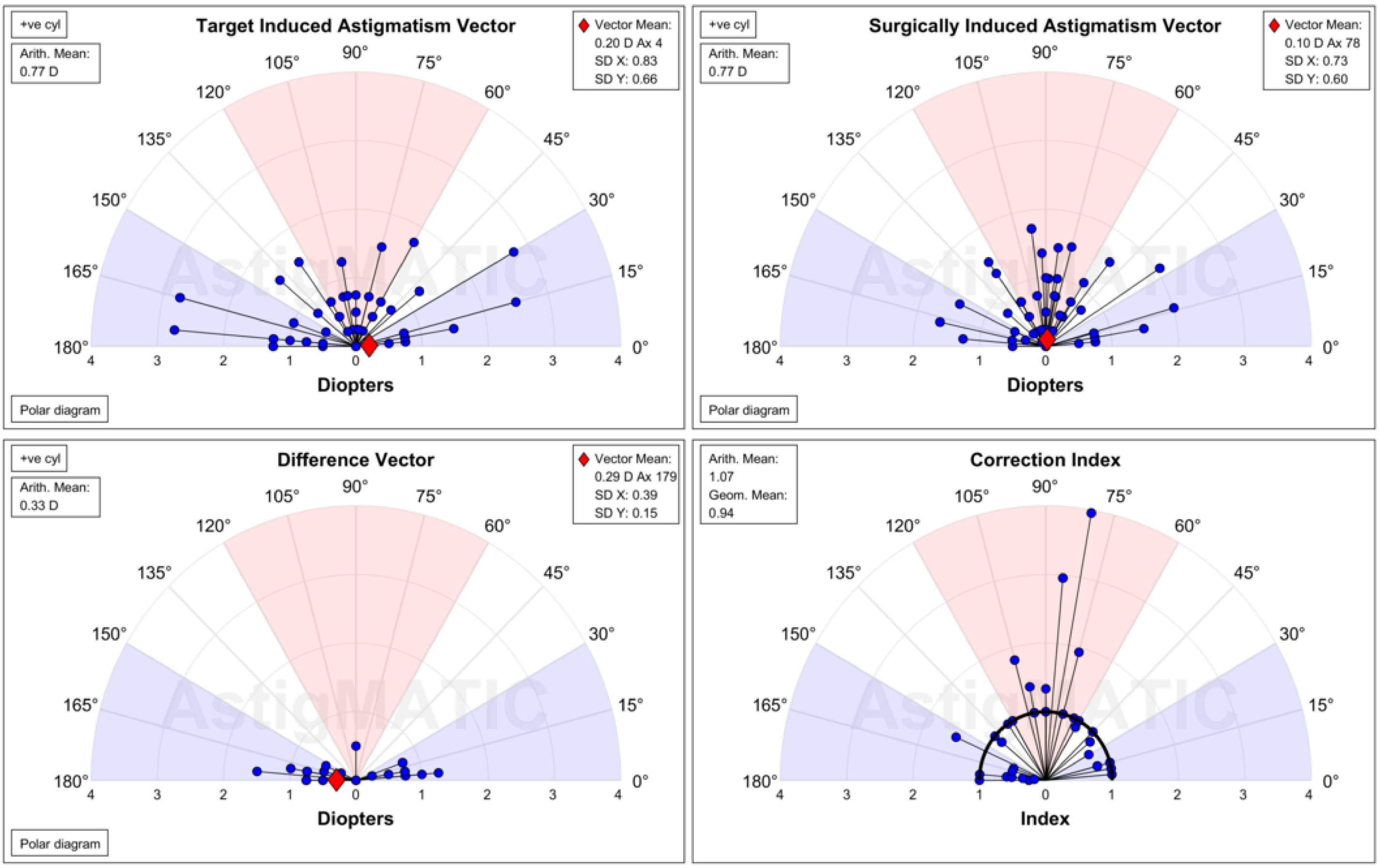
	Preop			6 Months FU		
	≤ 35 years old	**≥ 40 years old**	**p-value**	**≤ 35 years old**	**≥ 40 years old**	**p-value**
RMS Total						
mean ± SD	1.15 ± 0.48	0.93 ± 0.56	0.046	1.00 ± 0.37	1.08 ± 0.50	0.401
range	0.42, 2.11	0.33, 2.81		0.48, 2.24	0.39, 2.43	
RMS ASTG						
mean ± SD	1.06 ± 0.52	0.79 ± 0.61	0.033	0.68 ± 0.43	0.81 ± 0.45	0.198
range	0.10, 2.00	0.05, 2.76		0.07, 1.96	0.29, 2.09	
RMS SA						
mean ± SD	0.22 ± 0.07	0.23 ± 0.06	0.826	0.36 ± 0.18	0.32 ± 0.26	0.355
range	0.10, 0.45	0.12, 0.37		-0.03, 0.87	-0.10, 0.92	
RMS COMA						
mean ± SD	0.19 ± 0.14	0.23 ± 0.12	0.194	0.34 ± 0.24	0.34 ± 0.24	0.289
range	0.01, 0.56	0.03, 0.55		0.39, 0.18	0.04, 1.10	
RMS HOA						
mean ± SD	0.41 ± 0.12	0.40 ± 0.09	0.856	0.67 ± 0.17	0.68 ± 0.38	0.896
range	0.21, 0.75	0.26, 0.63		0.24, 1.09	0.26, 2.02	
RMS SPHLK						
mean ± SD	0.27 ± 0.06	0.26 ± 0.06	0.371	0.44 ± 0.16	0.43 ± 0.28	0.892
range	0.14, 0.47	0.15, 0.41		0.18, 0.89	0.12, 1.39	
RMS COMLK						
mean ± SD	0.29 ± 0.14	0.30 ± 0.10	0.645	0.48 ± 0.16	0.50 ± 0.31	0.767
range	0.08, 0.70	0.11, 0.55		0.17, 0.88	0.10, 1.47	

Supplemental Table. Corneal wavefront aberrations outcomes at 6 months postop. RMS: root mean square; ASTG: astigmatism; SA: spherical aberration; HOA high order aberration; SPHLK: spherical like; COMLK: coma like.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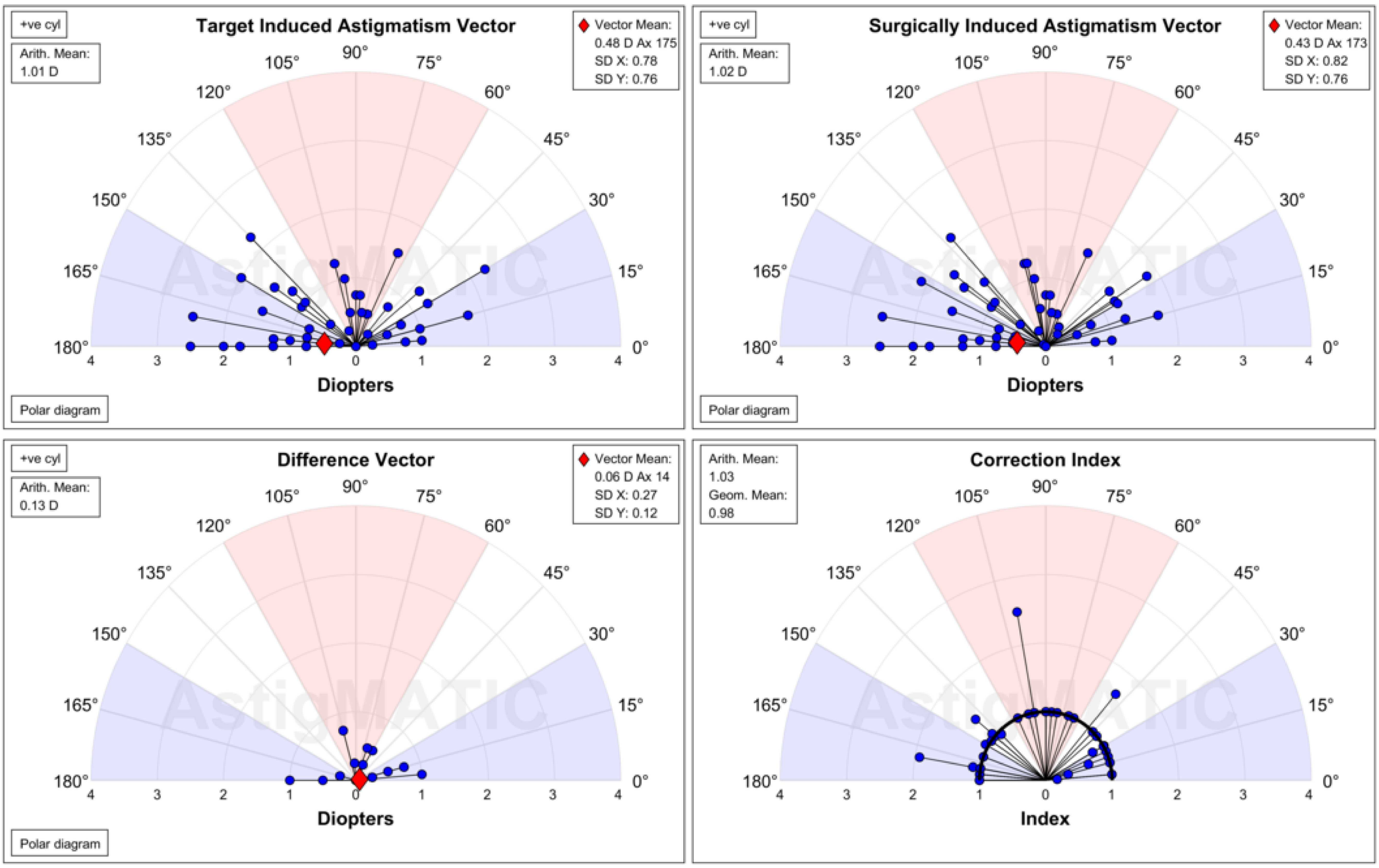
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