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Laser keratomileusis in treatment of anisometropic amblyopia in adults

Pidro Ajla[1]*, Ahmedegović-Pjano Melisa[1], Mravičić Ivana[2], Grišević Senad[1], Biščević Alma[1], Pidro Aida[3]

Abstract:

PURPOSE: To compare and evaluate improvement in corrected distant visual acuity (CDVA) between myopia and hyperopia after laser *in situ* keratomileusis (LASIK) in adult patients with anisometropic amblyopia.

MATERIALS AND METHODS: This prospective clinical study included 103 amblyopic eyes (103 patients), which underwent LASIK correction of refractive error from January 2013 to January 2018. Uncorrected distance visual acuity (UDVA), CDVA, spherical equivalent (SE), postoperative astigmatism, and intraocular pressure were evaluated at time points of 1, 6, and 12 months.

RESULTS: Patients were divided into two groups according to refractive error. Group 1: Forty-six patients with myopia and Group 2: Fifty-seven patients with hyperopia. Mean CDVA (logarithm of the minimum angle of resolution [logMAR]) preoperatively was 0.23 ± 0.16 in Group 1 and 0.40 ± 0.19 in Group 2. Postoperative CDVA (logMAR) was 0.17 ± 0.13 in Group 1 and 0.32 ± 0.17 in Group 2. There was statistically significant increase in UDVA ($P < 0.0001$) postoperatively and no change during the follow-up period of 12 months in both groups. Group 1 showed more expectable results, 95% of variability SE achieved was dependent on SE intended ($R^2 = 0.95$), while in Group 2, the percentage was slightly lower of expected 87% ($R^2 = 0.87$). There was statistical significance in respect of CDVA change postoperatively and preoperatively in both groups. Correlation factors are low, in Group 1 $r = -0.53$ and in Group 2 $r = -0.39$.

CONCLUSION: LASIK can improve CDVA in a considerable portion of amblyopic eyes, both myopic and hyperopic. Eyes with better initial CDVA and those with myopia were associated with greater improvement in postoperative CDVA.

Keywords:

Amblyopia, anisometropia, laser *in situ* keratomileusis

Introduction

Amblyopia, defined as poor vision due to abnormal visual experience early in life, affects approximately 3% of the population.[1] Anisometropic amblyopia is a unilateral decrease in visual acuity occurring with unequal, uncorrected refractive error that is present before 6 years of age.[2]

The traditional treatment consists of correcting the refractive anomaly with spectacles or contact lenses, occlusion therapy, and penalization therapy.[3] In recent years, many surgical procedures have been used to treat refractive errors. Refractive surgery, such as laser *in situ* keratomileusis (LASIK), is a potential alternative treatment for anisometropia in adults.[4]

In our study, we evaluated the efficacy, stability, and safety of LASIK in adult patients with anisometropic amblyopia.

Materials and Methods

In this prospective study, we enrolled 103 eyes of 103 adult patients previously diagnosed

[1]*Eye Clinic Svjetlost, Sarajevo, Bosnia and Herzegovina,* [2]*University Eye Clinic Svjetlost, Zagreb, Croatia,* [3]*Department of Ophthalmology, General Hospital Sarajevo, Sarajevo, Bosnia and Herzegovina*

***Address for correspondence:**
Dr. Pidro Ajla, Kalemova 9, Sarajevo, Bosnia and Herzegovina.
E-mail: ajlapidro1@gmail.com

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with anisometropic amblyopia, who underwent LASIK surgery at our clinic in the time period from January 2013 to January 2018. All eyes were amblyopic and received the standard amblyopia treatment in early childhood (occlusion and/or optical penalization). There were 46 myopic eyes in Group 1 and 57 hyperopic eyes in Group 2.

Inclusion criteria were: corrected distant visual acuity (CDVA) on dominant eye from 0.1 to 0.0 (logarithm of the minimum angle of resolution [logMAR]), CDVA on amblyopic eye from 0.7 to 0.1 (logMAR), at least two lines of difference of CDVA between two eyes, stable refraction within 1 year, age of 18 years or older, myopia up to −10.00D, hyperopia up to +6.00D, and astigmatism up to ±2.00D. Patients were instructed not to wear contact lenses before the surgery 7–30 days depending on the type of lenses.

Exclusion criteria were previously or present eye diseases (such as glaucoma, uveitis, retinopathy, and opacification of optic media), corneal topographic changes (any kind of corneal irregularity susceptible to keratoconus or other ectatic diseases), corneal thickness <480 μm, and concomitant diseases such as diabetes, autoimmune diseases, and recent pregnancy or breastfeeding in women.

Preoperative examination included uncorrected distant visual acuity (UDVA) and CDVA, autorefractometry (Grand Seiko GR-3100 K, Hiroshima, Japan), cycloplegic refraction, slit lamp examination, contact tonometry (I-care Finland Oy, Espoo, Finland), indirect ophthalmoscopy and corneal topography (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany), and Schirmer test. Visual acuity testing was carried out using LogMAR charts, which are more accurate in amblyopia and size scaling.[5]

All surgeries were performed using excimer laser Wavelight Allegretto Eye-Q 400 Hz (Wavelight Allegretto, Erlangen, Germany) and microkeratome Moria M2 for flap creation (Moria M2, Antony, France). During the first 10 postoperative days, all eyes received antibiotic-corticosteroid drops (Tobradex, Alcon, Fort Worth, TX, USA) four times daily and artificial tears (Blink, Abbott Medical Optics, Santa Ana, CA, USA) four times daily minimally for 1 month. Follow-up was 1, 6, and 12 months postoperatively. Slit lamp examination, UDVA, CDVA, and autorefraction were performed in all visits. Informed consent was obtained from all patients included in the study, conforming to local laws and in compliance with the principles of the Declaration of Helsinki and WHO guidelines. The study was approved by the Ethics Committee of Eye Clinic Svjetlost (SVJETLOST/1/2013).

Statistical calculation was performed with SPSS for Windows (19.0, SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel (11.0, Microsoft Corporation, Redmond, WA, USA). The comparison between the preoperative and postoperative periods was performed with the Wilcoxon signed-rank test while correlations with Pearson correlation test. A $P < 0.01$ was considered statistically significant.

Results

Among the 4347 cases examined, 103 eyes of 103 patients met the inclusion criteria for the study. Sixty-one patients (59.2%) were male and 42 (40.8%) were female. Mean age was 32.92 ± 8.38 years, ranging from 19 to 55 years. Table 1 shows the preoperative values of both groups. There were 46 myopic eyes in Group 1 with spherical equivalent (SE) −6.52 ± 2.07D and 57 hyperopic eyes with SE + 4.72 ± 1.15D in Group 2. Astigmatism in both groups was <±2.00D.

There was a statistically significant increase in UDVA in group one after LASIK ($P < 0.0001$) comparing all postoperative results to preoperative values. Wilcox signed-paired test did not show any statistically significant difference between postoperative values ($P = 0.222$ and $P = 0.317$). There was statistically significant change in CDVA preoperatively and CDVA postoperatively ($P < 0.0001$). When preoperative CDVA and UDVA at the end of follow-up period were compared, there was statistically significant difference.

Similar results were obtained in Group 2. There was statistically significant increase in UDVA ($P < 0.0001$) postoperatively and no change during the follow-up period of 12 months. Comparing preoperative and postoperative CDVA, we found significant change ($P < 0.0001$). Preoperative CDVA and postoperative UDVA also showed statistically significant change ($P < 0.0001$). Postoperative values of SE, UDVA, and CDVA in the follow-up period are presented in Table 2.

Scatter plots of SE achieved and SE intended for both groups are presented in Graphs 1 and 2. Group 1 showed more expectable results, 95% of variability SE achieved is dependent on SE intended ($R^2 = 0.95$), while in Group 2, the percentage was slightly lower 87% ($R^2 = 0.87$).

Achieved SE was within 1D in 95.65% of the cases in Group 1 and 80.70% of the cases in Group 2. In Group 1, 76% of eyes were within ± 0.5D, and only 47% of the eyes in Group 2 were within ± 0.5D at the end of the follow-up period.

Preoperative UDVA, preoperative SE as well as sex, age, and pachymetry do not show statistical significance in respect to change of CDVA postoperatively in

Group 1 [Table 3]. There is statistical significance in respect to preoperative CDVA. Correlation factor is low, and the correlation is negative (r = –0.53).

In Group 2, of all tested preoperative values, only CDVA showed statically significance in comparison to the increase in CDVA postoperatively (P = 0.003), as shown in Table 4. Correlation factor was very low and negative (r = –0.39).

Table 1: Preoperative patients' characteristics

	Group 1 (n=46)	Group 2 (n=57)
Sex (male/female)	47.8%/52.2%	68.4%/31.6%
Age	36.00±9.92	30.44±5.90
SE	–6.52±2.07 D	+5.26±1.14 D
Sphere	–5.91±2.05 D	+4.72±1.15 D
Astigmatism	–1.21±0.55 D	+1.08±0.57 D
UDVA (logMAR)	1.0±0.31	0.82±0.34
CDVA (logMAR)	0.23±0.16	0.40±0.19

UDVA=Uncorrected distance visual acuity, CDVA=Corrected distant visual acuity, logMAR=Logarithm of the minimum angle of resolution

Table 2: Postoperative results

	Group 1	Group 2
1 month		
SE (D)	–0.60±0.54	0.41±0.56
UDVA (logMAR)	0.22±0.14	0.34±0.19
CDVA (logMAR)	0.20±0.14	0.33±0.19
6 months		
SE (D)	–0.18±0.48	0.55±0.53
UDVA (logMAR)	0.21±0.15	0.33±0.18
CDVA (logMAR)	0.18±0.14	0.32±0.18
12 months		
SE (D)	–0.25±0.51	0.61±0.54
UDVA (logMAR)	0.19±0.15	0.32±0.18
CDVA (logMAR)	0.17±0.13	0.32±0.17

UDVA=Uncorrected distance visual acuity, CDVA=Corrected distant visual acuity, logMAR=Logarithm of the minimum angle of resolution, SE=Spherical equivalent

Table 3: Correlation in myopia group in change of corrected distant visual acuity (logarithm of the minimum angle of resolution)

	Sex	Age	CDVA	UDVA	Pachymetry	SE
Pearson's correlation	–0.04	0.11	–0.53	–0.09	–0.08	0.02
Significant (two-tailed)	0.80	0.49	0.0001	0.57	0.62	0.89

UDVA=Uncorrected distance visual acuity, CDVA=Corrected distant visual acuity, SE=Spherical equivalent

Table 4: Correlation in hyperopia group in change of corrected distant visual acuity (logarithm of the minimum angle of resolution)

	Sex	Age	CDVA	UDVA	Pachymetry	SE
Pearson correlation	0.06	–0.09	–0.39	0.13	–0.08	–0.13
Significant (two-tailed)	0.65	0.53	0.003	0.35	0.55	0.35

UDVA=Uncorrected distance visual acuity, CDVA=Corrected distant visual acuity, SE=Spherical equivalent

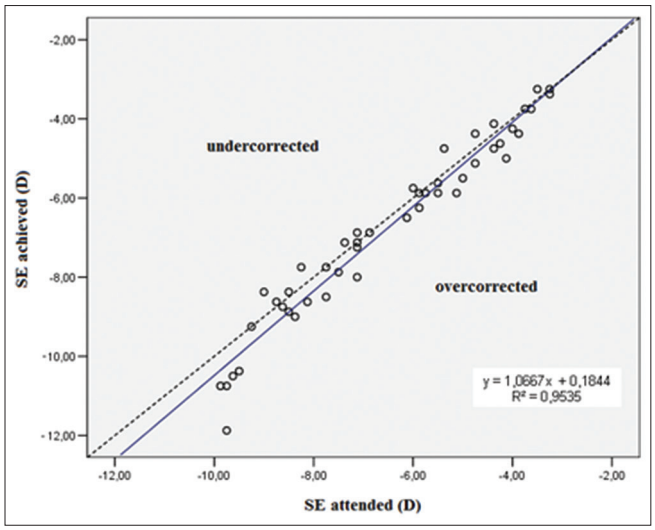
Discussion

It is well established that therapy of amblyopia is effective at young age when the visual system is sufficiently plastic for cortical correction.[6] In this study, we analyzed refractive results after LASIK in anisometropic amblyopic eyes in adults. By excluding astigmatism higher than ± 2.00D, this study focused on myopic and hyperopic anisometropia. There are no differences in gender and age between the two groups, as presented in Table 1. Postoperative refraction close to emmetropia was achieved in both groups, which is also reported by other authors.[7,8]

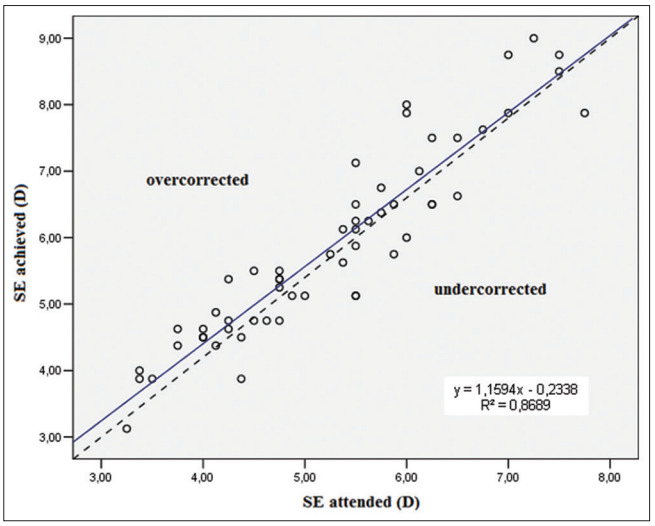
There was significant difference between UDVA preoperatively and UDVA postoperatively, but during the postoperative period of 12 months, there was still slight improvement in UDVA and postoperative SE, but it was not statistically significant. These results confirm that LASIK is highly effective, stable, and safe method for surgical correction of refractive errors in eyes with amblyopia, as it is reported for other groups.[9-12]

In our study, we found slightly better improvement in myopic eyes (62.07%) compared to hyperopic group (54.29%). The mean CDVA (logMAR) improved in Group 1 from 0.23 ± 0.16 preoperatively to 0.17 ± 0.13 postoperatively and from 0.40 ± 0.19 to 0.32 ± 0.17 in Group 2 postoperatively. Other postoperative results are shown in Table 2. Results of similar studies report improvement in adult amblyopic eyes after LASIK. The rates of improvement vary over a wide range. Agca *et al*.[12] reported improvement in CDVA in 60% of myopic and 33% of hyperopic eyes. Sakatani *et al*.[6] reported an improvement of CDVA in 42.8% of myopic eyes, and Dedhia and Behl[13] reported an improvement in 66.7% of patients after LASIK. Our results in both groups are the same or slightly better. In all studies, myopic group had more improvement in CDVA in comparison to hyperopic group.

Minification due to spectacle lenses in myopic eyes was suggested as a possible reason for this.[14] However, many other explanations are possible causes. Some authors suggest that amblyopia is truly resolved by forcing the amblyopic eye to look sharper and use functional visual acuity reserve by eliminating high refractive errors. Vuori *et al*.[15] proposed that image enlargement is not the source of CDVA improvement, but the changes in the plasticity of the visual cortex after the visual-input-balance between eyes are restored. In our study, both groups reached statistically significant level of improvement, CDVA preoperatively being significantly lower than UDVA postoperatively in all periods of follow-up. Even in high hyperopia, we were able to achieve using few principles: wearing a higher optical correction for a few



Graph 1: Scatter plots of spherical equivalent achieved versus spherical equivalent attended correction in Group 1



Graph 2: Scatter plots of spherical equivalent achieved versus spherical equivalent attended correction in Group 2

months may reduce the accommodative spasm and will allow a better correction of the true latent hyperopia. Further, the optical zone for hyperopic correction should not be <6.5 mm and preferably should be >6.7 or even 7 mm, with respectful larger flaps.[16] Some studies based on subjective manifest refraction, posthyperopic LASIK surgery, have shown significant regression in the first 12 months after surgery with more stable results from 12 months postoperatively. Higher degree hyperopic treatments (>+4D) have an even greater amount of regression.[17] This is why discreet initial overcorrection is systematic for hyperopia, to achieve long-term stability and avoid regression.

The trend of UDVA improvement continues throughout follow-up period, but not in statistically significant. Therefore, the plasticity of visual system is considered to be reserved for early childhood, but many studies suggest otherwise.[15-20] Chino *et al*.[21] reported reorganization of the visual cortex only hours after loss of one eye in cats and concluded that there is a great degree of plasticity even in adult visual system. Studies done on humans losing their sight on better-seeing eye for macular pathology and report recovery of visual acuity are again indicating certain level of plasticity.[22] Whatever the mechanism in these cases may be, there is an indication that amblyopia is treatable to certain extent and that by removal of high refractive errors can be key to improving adult amblyopia.

Unfortunately, we did not find strong predictor whether CDVA will improve. The only factor that showed statistical significance is preoperative CDVA. Lower values of CDVA (logMAR) showed more improvement in CDVA postoperatively. Correlation is not strong in Group 1 (−0.53) and even lower in Group 2 (−0.39), in both groups with negative correlation. Therefore, there is a trend that the patients with better visual acuity preoperatively have more CDVA improvement in both groups, where myopic group experienced somewhat better improvement.

Preoperative refractive error, preoperative UDVA, as well as sex, age, and pachymetry had no effect on mean postoperative CDVA in amblyopic eyes. This finding is in agreement with Cagil[8] and Agca,[12] who reported that the type of refractive error is not related to final CDVA.

However, in their studies, they did not find correlations in degrees of amblyopia and CDVA improvement. Our correlation was statistically significant, but very low. Anyhow, further testing and division in groups by levels of amblyopia are needed to make final conclusions on these parameters.

This study had its limitations because only visual acuity with glasses preoperatively was obtained. It would be better to have CDVA obtained with contact lenses for reducing visual aberrations due to spectacle lenses. This way we could reduce the effect of minification on improvement observed after refractive rehabilitation after LASIK. In addition, evaluation of the visual function is a complicated task and requires more than evaluating visual acuity. Future studies need to deal with contrast sensitivity and higher-order aberrations to complete the full evaluation of visual acuity.

Conclusion

LASIK can improve the CDVA in a considerable portion of amblyopic eyes, both myopic and hyperopic. Eyes with a better initial CDVA and those with myopia were associated with greater improvement in postoperative CDVA.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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