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Original Article

Evaluation of Retinal Ganglion Cell Layer Thickness in the Early Period After Femtosecond Laser-Assisted LASIK Surgery

Kemal Özülken*, Çağrı İlhan**

*Department of Ophthalmology TOBB ETU Medical School, Ankara, Turkey
** Hatay State Hospital, Hatay, Turkey

Abstract

Objectives: To evaluate the early effects of femtosecond laser-assisted in situ keratomileusis (LASIK) surgery in a healthy population on the retinal ganglion cell thickness (GCT), peripapillary retinal nerve fiber thickness (NFT), and central macular thickness (CMT) obtained by spectral domain optical coherence tomography (SD-OCT).

Materials and Methods: This case-control study included data from the right eye of 40 subjects without any disease other than refractive error and who had undergone femtosecond laser-assisted LASIK surgery. The preoperative, postoperative first hour, and postoperative third week GCT, NFT, and CMT values obtained by SD-OCT were compared.

Results: The mean age was 27.54 ± 5.99 years (18-45 years). GCT, NFT, and CMT were 18.43 ± 6.03 µm, 107.90 ± 9.01, and 234.3 ± 21.2 µm in the preoperative period; 18.05 ± 5.93 µm, 108.08 ± 8.92 µm, and 230.1 ± 22.6 µm at the postoperative first hour; and 17.86 ± 5.27 µm, 107.98 ± 10.13, and 236.3 ± 25.1 µm at the postoperative third week (p values were 0.159, 0.85, 0.254, respectively).

Conclusion: There was no change in GCT, NFT, and CMT values evaluated with SD-OCT in the early period after femtosecond laser-assisted LASIK surgery.

Keywords: LASIK, ganglion cell layer, retinal nerve fiber, intraocular pressure, OCT.

Introduction

Laser-assisted in situ keratomileusis (LASIK) is the most commonly used method in current refractive surgery practice worldwide.[1] After lifting corneal tissue, the predetermined amount of tissue in the corneal stroma is ablated by laser energy, and a wide range of refractive errors are corrected. Although it is generally accepted as an effective and reliable method, intraocular pressure (IOP) increases to very high levels even for a short time at the stage of corneal flap formation in both mechanical microkeratome and femtosecond laser-assisted LASIK surgery.[2] In this regard, the application of LASIK surgery in glaucoma patients or patients with suspected glaucoma is still controversial.[3]

Glaucoma is a progressive optic neuropathy with retinal ganglion cells and retinal nerve fiber damage. High IOP is considered to be the most important and interchangeable risk factor of glaucoma. Progressive disease causes changes in optical disk topography and retinal nerve fiber thickness (NFT).[3]

Optical coherence tomography (OCT) is a non-invasive imaging method that provides real-time in vivo images of the retina.[4] Spectral domain OCT (SD-OCT) performs 20,000

Address for Correspondence: Irmak Karaca, Kemal Özülken, Department of Ophthalmology TOBB ETU Medical School, Ankara, Turkey
Phone:+90 312 292 99 10 E-mail: kemalozulken@hotmail.com **ORCID-ID:** orcid.org/
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or more axial scans per second using 840 nm diode laser and provides high resolution imaging with low artifacts.[5] The quantitative and qualitative analysis of the peripapillary nerve fiber layer obtained by SD-OCT is a highly sensitive diagnostic method used for the detection of glaucomatous damage for many years.[6] Furthermore, improved SD-OCT software allows for the selective evaluation of internal retinal layers such as the ganglion cell layer and the inner plexiform layer.[7] The aim of this study was to investigate the effects of femtosecond laser-assisted LASIK surgery on different layers of the retina with SD-OCT images.

Materials and Methods

Patients who underwent femtosecond laser-assisted LASIK surgery in both eyes between 1 August 2018 and 1 March 2019 at TOBB ETU Hospital's Ophthalmology Department were included in the study. After obtaining the approval of the local ethics committee, detailed information was given to the patients before all applications, and written informed consent was obtained for interventional procedures. The Helsinki Declaration was conducted at all stages of the study.

Patients with spherical refractive error between -6.00 and +4.0 diopters (D) and/or patients with <3 D cylindrical refractive error, best corrected visual acuity (BCVA) with a Snellen chart of at least 20/20 (0.00 logMAR), no known eye disease (such as glaucoma, uveitis, or retinal dystrophies), neurological disease (such as epilepsy or inherited neuropathies), or systemic disease (such as severe vitamin deficiency or metabolic diseases), patients with central corneal thickness (CCT) > 500 µm, and patients with normal limits of NFT, central macular thickness (CMT), and normal macular architecture with SD-OCT measurement were included in the study. Patients outside the scope of this definition with any known eye or systemic disease, past eye trauma or surgery, a history of drug use or dependence, and those pregnant or lactating were excluded from the study.

All patients were subjected to a detailed eye examination and asked to discontinue use of soft contact lenses at least one week before the operation. Manifest and objective refractive errors, uncorrected visual acuity (UCVA), and BCVA values were obtained. While visual acuity values were obtained, a Snellen equation was used and the data were converted to logMAR values. IOP was measured with a Goldmann applanation tonometer, and anterior and posterior segment examinations were performed with a biomicroscope. NFT, ganglion cell thickness (GCT), and CMT values were measured without pupillary dilation by SD-OCT (Heidelberg Engineering, Inc., Heidelberg, Germany). CCT and corneal topography were evaluated in detail with Pentacam HR (Oculus, Wetzlar, Germany).

All surgical procedures were performed by an experienced refractive surgeon (KO) in a single center. After placement of the lid speculum with topical anesthesia with 0.5% proparacaine (Alcaine, Alcon, Fort Worth, TX, USA) and standard preoperative asepsis protocol, surgery began. The Alcon/WaveLight® FS200 (Alcon Surgical, Fort Worth, TX, USA) was used to create a flap thickness of 120 µm with a 9 mm flap diameter. Following flap lifting and drying of the stromal bed, stromal ablation was performed with Wavelight EX500 (Wavelight, Erlangen, Germany). After the stromal bed was irrigated with a balanced salt solution, the flap was repositioned on the stromal bed, and the operation was terminated. Topical postoperative medication, moxifloxacin 0.5% (Vigamox, Alcon, Fort Worth, TX), was applied three times a day for one week, along with a prescription for dexamethasone (Maxidex, Alcon, Fort Worth, TX) at decreasing dosages starting with five times a day for three weeks. Preservative-free artificial tear drops (Refresh, Allergan, Irvine, CA) were added eight times a day for two months. All the patients were instructed not to rub their eyes or go swimming for the first month to prevent flap displacement or infectious keratitis.

At the first postoperative hour, SD-OCT was re-evaluated. At this time, the scan was repeated if suboptimal results were encountered and reliable results were provided. Figure 1 demonstrates a sample of GCT and NFT reports measured by SD-OCT. Detailed ophthalmologic examination was performed on the postoperative first day, first week, and third week, including manifest refraction, visual acuity, IOP, and anterior and posterior segment examinations. In addition, SD-OCT evaluation was repeated in the third week postoperatively. All follow-up examinations were performed for all subjects.

The statistical study included data from the right eyes of all patients. The data obtained from the study were analyzed

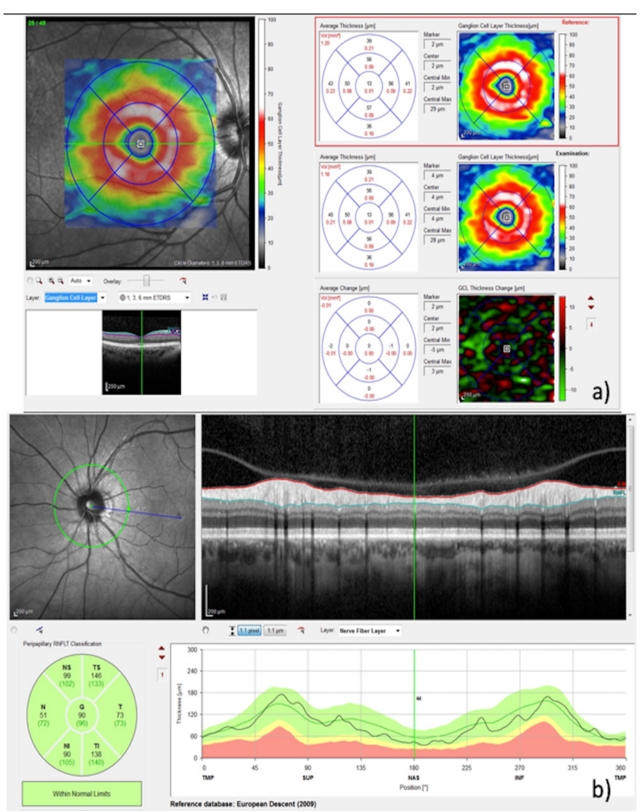

Figure 1. A sample of ganglion cell and nerve fiber thicknesses report measured by spectral domain OCT

using the Statistical Package for the Social Sciences (SPSS) 24.0 software (IBM Corp., New York, USA). Descriptive statistics were presented as mean ± standard deviation (SD). The normal distribution of the variables was tested using the Kolmogorov-Smirnov test. Since the data did not conform to the normal distribution, the difference between the non-parametric Friedman test and the dependent variables was analyzed. The correlation between Pearson correlation analysis was investigated. Statistical significance was set at p <0.05 for all tests.

Results

Of the 40 patients included in the study, 18 (45%) were male and 22 (55%) were female. The mean age of the patients was 27.54 ± 5.99 years (range 18 to 45 years). The preoperative mean spherical equivalent of the patients was -2.13 ± 1.82 D (+2.73 to 5.25 D) and the spherical equivalent of the postoperative third week was -0.23 ± 0.18 D (+0.45 to 0.38 D). The preoperative mean UCVA was 0.84 ± 0.22 logMAR (+1.60 to 0.30 logMAR), while it was 0.11 ± 0.04 logMAR (0.20 to -0.10 logMAR). Table 1 summarizes the preoperative and postoperative third week clinical characteristics of the subjects.

According to the results of the SD-OCT evaluation, preoperative mean GCT was 18.43 ± 6.03 µm (11 to 32 µm), and this value was 18.05 ± 5.93 µm (10 to 31 µm) at postoperative first hour and 17.86 ± 5.27µm (11 to 32 µm) at postoperative third week (p =0.159). The mean peripapillary global NFT were 107,90 ± 9,01 µm (90 to 134 µm) preoperatively, 108.08 ± 8.92 µm (88 to 131 µm) at postoperative first hour, and 107.98 ± 10.13 µm (91 to 135 µm) at postoperative third week (p =0.851).

Similarly, while preoperative CMT was 234.3 ± 21.2 mm (212 to 255 mm), this value was 230.1 ± 22.6 mm (207 to 253 mm) at the postoperative first hour and 236.3 ± 25.1 mm (205 to 267 mm) at the postoperative third week (p =0.254) (Table 2). There was a significant positive correlation between GCT, NFT, and CMT values preoperative, postoperative first hour, and postoperative third week (all p values were <0.001) (Table 3).

Table 1. Clinical characteristics of the subjects at preoperative and postoperative 3rd week.

	Preoperative	Postoperative 3rd Week
Spherical RE (D)	-1.70 ± 2.92 (-6.00 to 4.00)	-0,42 ± 0,35 (-1,00 to 0.75)
Cylindrical RE (D)	-0.86 ± 0.79 (-3.00 to 0.00)	-0.39 ± 0.21 (-0.75 to 0.00)
Spherical equivalent (D)	-2.13 ± 1.82 (+2.75 to 5.25)	-0.40 ± 0.18 (-1.13 to 0.00)
UCVA (logMAR)	0.84 ± 0.22 (1.60 to 0.30)	0.11 ± 0.04 (0.20 to -0,10)
BCVA (logMAR)	-0.12 ± 0.11 (0.10 to -0.30)	-0.09 ± 0.06 (0.00 to -0.20)
CCT (mm)	549.81 ± 23.52 (515 to 606)	489.00 ± 32.44 (430 to 543)

RE: refractive error; UCVA: uncorrected visual acuity; BCVA: best corrected visual acuity; CCT: central corneal thickness.

Table 2. GCT, NFT, and CMT values measured by SD-OCT.

		Preoperative	Postoperative 1st hour	Postoperative 3rd week	p value
GCT(mm)		18.43 ± 6.03	18.05 ± 5.93	17.86 ± 5.27	0.159
NFT (mm)	Global	107.90 ± 9.01	108.08 ± 8.92	107.98 ± 10.13	0.851
	Superior	110.95 ± 9.82	111.15 ± 9.63	111.05 ± 10.91	0.352
	Inferior	111.62 ± 10.74	110.92 ± 10,78	111.75 ± 8.42	0.843
	Temporal	84.90 ± 16.14	85.31 ± 15.69	86.30 ± 15.56	0.481
	Nasal	78.74 ± 7.11	78.31 ± 7.24	77.82 ± 7.14	0.287
CMT(mm)		234.29 ± 21.20	230.07 ± 22.63	236.31 ± 25.12	0.254

GCT: ganglion cell thickness; NFT: nerve fiber thickness; CMT: central macular thickness; SD-OCT: spectral domain optical coherence tomography.

Table 3. Details in correlation between GCT, NFT, and CMT values in preoperative, postoperative 1st week, and postoperative 3rd week.

	Preoperative		Postoperative 1st hour		Postoperative 3rd week	
	r value	p value	r value	p value	r value	p value
GCT and NFT	0.786	<0.001	0.792	<0.001	0.798	<0.001
GCT and CMT	0.822	<0.001	0.816	<0.001	0.812	<0.001
NFT and CMT	0.844	<0.001	0.848	<0.001	0.882	<0.001

GCT: ganglion cell thickness; NFT: nerve fiber thickness; CMT: central macular thickness.

Figure 2 demonstrates GCT, NFT, and CMT values preoperative, postoperative first hour, and postoperative third week (Figure 2).

Discussion

During LASIK surgery, IOP is known to be at very high levels for a period of time. Hernandez-Verdejo et al.[2] reported in their experimental studies that in the LASIK surgery performed with the help of mechanical microkeratome, the IOP increased to 122.5 mmHg and 160.5 mmHg with a mean of 21.4 sec and 15 sec, respectively. In femtosecond laser-assisted LASIK surgery, these values were found to be 89.2 mmHg and 119.3 mmHg for 40 sec and 52.8 sec, respectively.[2] The structural and functional effects of the IOP value above the normal value in both microkeratome and femtosecond laser-assisted LASIK surgery are not yet fully known. Therefore, recent studies have aimed to address concerns about the safety of LASIK surgery in glaucoma patients or in patients with suspected glaucoma.

Computer aided imaging methods are efficient, reliable, and objective and have an important role in the follow-up of glaucomatous patients. Among these, OCT is used more frequently than other methods by allowing direct structural evaluation by direct thickness measurement using the reflection of a near-infrared beam from the posterior segment structures.[8] In recent years, many studies with OCT have shown that there is no significant change in the NFT after both mechanical microkeratome and femtosecond laser-assisted LASIK surgery.[9-12] Although it has been reported that the evaluation of ganglion cell complex (nerve fiber, ganglion cell, and inner plexiform layers in the macular area) in glaucomatous patients does not contribute to the evaluation of peripapillary NFT. The investigation of GCT after LASIK surgery is a newer approach.[13,14]

Zivkovic et al.[15] reported no significant changes in the thickness of the ganglion cell-- inner plexiform layer after microkeratome assisted LASIK surgery. Zhang et al.[7] reported no significant change in the thickness of the nerve fiber layer and ganglion cell complex after femtosecond laser-assisted LASIK surgery. As a result of this study, which evaluated the GCT with SD-OCT in the early period after femtosecond laser-assisted LASIK surgery, it was observed that there was no significant change in GCT and NFT values similar to the literature, and results correlated with CMT.

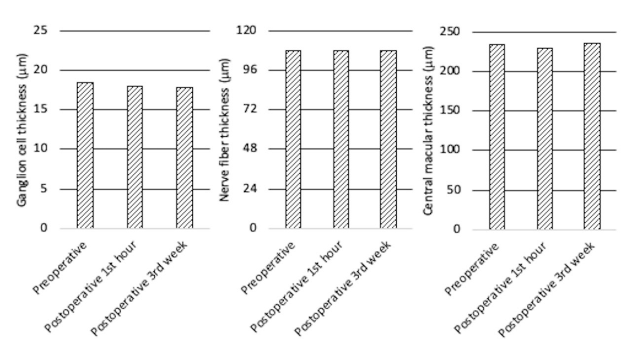

Figure 2. Demonstration of ganglion cell, nerve fiber, and CMT measurements in preoperative, postoperative 1st hour, and postoperative 3rd week.

In another study, Katsanos et al.,[16] examined the NFT after laser-assisted subepithelial keratomileusis (LASEK) and femtosecond laser-assisted LASIK surgery. In contrast to this study, they found that the temporal-inferior and average NFT values were significantly higher after femtosecond laser-assisted LASIK than the preoperative values. Moreover, they suggested that LASIK induced corneal changes might have affected postoperative image acquisition. Furthermore, they stated that they could not exclude increased postoperative NFT as a sign of axonal edema.

In a study conducted by Zhang and Zhou,[17] they showed that IOP elevations observed during LASIK may lead to retinal edema in the postoperative period by preventing ocular blood flow and axial transport in 102 eyes treated with a Ziemer LDV femtosecond laser (Ziemer Group, Port, Switzerland) and 102 eyes treated with an M2 microkeratome. They used Fourier-domain OCT to assess macular, ganglion cell complex and nerve fiber layer thicknesses, and they found that the mean foveal and parafoveal NFT values increased in both groups at the 30th minute after LASIK compared to preoperative values. In addition, they observed that the difference in NFT measurements disappeared on the first postoperative day and remained statistically similar during the one-year follow-up compared to preoperative values.

Similarly, in this study, SD-OCT measurements were performed at one hour after the procedure to investigate the changes in NFT and GCT in the short term after femtosecond assisted LASIK surgery, and no statistical difference between preoperative and postoperative measurements was found. This may be due to the fact that the OCT device used in this study is different. In addition, the time between the mean vacuum on and vacuum off sets generated by the different laser platforms and the increase in the maximum IOP values during the procedure may affect postoperative outcomes. The relatively short time between the average vacuum on-vacuum offsets generated by the new generation femtosecond laser platform used in this study could be the reason there was no increase in the NFT and GCT in this study.

Despite of the results of this study that reports no change in the GCT, NFT, and CMT measured by the SD-OCT in the early period, it cannot be concluded that femtosecond laser-assisted LASIK surgery is completely safe in subjects with glaucoma or glaucoma suspect. In this regard, every subject who candidate for refractive surgery should be detailed evaluated and presence of glaucoma risk factors should be revealed because this surgery may change corneal viscoelastic properties, corneal permeability, and topical antiglaucoma medication response.[18] Further studies evaluating long-term effects of femtosecond laser-assisted LASIK surgery with novel diagnostic tools, may help to overcome these diagnostic and management challenges in glaucomatous or glaucoma suspected subjects.

The fact that a new generation of SD-OCT devices with high sensitivity and resolution are used and a relatively homogeneous sampling is the strength of this study. However, the small number of samples, short follow-up period, and absence of SD-OCT measurements in the postoperative first day may be considered limitations. In conclusion, after femtosecond laser-assisted LASIK surgery, there was no change in the GCT, NFT, and CMT measured by the SD-OCT in the early period.

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