Original Article

Does Laser Iridotomy Cause Secondary Epiretinal Membrane?

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Abstract

Objectives: This study aimed to determine the frequency of epiretinal membrane (ERM) in the long term after neodymium-doped yttrium aluminum garnet laser iridotomy (LI) using spectral domain optical coherence tomography (SD-OCT).

Materials and Methods: This retrospective study included 94 eyes that underwent LI for primary angle-closure glaucoma, were followed for at least 4 years, and had no ERM before the procedure. The control group consisted of 66 eyes that were followed for suspected glaucoma did not have a previous ERM. We compared the ERM frequencies of the groups at the last visit. Additionally, ERM frequencies were compared between those who had cataract surgery in the post-LI period and those who did not.

Results: After a follow-up period of at least 4 years, ERM developed in 36 of 94 eyes (38.2%) in the LI group. Of these, 32 were stage 1 ERM (34.0%) and 4 were stage 2 ERM (4.2%). In the control group, ERM developed in 13 of 66 eyes (19.6%), 12 of which were stage 1 ERM (18.1%) and 1 was stage 2 ERM (1.5%) (p=0.012). ERM developed in 14 of 32 eyes (43.7%) who underwent phacoemulsification surgery after LI and in 22 of 62 eyes (35.4%) that underwent only LI without subsequent cataract surgery (p=0.435). ERM developed significantly more frequently in the 62 phakic eyes that underwent only LI than in the eyes in the control group (p=0.045)

Conclusion: LI appears to be a predisposing factor for the development of ERM, regardless of subsequent cataract surgery.

Keywords: Epiretinal membrane, laser iridotomy, spectral domain optical coherence tomography

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Introduction

Epiretinal membrane (ERM) is an avascular fibrocellular proliferation at the vitreomacular interface.[1,2] It mostly occurs idiopathically at older ages. However, it can also develop secondary to retinal vascular diseases, inflammatory diseases, trauma, repeated intravitreal injections, previous cataract and glaucoma surgery, and rhegmatogenous retinal detachment surgery.[3,4,5,6,7,8] Although ERMs are usually identified by fundus examination, optical coherence tomography (OCT) is more sensitive than slit-lamp examination.[9]

Primary angle-closure glaucoma (PACG) is one of the major causes of blindness worldwide. Although more than one mechanism may be effective in angle closure, the main pathology in most cases is pupillary block. Therefore, the first treatment option is neodymium-doped yttrium aluminum garnet (Nd:YAG) laser peripheral iridotomy (LI).[10] A temporary low-grade iritis may develop after the procedure. Additionally, iris pigments are scattered into both the anterior chamber and the posterior chamber.[11] While anterior segment complications such as corneal endothelial damage, iris bleeding, temporary intraocular pressure (IOP) elevation, and lens damage can often be observed after LI, posterior segment complications are encountered less frequently.[12,13,14]

It has been shown that the frequency of ERM increases after trabeculectomy and Ex-Press glaucoma filtration device implantation surgeries due to increased inflammation and IOP fluctuations.[8,15]

This study investigated the effect of LI on the frequency of ERM in the long term with spectral domain (SD)-OCT.

Materials and Methods

Ethical Approval

This retrospective study was approved by the Institutional Ethics Board of the University of Health Sciences Türkiye, İzmir Bozyaka Training and Research Hospital (reference number: 2023/152; date: 06/09/2023) and was performed in accordance with the principles of the Declaration of Helsinki.

Since the study was retrospective, informed consent was not required.

Participants

The records of patients diagnosed with PACG, primary angle-closure (PAC), or as a primary angle-closure suspect (PACS) and treated with LI in the glaucoma unit of our clinic between January 2017 and June 2019 were retrospectively examined. LI was applied to 312 eyes. Reliable pre-procedural OCT records could not be found for 71 of these eyes, and 88 eyes did not have a follow-up period of at least 4 years. Exclusion criteria were as follows: 1) history of ocular surgery (including cataract) before LI; 2) ocular surgery other than uncomplicated phacoemulsification surgery during the follow-up period after LI; 3) any vitreomacular interface disease (such as posterior vitreous detachment, vitreomacular adhesion, vitreomacular traction, macular hole, pseudohole, or ERM) at the first visit; 4) age-related macular degeneration or any retinal vascular disease; 5) retinal argon laser treatment for any reason; 6) exfoliation material in the anterior segment; 7) anti-vascular endothelial growth factor treatment; 8) media opacity impeding reliable OCT imaging (defined as signal strength >6); 9) axial length (AL) <21 mm or >26 mm; and 10) spherical refraction greater than ±5 diopters (D) or cylindrical refraction greater than ±3 D. Additionally, eyes with acute angle-closure glaucoma treated with LI were excluded from the study. Another 59 eyes were not included in the study due to the exclusion criteria. Thus, 94 eyes of 52 patients were included in the study.

The control group consisted of 66 eyes of 36 age-matched patients who were referred to the glaucoma unit due to suspicion of glaucoma, were examined annually due to risk factors, underwent imaging with the same SD-OCT device, had at least 4 years of follow-up, and met the selection criteria.

After at least 4 years of follow-up, the frequency of ERM was compared between eyes treated with LI and the eyes of controls. In addition, the frequency of ERM was compared between eyes that did and did not undergo cataract surgery after LI.

All subjects underwent a complete ophthalmologic examination. Visual acuity, IOP measurements, gonioscopy, optic nerve status, visual field examinations, number of medications, and the presence or absence of exfoliation were recorded. The best corrected visual acuity of all patients was measured according to the Snellen chart and converted to logarithm of the minimal angle of resolution (logMAR) values for statistical evaluations. AL was measured by optical biometry (IOLMaster 500, Carl Zeiss Meditec, Dublin, CA, USA). The trabecular meshwork was evaluated by gonioscopy using a goniolens with undilated pupil in a dark room. Images were taken using a Cirrus HD-OCT (Model 5000 Carl Zeiss Meditec, Inc., Dublin, CA, USA) at all visits. As previously described, eyes with iridotrabecular contact where at least 180 degrees of pigmented trabecular meshwork could not be seen on gonioscopic examination, IOP <21 mmHg, and no peripheral anterior synechiae were classified as PACS. Eyes with an iridotrabecular contact of at least 180 degrees and an IOP >21 mmHg or peripheral anterior synechiae detected on gonioscopic examination were defined as PAC. In addition to these findings, eyes that showed characteristic optic disc damage or loss of the retinal nerve fiber layer by other examination methods were defined as PACG.[16]

Laser Procedures

In all patients, 2% pilocarpine (Pilosed, Bilim ilaç, İstanbul, Türkiye) was instilled 3 times at 5-minute intervals before the procedure. A Q-switched Nd-YAG laser device was used for the procedure (Tango, Ellex, Adelaide, Australia). LI was applied by an experienced glaucoma specialist (N.T.) in the areas where the iris was thin in the upper quadrants (between 10 and 2 o'clock) using an Abraham iridotomy contact lens (Ocular Instruments Inc.). The power started at 2 mJ and went up to 6 mJ. The number of shots varied with iris thickness. The total energy used and the number of shots were recorded. Observation of the passage of aqueous humor from the posterior chamber to the anterior chamber and the spread of iris pigments from the iridotomy area indicated sufficient LI patency. One hour later, the patients were examined again. The patency of the LI was evaluated both directly and by retroillumination during slit-lamp examination. In 4 eyes evaluated as having insufficient LI patency, the procedure was repeated and the number of shots and energy used were added to the values of the first procedure. Topical loteprednol etabonate 0.5% (Lotemax, Bausch+Lomb, NY, USA) was prescribed to all patients 4 times a day for 1 week.

Optical Coherence Tomography Imaging

All OCT scans were performed with SD-OCT (Cirrus HD-OCT 5000, Carl Zeiss Meditech, Dublin, CA, USA) which has an A-scan velocity of 27,000 scans/second with a 5-µm axial and 15-µm lateral resolution and a scanning depth of 2 mm. The instrument uses light of 840 nm wavelength. The Macular Cube protocol acquires 128 B-scans, each composed of 512 A-scans. Central macular thickness (CMT) was calculated using the Early Treatment Diabetic Retinopathy Study (ETDRS) grid. CMT was defined as the mean thickness of the macula on the central 1 mm of the ETDRS grid. All measurements were performed by the same technician. All OCT images were evaluated by two experienced researchers (O.A., N.T.). There was consensus on all images.

ERM staging was performed using the classification described by Govetto et al.[17] According to this staging, in stage 1 ERM, the foveal contour is preserved and the retinal layers can be well distinguished (Figure 1). In stage 2 ERM, retinal layers can be distinguished but the foveal depression has disappeared. Additionally, tension in the outer nuclear layer is evident (Figure 2). In stage 3, in addition to stage 2, an ectopic inner foveal layer (EIFL) is seen passing through the central fovea. In stage 4, retinal thickness has increased significantly. There is a significant deterioration in the macula. The EIFL is also seen at this stage, but the retinal layers cannot be distinguished.

Statistical Analysis

SPSS version 26 program (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis of the study. Descriptive data were expressed as mean and standard deviation. Independent

t-test was used for comparisons of continuous variables between the LI group and the control group. The chi-square test was used for categorical variables. All statistical analyses were 2-sided and a p value lower than 0.05 was considered statistically significant.

Results

The clinical and demographic characteristics of the patients are shown in Table 1.

Nd:YAG LI was applied to a total of 94 eyes, including 30 eyes with a diagnosis of PACS, 33 eyes with a diagnosis of PAC, and 31 eyes with a diagnosis of PACG. A mean of 15.01±5.03 mJ of energy was used in a mean of 5.2±2.3 shots. The mean IOP was 16.7±3.2 mmHg before LI and 16.1±1.9 mmHg at the last follow-up (p=0.015). A mean of 1.59±1.3 topical antiglaucoma drugs were used before LI, while 1.18±1.2 were used at last follow-up (p<0.001). Uncomplicated phacoemulsification surgery was performed in 32 of the eyes in the LI group an average of 13.9±9.1 months after the procedure.

After a follow-up period of at least 4 years, ERM developed in 36 of 94 eyes (38.2%) in the LI group. Of these, 32 were stage 1 ERM (34.0%) and 4 were stage 2 ERM (4.2%). In the control group, ERM developed in 13 of 66 eyes (19.6%). Twelve of these were stage 1 ERM (18.1%) and 1 was stage 2 ERM (1.5%) (p=0.012) (Table 2). There was no development of stage 3 or 4 ERM in either group.

ERM developed in 14 of 32 eyes (43.7%) that underwent phacoemulsification surgery after LI. Twelve of these were stage 1 ERM (37.5%) and 2 were stage 2 ERM (6.2%). ERM developed in 22 of 62 eyes that underwent LI only (35.4%). Twenty of these were stage 1 ERM (32.2%) and 2 were stage 2 ERM (3.2%) (p=0.435) (Table 2).

ERM developed significantly more frequently in the 62 phakic eyes in the LI group than in the control group (p=0.045). At the end of the follow-up period, ERM developed in 10 of 30 eyes with PACS, 23 of 33 eyes with PAC, and 16 of 31 eyes with PACG (p=0.171). The mean IOP of patients in the LI group was 16.7 mmHg before the procedure and 17.3 mmHg at 1 hour after the procedure (p=0.053).

In the control group, visual acuity decreased from 0.06±0.09 logMAR to 0.09±0.13 logMAR during follow-up (p<0.001). In the LI group, it increased from 0.39±0.17 logMAR to 0.1±0.11 logMAR in those who had cataract surgery (p<0.001) and decreased from 0.1±0.12 logMAR to 0.14±0.15 logMAR in phakic eyes (p<0.001).

The CMT values of the LI and control groups were similar both at baseline and the last visit (Table 1).

Discussion

In this study, we tried to determine the long-term effect of Nd:YAG LI on the frequency of ERM. We observed that ERM developed significantly more in the eyes of the LI group than in controls. We found that phacoemulsification surgery performed after LI had no additional effect on the development of ERM.

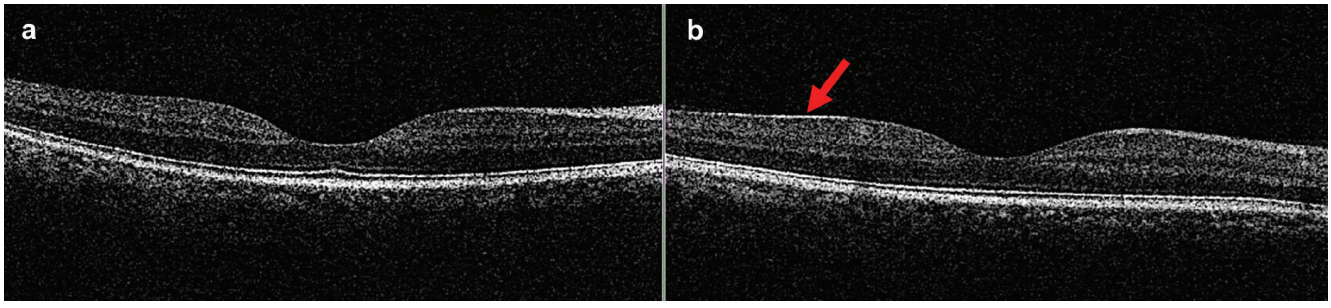

Figure 1. Two spectral-domain optical coherence tomography images of the same patient taken before Nd:YAG laser iridotomy (a) and after 56 months of follow-up (b). The red arrow shows the stage 1 ERM
Nd:YAG: Neodymium-doped yttrium aluminum garnet, ERM: Epiretinal membrane

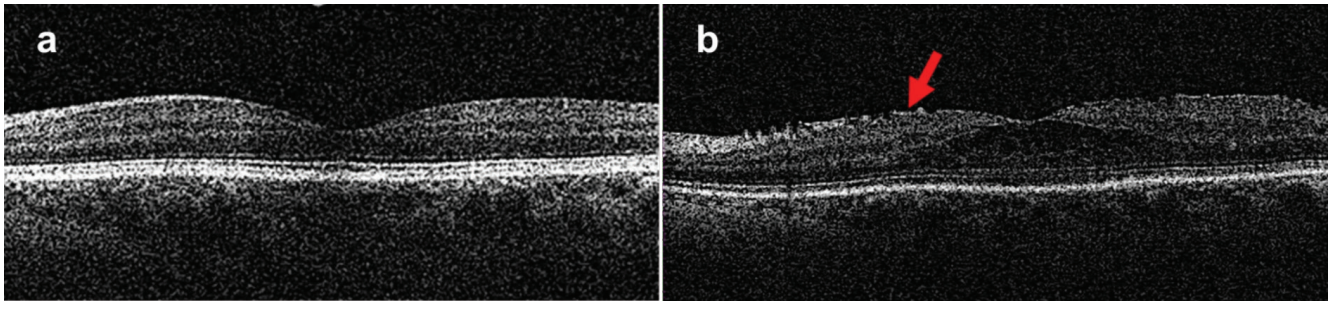

Figure 2. Two spectral-domain optical coherence tomography images of the same patient taken before Nd:YAG laser iridotomy (a) and after 61 months of follow-up (b). The red arrow indicates stage 2 ERM
Nd:YAG: Neodymium-doped yttrium aluminum garnet, ERM: Epiretinal membrane

Table 1. The clinical and demographic characteristics of the patients

	LI group (n=94)	Control group (n=66)	p value
Age (years)	64.03±8.2 (48-80)	66.2±5.9 (51-80)	0.063
Sex (F/M)	33/19	17/19	0.131
BCVA (logMAR) at baseline	0.2±0.2	0.06±0.09	**<0.001**
BCVA (logMAR) at last visit	0.13±0.14	0.09±0.13	0.097
IOP (mmHg)	16.7±3.2	16.1±2.6	0.244
AL (mm)	23.35±0.9	23.31±0.9	0.781
CMT (µm) at baseline	246.6±19	248.1±19	0.636
CMT (µm) at last visit	262.4±21	260.9±21	0.658
Follow-up time (months)	59.1±5.8	55.05±4.1	**<0.001**

Significant p values (<0.05) are indicated in bold. LI: Laser iridotomy, F: Female, M: Male, BCVA: Best corrected visual acuity, logMAR: Logarithm of the minimal angle of resolution, IOP: Intraocular pressure, AL: Axial length, CMT: Central macular thickness

Table 2. The frequency of ERM between the phakic and pseudophakic eyes in the LI group and between the LI and control groups

	LI group				Control group	p value*
	Phakic LI	Pseudophakic LI	p value	Total		
ERM, n/total (%)	22/62 (35.4)	14/32 (43.7)	0.435	36/94 (38.2)	13/66 (19.6)	**0.012**

*LI vs. control group. Significant p values (<0.05) are indicated in bold. ERM: Epiretinal membrane, LI: Laser iridotomy

Vieira et al.[8] attempted to determine the frequency of ERM after trabeculectomy in eyes diagnosed with primary open-angle glaucoma. For this purpose, they retrospectively examined 50 eyes of 40 patients with an average follow-up of 27.5 months. They observed that ERM developed in 28 of 50 eyes (56%), 19 (38%) of which were cellophane macular reflex (CMR) and 9 (18%) were premacular fibrosis (PMF). They reported that 16 of these patients had preoperative OCT, 3 of them (18.8%) developed ERM, and 4 of them (25%) had progression from CMR to PMF. They observed that intraoperative antimetabolite use or phacoemulsification surgery combined with trabeculectomy had no additional effect on the development of ERM. In our study of 94 eyes that underwent LI, ERM developed in 36 eyes (38.2%) within an approximately 5-year follow-up period. The lower prevalence of ERM development despite the longer follow-up in our study may be attributed to several factors. First, it can be considered that trabeculectomy is a more traumatic surgery for ocular tissues than LI. The resulting increased inflammation may cause more secondary ERM development. Another factor may be greater IOP fluctuations after trabeculectomy. No large IOP fluctuations are seen after LI except in acute angle-closure glaucoma. Patients with acute angle-closure glaucoma were not included in our study.

Loiudice et al.[15] reported that over a 6-month follow-up with SD-OCT, ERM developed in 18 of 54 eyes (34%) in which they implanted an Ex-Press glaucoma filtration device due to primary open-angle glaucoma. They observed that ERM developed in 9 (17%) of these patients' fellow eyes treated with only topical antiglaucoma drugs as the control group. They also reported that the combined phacoemulsification surgery had no effect on the development of ERM. The authors concluded that although the pathophysiology of ERM development after this surgery is not fully known, the lower incidence of ERM might be explained by the presence of less inflammation and less IOP fluctuations compared to trabeculectomy. The rate of ERM was higher in our study, but we think this is due to our long follow-up period, not to inflammation or IOP fluctuation. In addition, in the study by Loiudice et al.[15], there was a significant increase in visual acuity in eyes that underwent combined surgery, whereas there was no significant change in those that received only the Ex-Press glaucoma filtration device implant. In our study, there was a significant increase in visual acuity in patients in the LI group who underwent cataract surgery. However, there was a decrease in visual acuity in both the phakic patients who underwent LI and the patients in the control group. We think that this may be due to refractive changes or nuclear thickening that may occur over the long follow-up period.

Acharya et al.[18] and Sar et al.[19] reported cases of macular hole developing after Nd:YAG LI. In both cases, the authors thought that the shock waves generated during Nd:YAG LI may be responsible for the development of macular hole. According to this theory, during the procedure, the shock waves that occur during photodisruption and plasma formation in the anterior chamber first reach the vitreous. There they cause contraction of the vitreous fibers, resulting in traction at the vitreomacular interface that may cause a macular hole.

Similar to the authors above, we think that inflammation occurring after LI and the changes at the vitreomacular interface caused by shock waves associated with the procedure may be responsible for the development of ERM.

Cataract surgery is known to be one of the causes of secondary ERM.[9,20] In this study, we compared the ERM frequencies in eyes treated with LI alone and eyes in which cataract surgery was performed after LI. Similar to the studies of both Vieira et al.[8] and Loiudice et al.[15], we observed that cataract surgery did not have an additional effect on the frequency of ERM.

Study Limitations

The first limitation of our study was that it was retrospective and included data from a limited number of patients. Another limitation was that glaucoma stage was not evaluated. In addition, determining the frequency of ERM progression from early stages to advanced stages during an average 5-year follow-up after LI would also be very valuable. Despite these limitations, to our knowledge this study was the first study to evaluate the frequency of ERM after LI.

Conclusion

Although studies with more eyes are needed, Nd:YAG LI appears to be a predisposing factor for the development of ERM, regardless of subsequent cataract surgery.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Institutional Ethics Board of the University of Health Sciences Türkiye, İzmir Bozyaka Training and Research Hospital (reference number: 2023/152; date: 06/09/2023) and was performed in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: N.T., Concept: O.A., N.T., Design: O.A., N.T., Data Collection or Processing: O.A., N.T., Analysis or Interpretation: O.A., Literature Search: O.A., Writing: O.A., N.T.

Conflict of Interest: No conflict of interest was declared by the authors.

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