DOI: 10.14744/eer.2023.48403
Eur Eye Res 2024;4(1):16–23

ORIGINAL ARTICLE

The effect of ectopic inner foveal layer thickness on metamorphopsia in idiopathic epiretinal membranes

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Abstract

Purpose: The objective is to determine the effect of ectopic inner foveal layer (EIFL) thickness on preoperative and postoperative best-corrected visual acuity (BCVA) and metamorphopsia scores in stage 3 epiretinal membranes (ERM).

Methods: Thirty eyes of 28 patients were included in the study. All patients underwent uncomplicated vitrectomy and membrane peeling. EIFL, central foveal thickness (CFT), outer nuclear layer (ONL), inner nuclear layer (INL), inner plexiform layer (IPL) thicknesses were measured preoperatively and postoperatively at 3 months using Spectralis spectral-domain optical cohorence tomography. Horizontal line (MH) and vertical line (MV) metamorphopsia scores were calculated using M-CHARTS. Postoperative changes in OCT parameters and visual functions and the correlations between them were analyzed.

Results: EIFL thickness, ONL thickness, and CFT were 143.1±19.1 µm, 189.3±48 µm, and 431.7±58 µm preoperatively, respectively. In the postoperative 3rd month, they were 131.2±17.3 µm, 163.5±45.1 µm, and 388.2±52.6 µm (P=0.004, P=0.001, P=0.001 respectively). BCVA (logMAR: Logarithm of the minimal angle of resolution), MH, and MV scores at the postoperative 3rd month were significantly lower than their preoperative values (P<0.001 in all three). Preoperative CFT was found to be correlated with preoperative MH and MV (P=0.031, P=0.02, respectively). Preoperative ONL thickness was correlated with MH and MV scores (P=0.049, P=0.014, respectively). Preoperative INL thickness was only positively correlated with the MH score (P=0.004). There was no correlation between preoperative - postoperative OCT parameters and postoperative visual functions.

Conclusion: EIFL thickness had no effect on metamorphopsia and BCVA in stage 3 ERM patients. It was thought that the formation of metamorphopsia in these patients might be due to changes in the outer retinal layers.

Keywords: Ectopic inner foveal layer; epiretinal membrane; metamorphopsia; optical coherence tomography.

Epiretinal membranes (ERM) is a common vitreomacular interface pathology that increases with age and is characterized by avascular fibrocellular proliferation on the inner retinal surface.[1,2] Although it is usually asymptomatic, it may cause complaints such as decreased visual acuity, metamorphopsia, macropsia, micropsia,

Cite this article as: Akmaz O, Murat Tokac G, Murat Garlı M, Kerci SG, Aydin T. The effect of ectopic inner foveal layer thickness on metamorphopsia in idiopathic epiretinal membranes. Eur Eye Res 2024;4:16-23.

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Submitted Date: 11.05.2023 **Revised Date:** 11.06.2023 **Accepted Date:** 19.07.2023 **Available Online Date:** 20.03.2024

and monocular diplopia, depending on the location and thickness of the membrane and the severity of the distortion it causes in the retinal layers.[3,4] It is known that especially metamorphopsia strongly affects the vision-related quality of life.[5]

ERM is treated by peeling the membrane with pars plana vitrectomy (PPV) in symptomatic patients. Despite successful anatomical removal of the membrane and reduced traction on the retina, recovery of visual acuity and visual functions such as metamorphopsia may take a long time, and sometimes, these may not reach the expected levels.[6] Therefore, it is very valuable to determine the parameters with predictive value for the postoperative visual functions of patients. Spectral-domain optical coherence tomography (SD-OCT) is the most used imaging method for this purpose. It is possible to evaluate ERMs in detail preoperatively and postoperatively using SD-OCT.[7]

The ectopic inner foveal layer (EIFL) is a new OCT-based parameter identified by Govetto et al. in ERM patients.[8] It is described as a band containing the hyporeflective inner nuclear layer (INL) and the hyperreflective inner plexiform layer (IPL), passing the fovea transferably in ERM patients. A new ERM classification was reported by the same authors using EIFL via OCT images. According to this classification, stage 3 and stage 4 ERMs have EIFL.[9] The predictive value of the presence and thickness of the EIFL in terms of postoperative visual acuity prediction has been investigated in many studies.[10-12] However, there are a limited number of studies investigating its effect on metamorphopsia before and after surgery. Kim et al. observed that preoperative EIFL thickness and preoperative metamorphopsia scores were related, but this finding was not present postoperatively.[13] Yanagida et al. reported that there was a significant relationship between EIFL thickness and metamorphopsia scores both preoperatively and postoperatively.[14]

To the best of our knowledge, both stage 3 and stage 4 ERMs have been included in studies on this subject, including the studies mentioned above. The retinal structure is disrupted in stage 4 ERMs. For this reason, retinal layers cannot be distinguished from each other. In addition to the increase in EIFL thickness, it can be expected that this situation may cause deterioration of visual functions. Therefore, the aim of this study is to determine the effect of EIFL thickness on preoperative and postoperative best-corrected visual acuity (BCVA) and metamorphopsia scores in Stage 3 ERM patients without pathological changes in the outer retinal layers.

Materials and Methods

Ethical Approval

This study was approved by the Institutional Ethical Board of the Izmir Bozyaka University Training and Research Hospital (Reference Number: 2023/44 Date: March 29, 2023). Written informed consent was waived from the patients due to the retrospective nature of the study, and the study design was performed in accordance with the principles of the Declaration of Helsinki.

Patients

The records of the patients who were operated on with the diagnosis of ERM and followed up in the retina department of our clinic between January 2017 and November 2022 were reviewed retrospectively. Thirty eyes of 28 patients who were considered stage 3 according to this new classification were included in the study. Those with a visual acuity below 0.2, those with optic media opacity that may affect the OCT image quality, those who had ocular surgery other than uncomplicated cataract surgery, those with a history of trauma, those with ocular pathology that could lead to the development of secondary ERM, and those with vitreomacular interface pathology other than ERM were excluded from the study. Complete ophthalmologic evaluations of patients, including BCVA measurement, metamorphopsia evaluation with M-CHARTS (Inami Co., Tokyo, Japan), slit-lamp biomicroscopy, intraocular pressure measurement, fundus examination, and SD-OCT imaging, were performed both preoperatively and 3 months postoperatively. BCVA measurements were evaluated using the Snellen chart and converted to a logarithm of minimal angle of resolution (LogMAR) for statistical analysis.

Evaluation of the Metamorphopsia

The M-CHARTS system developed by Matsumoto et al. was used for the quantitative evaluation of metamorphopsia.[15] The patients with a BCVA of 0,2 and above were included in the study to make the measurements more reliable. In this system, there are 19 vertical lines arranged linearly at fixed intervals and separated by 0.2–2 degrees. After near refractive correction, the patient is asked to look at the point in the center of the lines from a distance of 30 cm, and the presence of metamorphopsia is questioned. The degree in which the points are apart from each other on the line segment where metamorphopsia disappears corresponds to the vertical metamorphopsia score (MV). Then, the M-CHARTS is rotated 90° and the same process is repeated, and the horizontal metamorphopsia score (MH) is determined. All measurements were calculated by the same experienced technician to whom clinical findings of the patients were masked.

OCT Imaging

Spectralis SD-OCT device (Heidelberg Engineering, Germany) in our clinic was used for qualitative and quantitative ERM evaluations. All measurements were performed by the same experienced technician. At least two SD-OCT scanning patterns were used at each control examination of the patients. Those with low OCT signal strength were not included in the study. The horizontal section passing through the fovea was evaluated. The classification scheme defined by Govetto et al. was used for ERM staging.[8] According to this, Stage 1: Mild ERMs with negligible anatomical and morphological impairment, in which the retinal layers are well differentiated and the foveal contour is preserved. Stage 2: It is the stage in which the retinal layers can be distinguished well, but the foveal depression disappears, stretching is evident in the outer nuclear layer (ONL), and a slightly more advanced retinal disorder is observed. Stage 3: It is the stage in which the foveal depression disappears, the EIFL passing through the central fovea is present, and the retinal layers can be distinguished. The INL seen as a hyporeflective band and the IPL seen as a hyperreflective band, can be clearly identified in the EIFL. Stretching in ONL is less pronounced than in stage 2. Stage 4: In this stage, there is a significant increase in retinal thickness and anatomical deterioration in the macula. EIFL is also seen at this stage, but it is not possible to evaluate the retinal layers.

The SD-OCT images of those with stage 3 ERM according to this classification were evaluated. EIFL and ONL thicknesses were measured manually using these images with the caliper function of Spectralis OCT. Preoperative EIFL thickness was measured from the central fovea between the outer border of the INL and the inner border of the internal limiting membrane (ILM). Postoperatively, it was measured between the outer border of the INL and the vitreoretinal interface (Fig. 1). ONL thickness was also measured from the central fovea, between the outer border of the outer plexiform layer (OPL) and the external limiting membrane (ELM). All manual measurements were made by 2 different retinal specialists and the averages of the measurements with differences were included in the study. Central foveal thickness (CFT), IPL, and INL thicknesses were automatically measured by the device from the foveal ring (central 1 mm area) determined according to the Early Treatment Diabetic Retinopathy Study (ETDRS) using the thickness map function and segmentation feature of Spectralis OCT.

Outer retinal layers were also evaluated on SD-OCT images, as they may affect visual functions. Irregularity, disruption of continuity, and the presence of intermittent hyporeflective areas in the ellipsoid zone (EZ) and ELM, which are normally seen as hyperreflective band, were considered pathological. These eyes were not included in the study. Patients with cystoid macular edema seen as hyporeflective intraretinal cystoid spaces on OCT were not included in the study. Those with lesions described as central bouquet abnormalities (CBA) by Govetto et al. to define cotton ball sign, foveolar detachment, and central acquired vitelliform lesions were also excluded from the study.[16] Retinal layers were determined as recommended by the IN-OCT Consensus.[17]

Surgical Procedure

Surgery was recommended for those with 0.5 or less visual acuity at the time of diagnosis, regardless of the presence of metamorphopsia. In those with better visual acuity, surgery

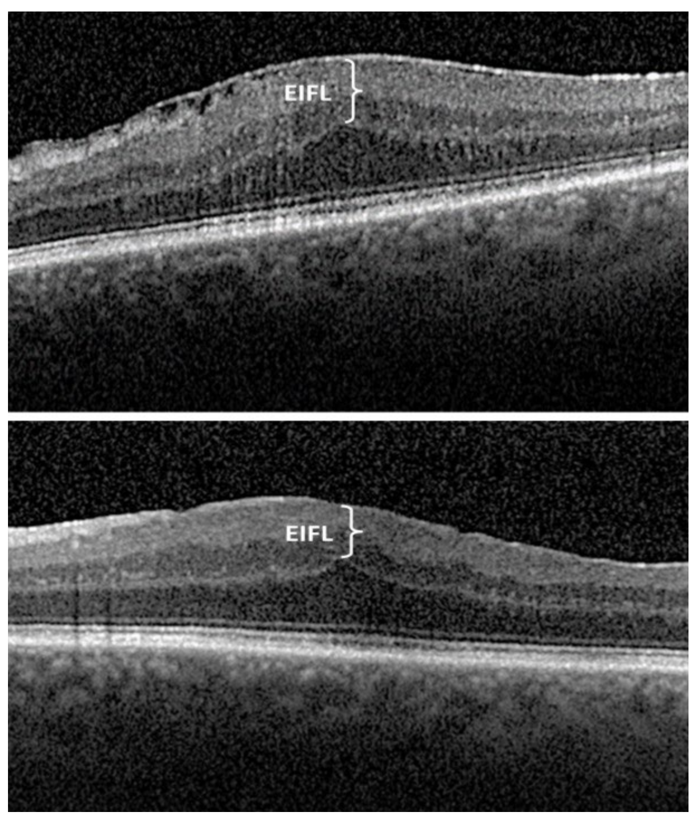

Fig. 1. Preoperative (a) and postoperative (b) Ectopic inner foveal layer (EIFL) appearance on optical coherence tomography image. Preoperative EIFL thickness was measured from the central fovea between the outer border of the inner nuclear layer (INL) and the inner border of the internal limiting membrane. Postoperatively, it was measured between the outer border of the INL and the vitreoretinal interface

was recommended if moderate or severe metamorphopsia was accompanied. In our clinic, we perform simultaneous cataract surgery for our patients over 55 years of age who have undergone PPV surgery, even if they do not have lens opacity. Because the most common complication of ERM surgery is cataract formation. We want to avoid a second surgery in these age groups which the risk of cataract development is increased. Since the youngest patient in this study was 59 years old (59–80 years old), all phakic patients underwent cataract surgery. Three-port standard PPV was applied to all patients by the same 2 surgeons (OA, SGK) using the 23G system. Phacoemulsification and foldable intraocular lens implantation into the capsular bag were performed simultaneously in all phakic cases. In patients whose posterior hyaloid was intact after core vitrectomy, intravitreal triamcinolone acetonide was injected to ensure visibility of the posterior hyaloid, and the posterior hyaloid was separated from the optic disc and retina from posterior to anterior with low aspiration. Following this procedure, trypan blue 0.15% (TB) was used to stain the ERM. The ERM was separated from the retinal surface with the help of micro forceps or the membrane peak and peeled off. After ERM peeling, ILM was stained using TB or brilliant blue 0.025%. The ILM was peeled off with the help of micro forceps. After peripheral retinal control, air or 20% sulfur hexafluoride (SF_6) was given to all cases as internal tamponade. Surgery was terminated after subconjunctival antibiotic and anti-inflammatory injections. No complications were observed in any patient.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS version 24, IBM, Chicago, IL, USA). Quantitative variables are presented as mean deviation±standard deviation. Qualitative variables are presented as numbers and percentages. Differences between preoperative and postoperative visual function parameters and OCT parameters were studied by the Wilcoxon rank sum test. The correlation between visual function parameters and OCT parameters was studied with Spearman correlation tests. A p-value of 0.05 was determined statistically significant in all statistical analyses.

Results

Thirty eyes of 28 patients were included in the study. 15 of the patients were female and 13 were male. Their mean age was 68.07±5.8 (minimum 59-maximum 80 years old). 6 eyes were pseudophakic. Cataract surgery was performed simultaneously with ERM surgery in 24 eyes.

Table 1. Visual functions and OCT parameters at baseline and 3 months postoperatively

	Baseline	At 3 months	P-value
BCVA (LogMAR)	0.46±0.15	0.23±0.14	<0.001
MH	0.55±0.34	0.19±0.17	<0.001
MV	0.47±0.28	0.24±0.15	<0.001
CFT (µm)	431.7±58	388.2±52.6	0.001
EIFL (µm)	143.1±19.1	131.2±17.3	0.004
ONL (µm)	189.3±48	163.5±45.1	0.001
INL (µm)	52.9±13.3	55.8±16.1	0.266
IPL (µm)	41.6±8.9	39.6±9.1	0.327

BCVA: Best-corrected visual acuity; MH: Metamorphopsia score for horizontal line; MV: Metamorphopsia score for vertical line; CFT: Central foveal thickness; EIFL: Ectopic inner foveal layer; ONL: Outer nuclear layer; INL: Inner nuclear layer; IPL: Inner plexiform layer. A P value < 0.05 is considered significant (Wilcoxon Rank Sum Test).

EIFL thickness, ONL thickness, and CFT were 143.1±19.1 µm, 189.3±48 µm, and 431.7±58 µm preoperatively, respectively. In the postoperative 3rd month, they were 131.2±17.3 µm, 163.5±45.1 µm, and 388.2±52.6 µm (P=0.004, P=0.001, P=0.001, respectively). No significant change was observed in the average thickness of the IPL and INL layers at the central 1 mm (P=0.327, P=0.266, respectively) (Table 1). BCVA (LogMAR), MH, and MV scores were significantly lower than their preoperative values (All three P<0.001) (Table 1).

Considering the correlations between preoperative OCT parameters and preoperative visual functions, we observed that preoperative CFT was correlated with both MH and MV (P=0.031, P=0.02, respectively). We found that preoperative ONL thickness was also correlated with MH and MV scores (P=0.049, P=0.014, respectively). In addition, we observed that INL thickness was only positively correlated with the MH score (P=0.004) (Table 2).

There was no correlation between postoperative OCT parameters and postoperative visual functions (Table 3). Moreover, we did not detect any correlation between preoperative OCT parameters and postoperative visual functions (Table 4).

We observed a negative correlation between the preoperative MH score and its change in the postoperative 3rd month (r=–0.849 P<0.001). We also observed a negative correlation between the preoperative MV score and its change in the postoperative 3rd month (r=–0.821 P<0.001). In addition, there was no correlation between preoperative BCVA and MH (r=0.055, P=0.771). No correlation was found between these two in the postoperative period either (r=0.199, P=0.276). There was no correlation between preoperative BCVA and MV (r=0.214, P=0.255). There was

Table 2. Correlation between preoperative OCT parameters and preoperative visual functions

Preoperative visual functions	Preoperative OCT parameters				
	CFT	EIFL	ONL	INL	IPL
BCVA (LogMAR)					
r	0.324	−0.215	0.343	0.071	0.217
P-value	0.080	0.253	0.064	0.708	0.249
MH					
r	0.395	0.244	0.361	0.514	0.118
P-value	0.031	0.194	0.050	0.004	0.536
MV					
r	0.550	0.131	0.445	0.350	0.231
P-value	0.002	0.491	0.014	0.058	0.219

BCVA: Best-corrected visual acuity, MH: Metamorphopsia score for horizontal line, MV: Metamorphopsia score for vertical line, CFT: Central foveal thickness, EIFL: Ectopic inner foveal layer, ONL: Outer nuclear layer, INL: Inner nuclear layer, IPL: Inner plexiform layer. A P value < 0.05 is considered significant (Spearman Correlation Test).

Table 3. Correlation between postoperative OCT parameters and postoperative visual functions

Postoperative visual functions	Postoperative OCT parameters				
	CFT	EIFL	ONL	INL	IPL
BCVA (LogMAR)					
r	−0.020	−0.060	−0.026	−0.024	0.037
P-value	0.916	0.752	0.893	0.901	0.845
MH					
r	0.160	−0.296	0.082	0.099	0.278
P-value	0.399	0.113	0.668	0.605	0.137
MV					
r	0.177	0.146	0.178	0.117	0.350
P-value	0.349	0.440	0.346	0.540	0.058

BCVA: Best-corrected visual acuity; MH: Metamorphopsia score for horizontal line; MV: Metamorphopsia score for vertical line; CFT: Central foveal thickness; EIFL: Ectopic inner foveal layer; ONL: Outer nucleer layer; INL: Inner nucleer layer; IPL: Inner plexiform layer. A P value < 0.05 is considered as significant (Spearman Correlation Test).

Table 4. Correlation between preoperative OCT parameters and postoperative visual functions

Postoperative visual functions	Postoperative OCT parameters				
	CFT	EIFL	ONL	INL	IPL
BCVA (LogMAR)					
r	−0.045	−0.313	−0.036	0.046	0.080
P-value	0.815	0.093	0.849	0.808	0.674
MH					
r	0.041	−0.264	0.031	0.134	−0.178
P-value	0.830	0.158	0.870	0.481	0.346
MV					
r	0.152	−0.182	0.284	−0.044	0.063
P-value	0.422	0.335	0.129	0.818	0.740

BCVA: Best-corrected visual acuity; MH: Metamorphopsia score for horizontal line; MV: Metamorphopsia score for vertical line; CFT: Central foveal thickness; EIFL: Ectopic inner foveal layer; ONL: Outer nuclear layer; INL: Inner nuclear layer; IPL: Inner plexiform layer. A P value < 0.05 is considered significant (Spearman Correlation Test).

no correlation between them in the postoperative period either (r=0.193, P=0.291).

Discussion

In this study, we found that EIFL thickness had no effect on BCVA, MH, and MV preoperatively and at the 3rd month postoperatively in patients with stage 3 ERM according to the OCT-based ERM classification defined by Govetto et al.[8] We observed that preoperative CMT and ONL thickness were positively correlated with preoperative MH and MV scores. We did not find a significant difference in INL and IPL thicknesses before and after surgery. Furthermore, we observed that the functional benefits of surgery decreased as the preoperative metamorphopsia scores of the patients increased.

As a result of the progressive displacement and reorganization of the inner retinal layers toward the center of the macula due to chronic anteroposterior and centripetal tractions caused by ERM, the continuous EIFL is formed, extending along the fovea. According to the OCT-based ERM classification, stage 3 and stage 4 ERMs have EIFL.[8] The presence and increased thickness of the EIFL in ERM patients are thought to be associated with lower visual acuity. Govetto et al. operated and followed 111 eyes with ERM, including patients from 4 stages, for 12 months postoperatively, and observed that the presence of EIFL was a negative prognostic factor for postoperative anatomical and functional recovery.[9] They also stated that EIFL thickness was negatively correlated with BCVA both in the preoperative and postoperative periods. Doguizi et al. examined 121 eyes with ERM and observed that the presence of EIFL, its thickness, and CFT were key indicators for vision loss.[10] They also suggested that the EIFL thickness in the preoperative period could be used to determine the timing of surgery.

Contrary to these studies, Coppola et al. did not include stage 4 ERMs as in our study and reported that the presence of preoperative EIFL did not correlate with preoperative BCVA.[18] They defined stage 1 and 2 ERMs as the group without EIFL, and stage 3 ERMs as the group with EIFL, and they followed these patients for 12 months after surgery. They observed that patients with EIFL, unless there is no disorganization in the inner retinal layers, achieve good visual acuity similar to those without EIFL, even though it's later. They also reported that the increase in visual acuity was associated with baseline BCVA.

The presence of metamorphopsia as well as decreased visual acuity in ERM patients, negatively affects the visual quality.[19] Kim et al., in their study, in which they included 84 patients with stage 2, 3, and 4 ERM, observed a decrease in visual acuity and an increase in metamorphopsia scores as the ERM stage increased in the preoperative period.[13] They reported that EIFL thickness was correlated with metamorphopsia scores in the preoperative period. Alkabes et al. examined 60 eyes with stage 3 and stage 4 ERM and found that metamorphopsia scores were significantly correlated with EIFL thickness and CFT.[20] The same authors stated that visual acuity decreases as the EIFL thickness increases. Furthermore, Yanagida et al. reported that there was a significant relationship between EIFL thickness and metamorphopsia scores both preoperatively and postoperatively.[14]

In this study, we observed that postoperative EIFL thickness decreased significantly, BCVA (LogMAR), MH, and MV decreased significantly compared to the preoperative period. However, we found no correlation between BCVA, MH, MV, and EIFL thickness neither in the preoperative nor in the postoperative period. We think that there may be two reasons why our results differ from the studies mentioned above, apart from the study of Coppola et al.[18] First, the fact that stage 4 ERM patients were not included in this study, like the study of Coppola et al., may have caused this difference.[18] Because the deterioration in visual functions may be more than the increase in EIFL thickness due to the disorganization of the retinal layers in stage 4 ERM patients. Another reason for this difference may be that those with pathological changes in the outer retinal layers, such as CBA, ELM, and EZ damage that adversely affect visual functions, were not included in the study.[9,12,21] In addition, when these results were evaluated, as Kim et al. also stated earlier, in terms of prognosis prediction, the ERM stage in the new classification made according to the presence of EIFL can be considered to be more useful than EIFL thickness.[13]

Since we did not see a significant difference in INL and IPL thicknesses before and after surgery, we thought that the formation of metamorphopsia in this patient group may be due to changes in the outer retinal layers. We observed that preoperative CMT and ONL thickness were positively correlated with preoperative MH and MV scores. ONL thickness may increase due to tangential and centripetal tractions extending to photoreceptors, photoreceptors may be displaced due to these tractions, and as a result, metamorphopsia may develop. Because we observed that both ONL, CFT and metamorphopsia scores decreased when these tractions were removed with surgical treatment. In addition, we found a negative correlation between preoperative MH and MV scores, and their changes in the postoperative 3rd month. In this patient group, we think that it would be appropriate to perform ERM surgery before severe metamorphopsia findings occur, as suggested by Kinoshita et al.[22]

Our study had some limitations. The first of these limitations was that it was performed retrospectively in a small group of patients. Therefore, we could not examine changes in other visual functions, such as aniseikonia and contrast sensitivity after surgery in this patient group. Another limitation was the short follow-up period. Since it has been shown that EIFL thickness or metamorphopsia scores may change in some patients up to 12 months, it may be beneficial to conduct studies with longer follow-up periods in which more patients are included.[9,18] The strengths of our study were that, as far as we know, it was the first study to investigate the effect of EIFL thickness on metamorphopsia in stage 3 patients, and that those with outer retinal pathology such as CBA, EZ injury, and ELM damage were not included.

Conclusion

We observed that EIFL thickness had no effect on preoperative and postoperative 3rd month metamorphopsia scores and BCVA in stage 3 ERMs, in which retinal layers can be distinguished. In addition, we believe that the ERM stage in this new classification, which we routinely use in our daily practice, is more prognostic than EIFL thickness.

Ethics Committee Approval: This study was approved by Izmir Bozyaka Education and Research Hospital Ethics Committee 29.03.2023 date; number 2023/44).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: O.A., M.G.T., M.G., S.G.K., T.A.; Design: O.A., M.G.T., M.G., S.G.K., T.A.; Supervision: O.A., M.G.T., M.G., S.G.K., T.A.; Resource: O.A., M.G.T., M.G.; Materials: O.A., M.G.T., M.G.; Data Collection and/or Processing: O.A., S.G.K., T.A.; Analysis and/or Interpretation: O.A., M.G.T., M.G.; Literature Search: O.A., M.G.T.; Writing: O.A., M.G.; Critical Reviews: O.A., S.G.K., T.A.

Conflict of Interest: None declared.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study received no financial support.

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