Ganglion Cell Complex Thickness Changes Following Removal of Long-Standing Epiretinal Membrane

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ABSTRACT

Objective: To investigate retinal structural changes following removal of long-standing epiretinal membrane (ERM).

Materials and Methods: This retrospective observational study included 15 eyes of 15 patients who underwent PPV with ERM peeling. Fellow eyes served as controls. Best-corrected visual acuity (BCVA), CMT, GCC, GCL, IPL, and RNFL thicknesses were assessed preoperatively and at postoperative week 1 and months 1, 3, and 6 using spectral-domain optical coherence tomography.

Results: The mean preoperative disease duration was 34.6 ± 24.4 months (range, 20–99 months). BCVA improved significantly from 0.30 ± 0.17 preoperatively to 0.65 ± 0.29 at postoperative month 6 (p=0.031). CMT decreased significantly during follow-up (overall Friedman test, p<0.001). GCC thickness demonstrated significant thinning after surgery (overall p=0.030), whereas GCL, IPL, and RNFL measurements did not reveal any significant change. Preoperative BCVA was not correlated with GCC, GCL, IPL, or RNFL thicknesses (all p>0.05).

Conclusions: Removal of long-standing ERM resulted in significant visual and anatomical improvements. Postoperative GCC thinning may reflect retinal remodeling following release of chronic traction; however, progressive neuronal loss cannot be excluded on the basis of the present data.

Keywords: Epiretinal Membrane, Pars Plana Vitrectomy, Ganglion Cell Complex, Inner Plexiform Layer, OCT

INTRODUCTION

Epiretinal membrane (ERM) is a common vitreomacular interface disorder characterized by fibrocellular proliferation on the inner retinal surface, leading to retinal distortion, macular thickening, metamorphopsia, and progressive visual impairment. Its prevalence increases with age and ranges from approximately 5% to 30% in elderly populations, making it one of the most frequently encountered macular disorders in clinical practice [1,2].

Pars plana vitrectomy (PPV) with ERM peeling has become the standard treatment for symptomatic ERM and generally provides favorable anatomical and functional outcomes[2-4]. Nevertheless, postoperative visual recovery varies considerably among patients despite successful membrane removal. Consequently, considerable attention has been directed toward identifying structural biomarkers that may reflect disease severity and predict visual outcomes after surgery[2,5-8].

The optimal timing of surgery for idiopathic ERM remains controversial. Although pars plana vitrectomy effectively relieves traction, prolonged retinal traction before surgery may induce irreversible retinal remodeling involving both

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the inner and outer retinal layers. Several studies have suggested that longer disease duration before surgical intervention may adversely affect postoperative anatomical recovery and visual function, emphasizing the importance of evaluating the duration of ERM prior to surgery as a potential prognostic factor[1,2,6].

Previous investigations have demonstrated that abnormalities involving the outer retina, particularly disruption of the ellipsoid zone and photoreceptor layers, are associated with poorer postoperative visual outcomes[6-8]. However, increasing evidence suggests that inner retinal alterations may also play a critical role in determining visual function. Among the inner retinal parameters, GCIPL and GCC measurements have emerged as important indicators of retinal integrity and visual prognosis[5,6,9]. The GCC, consisting of the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL), contains a substantial proportion of retinal ganglion cells responsible for visual signal transmission [10]. Chronic tangential traction induced by ERM may alter the architecture of these layers, resulting in structural and functional impairment[5,9,10].

Several studies have demonstrated postoperative reductions in GCC and GCIPL thickness following ERM surgery, suggesting that tractional injury, retinal remodeling, and surgical manipulation may influence the integrity of the inner retina[9,11]. Similarly, long-term changes in peripapillary RNFL thickness have been reported after ERM surgery, although their clinical significance remains controversial[12]. Despite these observations, the relationship between postoperative changes in GCC, GCL, IPL, RNFL, and visual recovery remains incompletely understood.

Therefore, the aim of the present study was to evaluate longitudinal changes in visual acuity, macular thickness, GCC, GCL, IPL, and RNFL measurements following removal of long-standing ERM . Additionally, we investigated the relationship between retinal structural parameters and functional outcomes during the postoperative follow-up period.

MATERIALS AND METHODS

This retrospective observational study included 15 eyes of 15 patients who underwent pars plana vitrectomy (PPV) with epiretinal membrane (ERM) peeling. Only patients with a documented disease duration of at least 20 months were included. The fellow eyes of the same patients, provided that they met the eligibility criteria, were used as the control group. All surgical procedures and clinical evaluations were performed at the Department of Ophthalmology, Kırşehir Ahi Evran University Training and Research Hospital, between December 2024 and December 2025. The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Research Ethics Committee of Kırşehir Ahi Evran University. Written informed consent was obtained from all participants prior to enrollment.

Patients presenting with symptomatic ERM associated with decreased visual acuity and/or metamorphopsia were deemed eligible for inclusion. The diagnosis of ERM was established based on fundus examination and spectral-domain optical coherence tomography (SD-OCT) findings. Representative SD-OCT images of ERM are shown in Figure 1. ERM stage was determined according to the OCT-based classification proposed by Govetto et al.[13]Stage 1 was characterized by the presence of a foveal pit and preserved retinal layers. Stage 2 was defined by the absence of the foveal pit while retaining well-defined retinal layers. Stage 3 was characterized by the presence of a continuous ectopic inner foveal layer (EIFL) crossing the central fovea. Stage 4 was defined by a thick EIFL associated with disruption of normal retinal architecture and loss of identifiable retinal layers. Only eyes with stage 2–4 ERM were eligible for inclusion in the study.

The inclusion criteria were as follows: age between 55 and 85 years, refractive error within ±5.0 diopters spherical equivalent and ±3.0 diopters cylindrical error, preoperative best-corrected visual acuity (BCVA) ranging from 0.1 to 0.5 on the Snellen visual acuity chart, intraocular pressure (IOP) ≤21 mmHg, and adequate fixation and cooperation for reliable OCT imaging.

The exclusion criteria included: (1) concomitant retinal disorders, including macular hole, rhegmatogenous retinal detachment, age-related macular degeneration, and uveitis; (2) ocular diseases potentially affecting the retinal nerve fiber layer (RNFL), such as glaucoma, optic neuropathies, or a history of retinal laser photocoagulation; (3) previous intraocular surgery other than uncomplicated cataract extraction; (4) poor-quality SD-OCT images resulting from media opacities, incomplete examinations,

or segmentation artifacts; (5) a history of ocular trauma; and (6) intraoperative use of gas tamponade, which may influence postoperative RNFL measurements. Fellow eyes without retinal pathology, including ERM, age-related macular degeneration, or macular hole, and without any of the aforementioned exclusion criteria, were included as controls.

All participants underwent a comprehensive ophthalmic examination preoperatively and at postoperative week 1 and months 1, 3, and 6. The examination protocol included assessment of BCVA, measurement of IOP using Goldmann applanation tonometry, slit-lamp biomicroscopy, dilated fundus examination and OCT.

All surgeries were performed under general anesthesia by two experienced vitreoretinal surgeons (Ö.K. and K.Ö.), who followed the same guidelines, using a 25-gauge three-port transconjunctival PPV system (EVA Nexus; D.O.R.C., Zuidland, the Netherlands). Following core vitrectomy, the posterior hyaloid was carefully detached and removed when present. The macular area was stained with a dual dye solution (D.O.R.C., Zuidland, the Netherlands) to enhance membrane visualization, and ERM peeling was subsequently performed using end-gripping forceps. (Figure 2). No internal limiting membrane peeling was carried out.

Macular imaging was performed using SD-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany). All scans were acquired by an experienced technician masked to the study design and clinical data. Central macular thickness (CMT) was obtained from the central 1-mm-diameter circle of the Early Treatment Diabetic Retinopathy Study (ETDRS) grid using the built-in Heidelberg Eye Explorer software (version 6.0.9.0). Ganglion cell complex (GCC) measurements were obtained using the macular

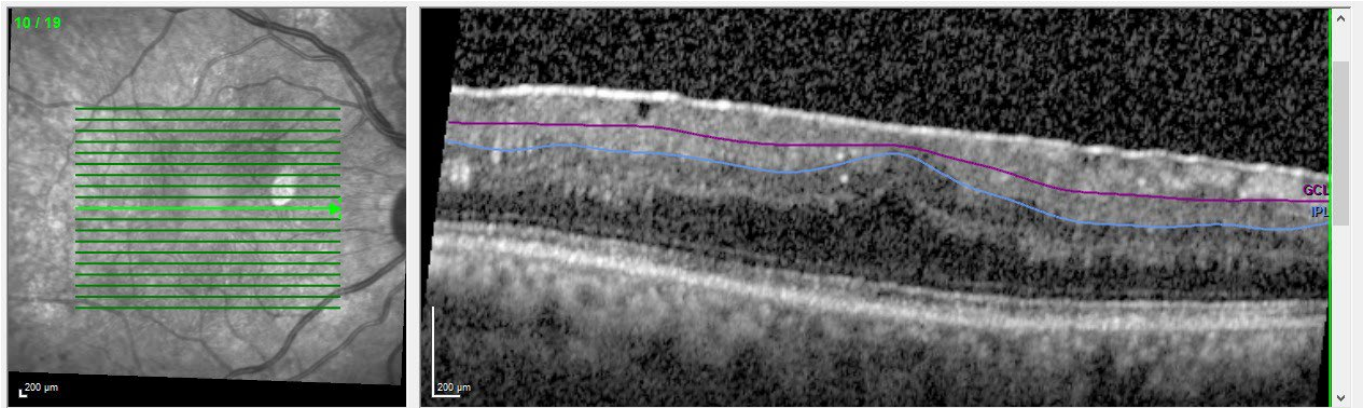

Figure 1: *Preoperative ERM and Retinal Layer Thicknesses*

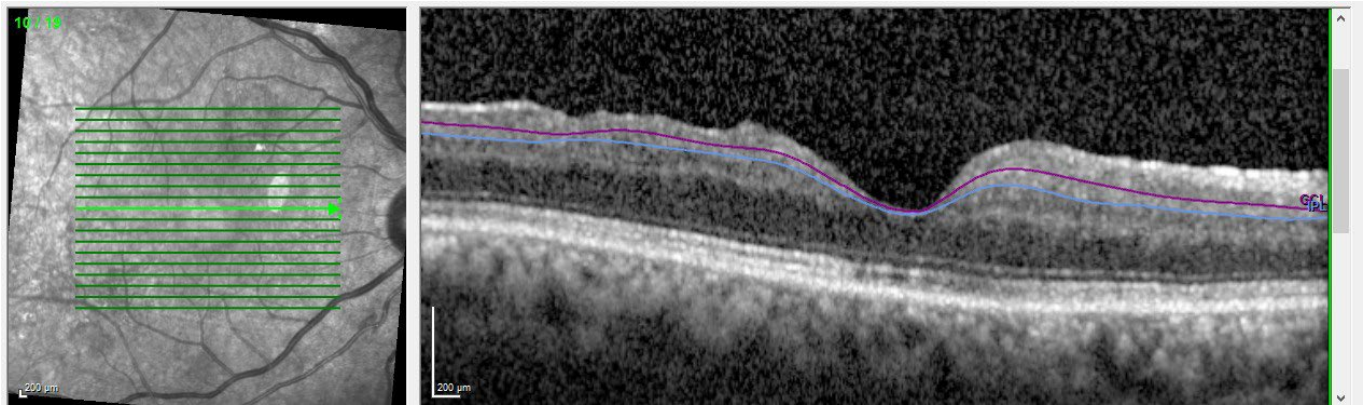

Figure 2 : *Postoperative Retinal Layer Thicknesses*

volume scan protocol of the spectralis spectral-domain optical coherence tomography device. Automated retinal layer segmentation provided by the device software was used to determine retinal layer thicknesses. GCC thickness was defined as the combined thickness of the macular retinal nerve fiber layer (mRNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL). The average GCC thickness generated by the software within the scanned macular region was recorded and included in the statistical analysis. In addition, the presence of ellipsoid zone (EZ) disruption was assessed on preoperative OCT images in eyes with ERM.

Statistical Analysis

Statistical analyses were performed using Jamovi software (Version 2.7.35; The jamovi project, Sydney, Australia). The normality of continuous variables was assessed using the Shapiro–Wilk test. Descriptive data were presented as mean ± standard deviation (SD). Since the control group consisted of fellow eyes of the same patients, baseline comparisons between ERM eyes and fellow-eye controls were performed using the Wilcoxon signed-rank test. Longitudinal changes in visual acuity (VA), central macular thickness (CMT), ganglion cell layer thickness (GCL), ganglion cell complex thickness (GCC), inner plexiform layer thickness (IPL), and retinal nerve fiber layer thickness (RNFL) were evaluated using the Friedman test. When a significant overall Friedman test was identified, pairwise comparisons were explored using the Wilcoxon signed-rank test. No formal adjustment for multiple pairwise comparisons was applied; therefore, these post-hoc p-values were interpreted as exploratory, and the overall Friedman test was considered the primary test of longitudinal change. Correlations between preoperative visual acuity and preoperative retinal structural parameters were assessed using Spearman rank correlation analysis. Correlations between postoperative follow-up time and repeated measurements were not retained because repeated observations obtained from the same eyes are not independent. All tests were two-sided, and a p value <0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 70.33 ± 5.72 years, and 53.3% were male. Preoperatively, visual acuity was significantly lower in ERM eyes compared with the fellow-eye controls (0.3 ± 0.2 vs 0.7 ± 0.2, p<0.001). Similarly, macular thickness, ganglion cell thickness, inner plexiform layer thickness, ganglion cell complex thickness, and retinal nerve fiber layer thickness were significantly different between ERM eyes and control eyes (Table 1, all p<0.01).

According to the Govetto classification, 6 eyes (40%) were stage 2, 5 eyes (33.3%) were stage 3, and 4 eyes (26.7%) were stage 4. Preoperative ellipsoid zone disruption was detected in 3 of the 15 ERM eyes (20%). The mean disease duration from the initial diagnosis was 34.6 ± 24.4 months (20-99 months) (Table 1).

Visual acuity improved during follow-up, increasing from 0.30 ± 0.17 preoperatively to 0.65 ± 0.29 at postoperative month 6. The overall Friedman test demonstrated a significant longitudinal change in visual acuity (p=0.0306). Exploratory pairwise comparisons showed improvement at postoperative month 1 (p=0.0096), month 3 (p=0.0278), and month 6 (p=0.0313); these pairwise p-values were not adjusted for multiple comparisons and should therefore be interpreted cautiously.

Central macular thickness decreased from 489.0 ± 103.3 µm preoperatively to 371.5 ± 78.4 µm at month 6. The overall longitudinal change in CMT was statistically significant (Friedman $\chi^2(4)=26.497$, p<0.001). Exploratory pairwise comparisons showed reductions at postoperative month 1 (p=0.013), month 3 (p=0.032), and month 6 (p=0.037); these pairwise p-values were not adjusted for multiple comparisons and should therefore be interpreted cautiously.−GCC thickness showed a significant overall longitudinal change (Friedman p=0.0296); exploratory pairwise comparisons suggested reductions at postoperative month 1 (p=0.046) and month 6 (p=0.029). No significant longitudinal changes were detected in ~~GC~~GCL, IPL, or RNFL measurements (Table 3).

Spearman correlation analysis demonstrated no significant association between preoperative visual acuity and GCL thickness (r=0.073, p=0.797), IPL thickness (r=0.180, p=0.521), GCC thickness (r=0.011, p=0.969), or RNFL thickness (r=−0.076, p=0.788) (Table 4).

Table 1. *Baseline Characteristics and Preoperative Comparison Between ERM Eyes and Fellow-Eye Controls*

Parameter	ERM Eye (n=15)	Fellow-Eye Control (n=15)	p value
VA	0.3 ± 0.2 (0.1–0.6)	0.7 ± 0.2 (0.5–1.0)	<0.001
CMT (µm)	489.0 ± 103.3 (367–732)	292.3 ± 52.1 (231–425)	0.00065
GCL (µm)	46.0 ± 14.0 (21–76)	21.7 ± 10.6 (9–42)	0.00196
IPL (µm)	45.5 ± 11.4 (22–66)	25.0 ± 7.1 (16–42)	0.00098
GCC (µm)	189.1 ± 74.4 (76–322)	60.7 ± 21.2 (34–104)	<0.0001
RNFL (µm)	97.6 ± 71.2 (13–248)	14.1 ± 4.8 (9–27)	<0.0001

VA:Visual Acuity, CMT: Central macular thickness, GCL: Ganglion cell layer thickness, IPL: Inner plexiform layer thickness, GCC: Ganglion cell complex thickness, RNFL: Retinal nerve fiber layer thickness

Table 2. *Longitudinal Changes in Visual Acuity and OCT Parameters Following ERM Surgery*

Parameter	Preop	1. Week	p	1. Month	p	3. Month	p	6. Month	p
VA	0.30 ± 0.17	0.33 ± 0.16	0.582	0.52 ± 0.26	0.0096	0.58 ± 0.33	0.0278	0.65 ± 0.29	0.0313
CMT (µm)	489.0 ± 103.3	431.4 ± 75.9	0.068	416.5 ± 83.0	0.013	431.9 ± 122.8	0.032	371.5 ± 78.4	0.037
GCL (µm)	46.0 ± 14.0	40.3 ± 13.7	0.116	34.8 ± 13.0	0.088	34.7 ± 12.4	0.064	32.7 ± 11.7	0.121
GCC (µm)	189.1 ± 74.4	155.0 ± 66.3	0.073	140.9 ± 61.0	0.046	151.8 ± 71.0	0.054	130.7 ± 50.5	0.029
RNFL (µm)	97.6 ± 71.2	75.7 ± 61.1	0.296	71.1 ± 59.1	0.163	80.1 ± 64.1	0.534	64.5 ± 37.0	0.084

VA:Visual Acuity, CMT: Central macular thickness, GCL: Ganglion cell layer thickness, GCC: Ganglion cell complex thickness, RNFL: Retinal nerve fiber layer thickness

Table 3. *Friedman Test Results for Longitudinal Changes in Visual and Retinal Structural Parameters*

Parameter	p-value
VA	0.0306
CMT	<0.001
GCL	0.0624
GCC	0.0296
IPL	0.0842
RNFL	0.2778

VA:Visual Acuity, CMT: Central macular thickness, GCL: Ganglion cell layer thickness, GCC: Ganglion cell complex thickness, RNFL: Retinal nerve fiber layer thickness

Table 4. *Spearman Correlation Analysis Between Preoperative Visual Acuity and Retinal Structural Parameters*

Variable	Parameter	Spearman's r	p value
Preoperative visual acuity (VA)	GCL	0.073	0.797
	IPL	0.180	0.521
	GCC	0.011	0.969
	RNFL	-0.076	0.788

VA:Visual Acuity, CMT: Central macular thickness, GCL: Ganglion cell layer thickness, GCC: Ganglion cell complex thickness, RNFL: Retinal nerve fiber layer thickness

DISCUSSION

In the present study, PPV for long-standing ERM resulted in significant visual improvement accompanied by a marked reduction in macular thickness during the six-month follow-up period. GCC measurements demonstrated a progressive decrease over time, whereas GCL, IPL, and RNFL remained relatively stable. Most eyes in the present cohort were categorized as stage 2 or stage 3 according to the Govetto classification13, indicating that the postoperative structural and functional changes primarily represent the response of eyes with intermediate-to-advanced ERM.

Improvement in visual acuity after ERM surgery is a well-established finding and is generally attributed to the release of tractional forces affecting the macula[2-4]. Ozdek et al. reported that both anatomical and functional restoration may continue for months or even years following surgery, reflecting ongoing retinal remodeling processes[2]. Likewise, Chua et al. emphasized that visual rehabilitation frequently extends beyond the early postoperative period despite successful anatomical correction[1].

A noteworthy finding of the present study is that all patients had long-standing ERM before undergoing surgery, with a mean preoperative disease duration of 34.6 months. Chronic retinal traction is thought to induce progressive structural remodeling of both the inner and outer retina, which may influence postoperative anatomical and functional recovery. Previous studies have suggested that prolonged disease duration before surgery may be associated with more advanced retinal alterations and less favorable visual outcomes, although the available evidence remains inconclusive[1,2,6]. Despite the relatively long preoperative disease duration in our cohort, significant postoperative visual improvement was achieved, suggesting that surgical intervention may still provide meaningful functional benefits even in long-standing ERM. The significant reduction in central macular thickness observed in our study is consistent with previous investigations showing reversal of traction-induced retinal thickening after ERM removal[2,3].

Another notable finding of our study was the significant decrease in GCC thickness during the follow-up. Previous studies have demonstrated postoperative reductions in GCC and GCIPL thickness after ERM surgery[9,11]. Lee and Yu reported significant GCIPL thinning six months after surgery and found that greater reductions in GCIPL thickness were associated with poorer postoperative visual outcomes[9]. Similarly, Cunha et al. demonstrated postoperative GCC thinning despite significant visual improvement and reported correlations between GCC measurements and retinal sensitivity assessed by microperimetry[11].

The postoperative reduction in GCC thickness observed in the present study may reflect retinal remodeling following release of chronic traction. However, the present data cannot establish the underlying biological mechanism, and progressive neuronal loss cannot be excluded. Previous OCT-based studies have similarly suggested that

postoperative GCC thinning may accompany restoration of retinal anatomy after relief of mechanical stress[9,11,14]. Unlike many recent studies, ILM peeling was not performed in our cohort. Therefore, the observed GCC changes may be related to ERM removal and release of traction rather than to potential trauma associated with ILM peeling, although this interpretation remains speculative. Interestingly, visual acuity improved despite the reduction in GCC thickness. Similar contrasts between structural and functional recovery have been reported in previous studies evaluating postoperative retinal changes after ERM surgery[9,11].

Another finding was the absence of significant RNFL alterations during the six-month follow-up period. Although several studies have demonstrated postoperative RNFL thinning after ERM surgery, these changes are often observed during longer follow-up periods[12]. Bae et al. reported an initial increase in RNFL thickness followed by gradual thinning of the global and temporal sectors over several years after surgery[12].

Recent evidence suggests that GCC-related parameters may serve as valuable biomarkers of postoperative visual prognosis. Lai et al. demonstrated that increased preoperative GCL and IPL thicknesses were associated with worse postoperative visual outcomes[6]. Furthermore, Cunha et al. reported significant correlations between GCC measurements and retinal sensitivity, highlighting the importance of ganglion cell integrity in visual function[11]. More recently, Zhan et al. showed that preservation of ganglion cell layer plexus microvasculature was independently associated with better postoperative visual acuity and retinal sensitivity[15].

Because only three eyes demonstrated EZ disruption, meaningful subgroup analysis was not feasible. Previous studies have identified photoreceptor integrity, particularly preservation of the ellipsoid zone, as one of the most important predictors of postoperative visual recovery following ERM surgery[7]. Although the limited sample size precluded subgroup analyses in the present study, assessment of EZ status may provide valuable prognostic information and warrants further investigation in larger prospective cohorts.

The present study has several limitations. First, the retrospective design and relatively small sample size may have limited statistical power. Second, the follow-up period was restricted to six months and therefore may not fully capture long-term retinal changes. Third, the use of fellow eyes as controls may represent a limitation because subclinical vitreomacular interface alterations may exist even in clinically unaffected eyes. Fourth, no formal correction for multiple comparisons was applied to the exploratory pairwise Wilcoxon signed-rank tests; consequently, pairwise p-values, particularly those close to the 0.05 threshold, should be interpreted cautiously. A strength of the study is the analysis of an older patient cohort with long-standing ERM.

In conclusion, PPV with ERM peeling resulted in significant visual and anatomical improvement during the six-month follow-up period, even in an older patient group with a longer disease duration. Although GCC thickness decreased significantly after surgery, RNFL measurements remained relatively stable throughout follow-up. Postoperative GCC thinning may reflect retinal remodeling after release of chronic traction; however, progressive neuronal loss cannot be excluded. Larger prospective studies with longer follow-up are required to clarify the clinical and biological significance of these postoperative GCC changes.

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