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Evaluation of retinal neurodegeneration and choroidal thickness following vitrectomy surgery in patients with preexisting epiretinal membrane

 Muhammed Mustafa Kurt,  Tugba Cetinkaya*Samsun Gazi State Hospital, Department of Ophthalmology, Samsun, Turkey*

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Abstract

To investigate neurodegenerative alterations, retinal and choroidal thickness measurements in patients who underwent pars plana vitrectomy (PPV) and the epiretinal membrane (ERM)+inner limiting membrane (ILM) peeling using swept-source optical coherence tomography (SS-OCT). The study was designed retrospectively. The eyes underwent PPV and ERM+ILM peeling comprised the study group, the fellow eyes served as the control group. Best-corrected visual acuity (BCVA), intraocular pressure (IOL), and SS-OCT measurements, including central macular thickness (CMT), ganglion cell layer (GCL)+ and GCL++ thickness, and choroidal thickness (ChT) were analyzed. Inter- and intragroup analyses of these parameters were performed at baseline and 6th month of the postoperative period. The patients had a mean age of 68.63 years. In the study group, the initial BCVA (0.95 ± 0.53 logMAR) showed a slight improvement to 0.79 ± 0.49 logMAR at the 6th month of the postoperative period ($P=0.059$). Only baseline CMT (441.18 ± 99.26 mm) significantly reduced to 377.36 ± 80.26 mm at the final visit ($P=0.042$). Preoperative GCL+ thickness, GCL++ thickness and ChT measurements decreased slightly at the final visit of the postoperative period ($P=0.483$, 0.939 and 0.193 , respectively). Normal fellow eyes had similar preoperative and postoperative BCVA, CMT, GCL thickness and ChT measurements ($P>0.05$ for both). Morphological results of ERM peeling surgery could be analyzed by using OCT to assess prognostic factors related to visual improvement. The outcomes of the study showed no significant visual function recovery following the ERM surgery. No GCL or choroidal thinning was noted. Significant CMT reduction was not associated with visual gain.

Keywords: Pars plana vitrectomy, epiretinal membrane, ganglion cell layer, choroidal thickness, optical coherence tomography

Introduction

Idiopathic epiretinal membrane (ERM) is a relatively common macular disorder in older individuals with a prevalence of about % 6 [1, 2]. ERM can distort foveal morphology with its traction on the macula, which may cause visual impairment and so decrease in visual acuity. The exact pathogenesis of ERM is still not clear. It is proposed that posterior vitreous detachment causes dehiscence in the internal limiting membrane of the retina, as a result, muller cells undergo hypertrophy and grow over the internal limiting membrane [3, 4].

Optical coherence tomography (OCT) is commonly used in the diagnosis and follow-up of retinal pathologies. The results of OCT studies have shown a thickening of the fovea and a disruption of the photoreceptors in the eyes with an ERM [5]. Pars Plana Vitrectomy (PPV) with peeling of ERM has been the gold standard treatment for ERM. The recurrence rate is further reduced when ERM and internal limiting membrane (ILM) peeling is done together [6].

Swept-source (SS) OCT provides a noninvasive imaging opportunity that measures the thickness of retinal layers and even choroidal thickness, thus offering a comprehensive assessment of retinal neurodegeneration, changes in the macula, optic nerve, peripapillary area and choroid for many ocular diseases. The purpose of this study was to measure topographic changes in the macula, including neurodegenerative retinal and choroidal thickness changes after pars plana vitrectomy combined with the inner limiting membrane (ILM) peeling in eyes with ERM.

*Corresponding Author: Muhammed Mustafa Kurt, Samsun Gazi State Hospital, Department of Ophthalmology, Samsun, Turkey
E-mail: musti_art@hotmail.com

Materials and Methods

The Institutional Review Board of Samsun Training and Research Hospital approved the present retrospective and cross-sectional study (GOKA/2021/10/12). Informed consent was obtained from all patients before the surgical intervention. The study was conducted in accordance with the principles of the Declaration of Helsinki. We reviewed the medical records of the patients with unilateral and idiopathic ERM who underwent PPV combined with ILM peeling at Samsun Gazi State Hospital from August 2019 to December 2020.

A total of 11 patients with grade 3 ERM were enrolled in the study. The eyes had ERM surgical procedures served as the study group, and the fellow eyes without any surgical procedures served as the control group. Eyes with mature cataract, macular diseases other than ERM, history of other ocular diseases (glaucoma, uveitis, corneal opacity, etc.) and high myopia (> -5 diopters) were excluded. The patients had a detailed ophthalmic examination including best-corrected visual acuity (BCVA, in logMAR unit), intraocular pressure (IOP, mmHg), anterior-posterior segment evaluation and OCT measurements. Intra- and inter-group comparisons of the BCVA, IOP and OCT parameters were performed at baseline (Initial visit, preoperative period) and 6th month of the postoperative period (final visit).

OCT measurement

We analyzed macular thickness in the 12-mm radial scan mode with Triton model SS-OCT (DRI OCT-1, Topcon, Tokyo, Japan). Retinal thickness was analyzed in 3 separate layers: (1) Central macular thickness (CMT), was measured from the ILM to retinal pigment epithelium (RPE) on the fovea, (2) Ganglion cell layer (GCL)+ thickness was measured between retinal nerve fiber layer and inner nuclear layer (INL) limit, and (3) GCL++ thickness was measured between ILM and INL boundaries. Choroidal thickness (ChT) was measured from the Bruch membrane to the sclera-choroidal interface under the fovea.

Surgical procedure

Follow-up duration after the surgery, the situation of the lens (phakic or pseudophakic) and was also evaluated. A standard 23-gauge (G) three-port PPV was performed by one the same surgeon (MMK) using the Constellation system (Alcon Laboratories, Inc., Fort Worth, TX, USA). After core vitrectomy, the ERM and ILM were peeled circumferentially from the retina with ILM-peeling forceps

in all cases. Finally, we performed a peripheral vitrectomy with shaving and careful inspection of the periphery over 360 degrees. Combined with PPV and ERM+ILM peeling, cataract surgery and implantation of a foldable acrylic intraocular lens (IOL) into the capsular bag were performed in all phakic eyes.

Statistical analysis

SPSS 21.0 software (IBM Corp., Armonk, NY, USA) was used to analyze the data. The constant parameters were demonstrated as the mean $\pm$ standard deviation. Normal distribution of the data was detected by using the Kolmogorov-Smirnov test. Independent samples t-test, Pearson and Spearman correlation tests were used for statistical analyses. A p-value of <0.05 was accepted as the statistical significance.

Results

We enrolled 22 eyes of 11 patients of whom 5 were males (45.5%) and 6 were females (54.5%) with a mean age of 68.63 years (range, 50–83). Seven phakic eyes underwent cataract surgery (phacoemulsification) and IOL implantation combined with PPV and ERM+ILM peeling, the remaining 4 eyes had PPV and ERM+ILM peeling alone.

In the study group, the baseline BCVA (0.95 ± 0.53 logMAR) slightly improved to 0.79 ± 0.49 logMAR at the 6th month of the postoperative period ($P=0.059$). The initial and final IOP values of the study group were similar (14.86 ± 3.72 versus 14.75 ± 3.38 , $P=0.226$). In the control group, the baseline BCVA (0.14 ± 0.01 logMAR) was similar to the final BCVA (0.15 ± 0.01 logMAR, $P=0.344$). Initial and final IOP values of the control group were also similar (14.48 ± 4.13 versus 14.66 ± 3.94 , $P=0.188$). The control group had better BCVA values both at baseline and final visits ($P<0.001$ for both). The study and control groups had similar IOP values both at baseline and final visits ($P>0.05$ for both).

Intra-group analysis of CMT, GCL+ and GCL++ thickness and ChT measurements are represented in table 1. Only preoperative CMT (441.18 ± 99.26 mm) significantly decreased to 377.36 ± 80.26 mm at the final visit of the postoperative period ($P = 0.042$). Preoperative GCL+ thickness, GCL++ thickness and ChT measurements showed insignificant reductions at the final visit of the postoperative period ($P=0.483$, 0.939 and 0.193 , respectively). No alterations in these parameters were observed in the control group including non-operated fellow eyes ($P>0.05$ for all).

Table 1. Preoperative and postoperative intra-group analysis of CMT, GCL+ thickness, GCL++ thickness and ChT parameters

Groups	Parameters (mm)	Preoperative	Postoperative (6 th Month)	P*
Study group	CMT	441.18 $\pm$ 99.26	377.36 $\pm$ 80.26	0.042**
	GCL+ Thickness	105.72 $\pm$ 44.76	84.18 $\pm$ 38.92	0.483
	GCL++ Thickness	132.63 $\pm$ 51.36	129.90 $\pm$ 50.08	0.939
	ChT	197.09 $\pm$ 88.31	178.81 $\pm$ 81.11	0.193
Control Group	CMT	235.80 $\pm$ 40.28	244.20 $\pm$ 36.98	0.310
	GCL+ Thickness	37.10 $\pm$ 10.06	39.20 $\pm$ 9.55	0.680
	GCL++ Thickness	41.20 $\pm$ 8.67	45.20 $\pm$ 11.24	0.556
	ChT	205.80 $\pm$ 68.52	192.30 $\pm$ 53.77	0.490

CMT: Central macular thickness, GCL: Ganglion cell layer, ChT: Choroidal thickness, *Statistically analyzed with independent sample t-test, **Statistically significant

Preoperative and postoperative inter-group analysis of CMT, GCL+ thickness, GCL++ thickness and ChT measurements are represented in table 2. Baseline and final CMT, GCL+ and GCL++ thickness measurements were lower in the control group when

compared to the study group ($P < 0.05$ for all). However similar preoperative and postoperative 6th-month ChT measurements were noted in the study and control groups.

Table 2. Preoperative and postoperative inter-group analysis of CMT, GCL+ thickness, GCL++ thickness and ChT parameters

Parameters (mm)	Study Group	Control Group	P*
CMT			
Preoperative	441.18	232.90	0.001**
Postoperative	377.36	244.20	0.001**
GCL+ Thickness			
Preoperative	105.72	39.36	0.015**
Postoperative	84.18	39.20	0.010**
GCL++ Thickness			
Preoperative	132.63	43.09	0.008**
Postoperative	129.90	45.00	0.011**
ChT			
Preoperative	197.09	213.09	0.710
Postoperative	178.81	192.3	0.702

CMT: Central macular thickness, GCL: Ganglion cell layer, ChT: Choroidal thickness, *Statistically analyzed with independent sample t-test, **Statistically significant

Discussion

ERM is common in elder adults and may cause vision impairment and metamorphopsia due to retinal wrinkle and distortion. Since the 1970s, vitrectomy has been used to remove an ERM. Recently, this surgical technique has been combined with ILM peeling to reduce ERM recurrence [1,7].

In the current study, we analyzed preoperative and postoperative CMT, GCL+ thickness, GCL++ thickness and ChT measurements of the eyes with ERM to assess the outcomes of surgical peeling of ERM and ILM combined with PPV. Our study results showed that only CMT was significantly decreased, but slightly thinning was observed in GCL and choroidal thickness after the ERM surgery. All initial and final thickness measurements were thicker in the eyes with ERM than in the unaffected fellow eyes other than similar ChT measurements. The normal fellow eyes had significantly better baseline and final BCVA values than the eyes with preexisting ERM. Although ERM surgery provided a slight visual gain this was not statistically significant.

Some prognostic factors affecting ERM surgery have been identified, such as preoperative visual acuity and symptom duration [8]. Previous studies used OCT to demonstrate the prognostic value of the structural integrity of the ellipsoid zone (EZ) and the presence of subretinal fluid after the ERM surgery [9-11]. Although thinner ganglion cell inner plexiform layer in the preoperative period seems to be a good prognostic factor [12], the effect of macular GCL thickness on the postoperative visual outcomes of the patients with ERM has not been clearly identified [13]. A study concluded that the visual gain in patients with preexisting ERM (Stage 3) was related to thinning of the inner retinal layers including GCL as well as the outer plexiform layer in the postoperative period [14]. Insignificant postoperative thinning in these layers might be a possible cause for insufficient visual function improvement following ERM peeling.

Alterations in the inner retinal layers including the ganglion cell layer have obtained growing attention in various retinal disorders such as ERM, which may be important in predicting postoperative visual function [15, 16]. The retina is a highly vascular and neuronal tissue; especially the GCL and INL provide connections within amacrine, Müller and horizontal. These cells form connections between the superficial and deep capillary plexus [17]. Müller cells also have an impact in providing the interconnection between retinal neurons and vessels, thus both neuronal and vascular changes may result in neuronal cell death and retinal edema and consequently vision loss in severe ERM [18]. So, the postoperative GCL and INL thinning can provide the repair of the neurovascular connections enabling better visual improvement [17].

Retinal layers in patients with ERM (especially the innermost layers) cannot be always well-segmented due to retinal traction. The different results in previous studies might be due to imaging at different ERM stages and using different OCT platforms and software [19, 20]. Different outcomes in morphologic and functional postoperative findings seemed to be significant among the three ERM stages of 2, 3 and 4. Morphological macular alterations expressed after stage 3 ERM surgery might show an impact on microvascular function [21]. Stage 4 ERM should not be included due to chronic and extensive displacement of the inner retinal layers that lead to photoreceptor disruptions and so impairment of neural transmission [22]. These alterations might not be completely reversible following ERM peeling.

Micro-vascular changes observed in the macula region, such as prominent capillary obstruction and tortuosity may be related to decreased blood flow speeds, which was demonstrated in fluorescein angiography images of the eyes with ERM [21]. The metabolic demand of the inner retina is mainly supplied by the superficial and deep retinal vasculature. Since the borders of GCL are located next to the deep capillary plexus, besides the superficial retina, deep retinal vessel density impairment might

be also observed in ERM, but it may be difficult to visualize in OCT angiography due to several artifacts. A study reported that parafoveal OCT angiographic measurements of the patients with ERM significantly recovered within 6 months in the postoperative period [23]. Moreover, a study demonstrated remarkable postoperative choroidal perfusion alterations in the OCT angiography images of the patients with preexisting ERM [24].

Our study has some limitations including the retrospective design, small number of patients and short-term postoperative follow-up. Prospective studies with a large population size and long-term follow-up should be conducted to investigate postoperative structural and functional effects of ERM surgery. Furthermore, the neurovascular unit should be evaluated with functional assessment, including electro-functional studies and microperimetry.

In conclusion, structural outcomes of PPV and ERM+ILM peeling can be assessed by using OCT to predict prognostic factors associated with visual function recovery. However, our study results concluded no significant visual acuity improvement after the ERM surgery. Only CMT reduction was noted in the postoperative period, whereas no GCL or choroidal thinning was observed.

Conflict of interests

The authors declare that they have no competing interests.

Financial Disclosure

All authors declare no financial support.

Ethical approval

The Institutional Review Board of Samsun Training and Research Hospital approved the present retrospective and cross-sectional study (GOKA/2021/10/12).

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