Outcomes of Internal Limiting Membrane Peeling in Epiretinal Membrane Surgery

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ABSTRACT

Purpose: To evaluate the structural and functional changes in the retinal layers after epiretinal membrane (ERM) surgery combined with internal limiting membrane (ILM) peeling.

Material and Methods: The files of patients who had surgery between 2015 - 2019 years were scrutinized retrospectively. Patients visual acuity and central foveal thickness, perifoveal and parafoveal retinal thickness, nasal and temporal inner and outer retinal thickness which were measured by spectral domain optic coherence tomography (SD-OCT) were recorded at preoperative and 12. months. The changes in the visual acuity, central foveal thickness, ellipsoid zone damage, dissociated optic nerve fiber layer (DONFL), subretinal deposit accumulation and foveal contour were evaluated.

Results: Fifty-one eyes of 51 patients and 40 healthy subjects as control were enrolled. Except perifoveal and parafoveal nasal outer retinal segment, all retinal layers were reduced in the 12 months. When the patients compared to the controls, inner retinal layers were thinner in all ERM patients. Whilst the mean outer retinal layer thickness in the temporal region was similar, it was thicker in the nasal region of the patient group. All patients had DONFL after the surgery. There wasn't any recurrence case. Four patients (% 7.8) had ellipsoid zone damage and 2 patients (% 3.9) had subretinal deposits.

Conclusions: ILM peeling may decrease the recurrence of ERM. However, it may lead to a decrease in the inner retinal layer thickness and changes in the retinal layer thickness. Further studies are needed to clarify long-term effects on the visual acuity.

Keywords: Dissociated optic nerve fiber layer, Epiretinal membrane, Internal limiting membrane.

INTRODUCTION

Epiretinal membrane (ERM) is fibrocellular contractile proliferation occurring on surface of internal limiting membrane (ILM), particularly at macula.[1] Although pathogenesis hasn't been fully understood, incomplete pathological posterior vitreal detachment is implied.[1]The ILM layer localized between retina and vitreous consists of Müller cell of basal membrane. It contains collagen fibers, glycosaminoglycan, laminin and fibronectin.[2] The Müller cells are most abundant glial cells in retina and they are present throughout neurosensory retina. These cells play an active role in the retina. The Müller cells are responsible from protection of all types retinal cell soma and retinal neurons.[3]

The contraction of ERM causes marked traction in ILM, retinal blood vessels and inner and outer retina.[4,5] The vitrectomy plus ERM peeling is decided by metamorphopsia and impaired vision.[6] In recent years, many ophthalmologists recommend ILM peeling together with ERM peeling.[7] In a survey about ILM peeling among ophthalmologists, the number of ophthalmologist recommending ILM peeling was increased compared to previous years.[7] In ERM surgery, benefits and potential harms of ILM peeling are controversial. It is likely to anticipate Müller cell defect and resultant structural and functional changes by ILM peeling. In preliminary study on ILM peeling, no significant difference was detected in visual acuity between groups. However, recurrent ERM rate was found to be lower in the group without ILM

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peeling .[8] There are studies showing that ILM peeling had no effect on visual acuity with decreased ERM recurrence and that ensured more rapid recovery of retinal folds.[9, 10] However, there are studies showing that ILM peeling caused structural retinal changes in addition to reduction recurrence rate.[11]

In our study, it was aimed to investigate whether structural changes developed in our patients underwent ILM peeling during epiretinal membrane surgery.

MATERIAL AND METHOD

We retrospectively reviewed files of patients who underwent idiopathic ERM surgery and ILM peeling between January, 2015 and May, 2019. The study was approved by Institutional Ethics Committee. The patients diagnosed as idiopathic epiretinal membrane were included to the study. Patients with maculopathy other than ERM, those with history of previous vitrectomy and patients with vitreomacular traction were excluded.

Clinical ERM classification was made based on fundus examination findings described by Gass:[12] grade 1, bright, cellophane membrane recognized on retinal surface without retinal distortion (clinically, cellophane maculopathy or premacular gliosis); grade 2, cellophane ERM leading irregular crinkling at retinal surface and ILM (surface crinkling maculopathy); grade 3, thick, opaque ERM covering underlying retinal vessels (clinically macular pucker). Age- and sex-matched healthy individuals without ocular problem other than refractive errors were included as controls. ERM plus ILM peeling was performed in all patients with ERM. Comprehensive ophthalmological examination, fundus imaging and SD-OCT imaging were performed at baseline and on months 3, 6, 9 and 12 in all patients. In all patients, visual acuity, central foveal thickness (CFT), perifoveal and parafoveal nasal and temporal inner and outer retinal thicknesses were recorded. In addition, dissociated optic nerve fiber layer, ellipsoid zone damage, subretinal deposition and foveal contour formation were also assessed on SD-OCT.

SD-OCT: Macular retinal thickness was measured using RTVue-100 Fourier-domain OCT (Optovue Inc., Fremont, CA, USA). In this study, scanning protocol was EMM5 which involves a macular area of 6 mm x 6 mm and 0.90 seconds of scan time with 21 horizontal and 21 vertical scans. Data were used to form a 5 mm x 5 mm map and whole retinal as well as inner and outer retinal thicknesses can be segmented for presentation of maps. Inner retinal thickness was defined as distance from vitreoretinal interface (VRI) to inner plexiform layer (IPL) whereas outer retinal thickness was defined as distance from IPL to photoreceptor inner segment/outer segment (IS/OS) junction and whole retinal thickness as distance from VRI to photoreceptor IS/OS junction. Macular area was assigned into 3 circles as concentric fovea (central circle with diameter of 1 mm), parafoveal (inner diameter: 1mm and outer diameter: 3 mm) and perifoveal (inner diameter: 3 mm and outer diameter: 5 mm).

Statistical analysis: Data were analyzed using IBMS SPSS version 20.0. Normal distribution of quantitative data was assessed using Kolmogorov-Smirnov test. Mean values were assessed using t test or Mann Whitney U test. Categorical variables were assessed using Chi-square test. A p value was considered as statistically significant. Correlation analysis was performed using Pearson's or Spearman's correlation tests where appropriate. Data are presented as mean ± standard deviation.

FINDINGS

The study included 51 patients with ERM and 40 healthy individuals as controls. Mean age was 68.4±7.6 years in ERM group whereas 69.3±6.7 years in the control group (p=0.594). Female: male (F: M) ratio was 35: 16 in ERM group and 28/12 in the control group (p=0.808. there was stage 2 ERM in 37 patients (72.5%) and stage 3 ERM in 14 patients (27.5%). Of the patients, 31 (60.8%) underwent vitrectomy alone while 20 patients underwent phako plus vitrectomy. Mean visual acuity was found as 0.88±0.50 logMAR before surgery and 0.26±0.20 logMAR on postoperative month 12 ($p<0.0001$). When retinal thicknesses before and on month 12 after surgery were compared, it was seen that there was thinning in all retinal layers other than perifoveal and parafoveal outer nasal retinal thicknesses (Table 1). When compared to controls, it was found that inner retinal layers were thinner while outer retinal layers were comparable in temporal but thicker in nasal regions on month 12 after surgery (Table 2). When correlation between visual acuity on postoperative month 12 and retinal thicknesses, it was found that there was significant, moderate positive correlation between preoperative CFT, inner retinal thickness, outer retinal thickness, postoperative thickness and inner retinal thickness (Table 3). Dissociated optic nerve fiber layer (DONFL) appearance was detected in all patients (Figure 1). No recurrence was detected. There was ellipsoid zone damage in 4 patients (7.8%) and subretinal deposit in 2 patients (3.9%).

Table 1: *Comparison of preoperative and postoperative visual acuity and OCT values.*

	Preoperative	Postoperative month 12	P value
Visual acuity (logMAR) mean ±SD	0.85±0.5	0.21±0.10	<0.0001
Total central fovea thickness (micron) mean ±SD	392.2±65.8	300.44±51.31	<0.0001
Inner Central fovea thickness (micron) mean ±SD	123.0±26.2	94.11±923.22	0.004
Outer Central fovea thickness (micron) mean ±SD	268.2±48.8	201.44±32.55	<0.0001
Parafoveal inner temporal quadrant(micron) mean ±SD	146.9±14.6	110.7±3.4	<0.0001
Parafoveal inner nasal quadrant(micron) mean ±SD	165.7±23.6	122.7±9.8	<0.0001
Perifoveal inner temporal quadrant(micron) mean ±SD	118.5±7.4	93.2±7.2	<0.0001
Perifoveal inner nasal quadrant(micron) mean ±SD	135.5±15.5	110.6±5.4	<0.0001
Parafoveal outer temporal quadrant(micron) mean ±SD	218.2±19.5	196.6±12.6	<0.0001
Parafoveal outer nasal quadrant(micron) mean ±SD	224.4±31.8	227.8±31.9	0.382
Perifoveal outer temporal quadrant(micron) mean ±SD	182.8±7.5	170.9±12.0	<0.0001
Perifoveal outer nasal quadrant(micron) mean ±SD	193.9±18.7	193.8±24.2	0.976

Table 2: *Comparison of OCT values between healhy controls and epiretinal membrane group.*

	Healthy control group. n=40	Epiretinal membrane group. n=51	P value
Total central fovea thickness (micron) mean±SD	253.44±18.90	300.44±51.31	<0.0001
Inner central fovea thickness (micron) mean±SD	72.04±9.75	94.11±23.22	<0.0001
Outer central fovea thickness (micron) mean±SD	182.84±13.51	207.44±32.55	0.003
Parafoveal inner temporal quadrant (micron) mean±SD	115.73±7.20	110.23±3.98	<0.0001
Parafoveal inner nasal quadrant (micron) mean±SD	127.55±14.34	119.04±12.50	0.018
Perifoveal inner temporal quadrant (micron) mean±SD	103.36±9.41	94.85±8.18	<0.0001
Perifoveal inner nasal quadrant (micron) mean±SD	116.10±14.31	109.31±6.22	0.028
Parafoveal outer temporal quadrant (micron) mean±SD	200.18±16.29	198.15±16.08	0.635
Parafoveal outer nasal quadrant (micron) mean±SD	196.67±7.17	238.08±39.99	<0.0001
Perifoveal outer temporal quadrant (micron) mean±SD	178.36±12.35	174.23±14.46	0.242
Perifoveal outer nasal quadrant (micron) mean±SD	184.73±14.46	200.00±29.77	0.012

Table 3: *Correlation analysis between postoperative visual acuity and retinal thicknesses.*

Parameter	Visual acuity on postoperative month 12	
	Correlation coefficient	p value
Preoperative central fovea thickness	0.60	***0.003***
Preoperative central inner retina thickness	0.73	***<0.00001***
Preoperative central outer retina thickness	0.58	***0.009***
Postoperative central fovea thickness	0.58	***0.006***
Postoperative central inner retina thickness	0.54	***0.003***
Postoperative central outer retina thickness	0.35	***0.116***

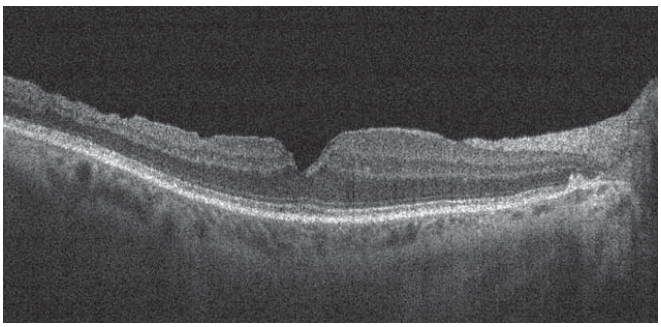

Figure 1: *Dissociated optic nerve fiber layer apperance.*

DISCUSSION

In ERM surgery, in addition to surgical techniques changed over time, ILM peeling together with epiretinal membrane is a controversial issue. There are several studies indicating that ILM peeling ERM surgery had no visual effect

but markedly reduced recurrence rate.[13] Similarly, we observed no recurrence. However, there are also studies demonstrating that ILM peeling caused some structural changes in retina.[11, 14-16] In our study, it was found there was thinning in all retinal layers other than inner nasal quadrant on postoperative month 12. When data obtained on postoperative month 12 wee compared with healthy controls, it was seen that perifoveal and parafoveal inner layers are thinner. In a study on patients with macular hole, it was found that there was thinning in ganglion cell layer and inner plexiform layer in both nasal and temporal regions in agreement with our study.[11] In another study, it was found that inner parafoveal retinal region was thinner in ERM patients underwent ILE peeling and that temporal region was thinner while nasal region was thicker at postoperative period when compared to healthy controls.[17]

Treumer et al. found that temporal region returned to normal while nasal region remained thick at mean follow-up of 4 years in patients underwent ILM peeling in ERM surgery.[18] In some studies, it was shown that there was retinal thinning in temporal retina with ILM peeling.[19, 20] The reason for thickness alteration in retinal regions with ILM feeling hasn't been understood. As known, Müller cells are present throughout all retinal layers, support retina and ILM is basal membrane of Müller cell. By ILM peeling, changes in retina may occur due to trauma in Müller cell. In a study (2018), the patient underwent ILM peeling were assessed immediately after peeling using intraoperative OCT and it was found that there was thickening in inner retinal layer which was considered as a marker for trauma.[21] In another study, thinner temporal region was explained by higher resistance of nasal retina against traction due to more compressed package of nerve fibers, ganglion cells and other retinal cells in papillomacular bundle.22 In the study by Yoshikawa et al. it was found that fovea was displaced towards optic disc. Authors suggested that the displacement will lead traction in temporal retina, causing thinner temporal retina.[23]

Tadayoni et al. (2001) observed abundant number of arcuate stria along optic nerve fiber which were darker than surrounding tissue by blue-free fundus images and defined this appearance as dissociated optic nerve fiber layer.[24] Authors proposed that there was defects in inner structure of retina in patients undergoing ILM peeling in ERM and macular hole surgeries and that these defects might be associated with optic nerve fiber based on their shape. In recent OCT studies, it was reported that these defects were limited to retinal nerve fiber layer.[25] It has been proposed that DONFL frequency is increased by mechanic trauma of ILM peeling as it was found that increased thickness of inner retina was associated with DONFL development by intraoperative OCT.[21] However, in another study, it was suggested that DONFL appearance can represent rearrangement of macular nerve fiber rather than true mechanical injury of retinal nerve fiber following ILM.[26] The frequency of DONFL varies across studies. In a study on patients underwent ILM peeling due to ERM and macular hole, DONFL frequency was found as 30%, 78% and 80% on months 1, 3 and 6, respectively.[26] In a study on ILM peeling for macular hole, DONLF rate was found as 100%.[27] This was attributed to use of en face OCT, suggesting that more clear assessment could be made by en face OCT.[27] Similarly, we found DONFL rate as 100% in our study. There are studies DONFL appearance can be at varying degrees.[27] Effects of these defects on retinal function are controversial. Some authors advocate that these defects are solely structural rather than being functional.[28, 29] In a study, no significant difference was found in visual acuity and retinal sensitivity between patients with and without DONFL. In support, no significant difference was found in retinal sensitivity when DONFL area and other retinal areas were compared..[30,31] On contrary, there are studies showing decreased retinal sensitivity.[32, 33] Nukada et al. suggested that this difference was related with areas selected to compare retinal sensitivity and that retinal sensitivity was lower in temporal region as DONFL defect was deeper in that region.[33]

In our study, we detected a significant, moderate positive correlation between postoperative visual acuity and preoperative central foveal thickness, inner and outer layer thickness, postoperative inner layer and central foveal thickness. The correlation between visual acuity and foveal thickness is controversial. In some studies, a correlation was detected between preoperative foveal thickness and visual acuity on month 6.[34, 36] Again, in another study, a correlation was detected between preoperative central foveal thickness and postoperative visual acuity and found that preoperative CFT was effective in time to achieve final visual acuity.[36] On contrary, there are studies that found no correlation between postoperative visual acuity and baseline retinal thicknesses.

Our study has some limitation including lack of ERM patients without ILM peeling as controls and limited sample size. Thus, effects of ERM peeling alone on retinal thickness changes and DONFL appearance could not be assessed.

CONCLUSION

ERM is an important pathology that impairs vision and causes metamorphopsia. Although ILM peeling in ERM surgery resulted in marked decrease in recurrent ERM,

it may lead thinning at inner retinal layers, DONFL and changes in retinal thickness. This may lead functional alterations. Effects on long-term results should have to be investigated.

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