

Internal Limiting Membrane Peeling in Epiretinal Membrane Surgery, is it a Safe Procedure?

Epiretinal Membran Cerrahisinde İnternal Limitan Membran Soyulması Güvenilir bir Prosedür müdür?

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ABSTRACT

Purpose: To assess the effect of internal limiting membrane (ILM) peeling on macular anatomy and function in the patients who underwent a surgery for idiopathic epiretinal membrane (ERM).

Materials and Methods: We studied a retrospective interventional case series of 20 eyes in 20 patients with idiopathic ERM. The study group (n= 10) who underwent “Pars plana vitrectomy (PPV), ERM removal and ILM peeling - double peeling,” and the control group (n= 10) who underwent “PPV, ERM removal without ILM peeling - single peeling” were statistically compared with each other by means of visual acuity, multifocal electroretinography, optical coherence tomography and microperimetry.

Results: ILM peeling do not affect the postoperative visual acuity, central macular thickness, microperimetry scores, N1 amplitudes and latencies statistically. However P1 amplitudes in ring1 decreased significantly in ILM peeled eyes (p=0.041). Besides, while foveal contour was recovered in 40% of the control group, none of the ILM peeled eyes had normal foveal contour at the end of the 3rd month.

Conclusion: Although ILM peeling do not reduce the visual acuity, it may result in an additional damage to the muller cells and the inner segments of the retina.

Key words: Epiretinal membrane, Internal limiting membrane, Electroretinogram, Microperimetry, Optical Coherence Tomography.

ÖZ

Amaç: Epiretinal membran (ERM) cerrahisi uygulanan hastalarda iç limitan membran (İLM) soyulmasının makula anatomisi ve fonksiyonları üzerine olan etkisinin değerlendirilmesi

Gereç ve Yöntemler: Retrospektif olarak tasarlanan çalışmaya idiyopatik ERM tanılı 20 hastanın 20 gözü dahil edilmiştir. Pars plana vitrektomi (PPV) ve ERM ile birlikte İLM soyulması ameliyatı yapılmış olan çalışma grubu hastaları (n=10) ile PPV ve İLM soyulmaksızın ERM soyulması ameliyatı yapılmış olan kontrol grubu hastaları (n:10) görme keskinliği, multifokal elektroretinografi, optik koherens tomografi ve mikroperimetri tetkikleri ile istatistiksel olarak karşılaştırılmıştır.

Bulgular: İLM soyulması, postoperatif görme keskinliğini, santral makula kalınlığını, mikroperimetrik değerleri, N1 amplitüdlerini ve latansları istatistiksel olarak etkilememektedir. Fakat birinci halkadaki P1 amplitüd değerleri İLM soyulan grupta belirgin olarak azalmaktadır.(p=0.041) Bununla birlikte 3.ayın sonunda, İLM soyulan gözlerin tamamında foveal kontur oluşmazken, kontrol grubundaki gözlerin % 40'ında foveal kontur oluşmuştur.

Sonuç: İLM soyulması makula üzerinde görme keskinliğini azaltacak bir etkiye yol açmamakla beraber, müller hücrelerinde ve iç retinal tabakada fazladan bir hasara neden olabilir.

Anahtar kelimeler: Epiretinal membran, İç Limitan Membran, Elektroretinografi, Mikroperimetri, Optik koherens tomografi.

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INTRODUCTION

Epiretinal membrane (ERM) is a vitreoretinal interface disorder characterized by avascular fibrocellular proliferation located on the surface of the internal limiting membrane (ILM) and in the macula.¹ It may cause vision loss, macropsy, micropsy or metamorphopsy.² Standard surgical treatment involves a pars plana vitrectomy (PPV) and ERM peeling procedure. In some studies published recently, ILM peeling was also recommended to decrease the recurrence of ERM.³⁻⁵

In some of these studies, it has been stated that ILM peeling had no unfavorable effect on the macula however in some of them, it has been reported that electrophysiological responses were deteriorated while the visual acuity was not affected.^{5,6,7} In this respect, peeling of the ILM in ERM surgery is still inconsistent and controversial.

The aim of the current study is to assess the macular anatomy and function between the patients who underwent a surgery for idiopathic ERM with and without ILM peeling by means of visual acuity, multifocal electroretinography (mfERG), optic coherens tomography (OCT) and microperimetry.

MATERIALS AND METHODS

We reviewed the records of the patients operated consecutively at our clinic (Gulhane Military Medical Academy, Haydarpaşa Training Hospital, Retina Department) with the diagnosis of idiopathic ERM. They were divided into two groups by matching age and sex, the study group (n= 10) who undergone "PPV, ERM removal and ILM peeling - double peeling," and the control group (n= 10) who undergone "PPV, ERM removal without ILM peeling - single peeling". Exclusion criterias were: the history of previous retinal detachment surgery, cryopexy, argon laser photocoagulation, penetrating or blunt ocular trauma, uveitis, glaucoma, vascular pathologies (retinal vein occlusion, diabetic or hypertensive retinopathy etc), complicated cataract surgery.

The following parameters were evaluated retrospectively: age, gender, ocular and systemic diseases, best corrected visual acuity (BCVA) in preoperative and postoperative third months, central macular thickness (CMT) measured using SD-OCT and results of microperimetry testing in which retinal sensitivity was determined and the macular electrical potential records measured by mfERG.

In all of the patients included in this study, 23G transconjunctival PPV was performed. A few drops of trypan blue solution (0.06%) was applied in all of the eyes for 40 seconds to stain the ERM following core vitrectomy and then the ERM was peeled by using end-opening forceps. Following this procedure, a few drops of Brilliant blue solution with a dose of 0.25 mg/mL was used in all of the cases for 40 seconds to stain the ILM. And then while the ILM was

peeled in the study group, the ILM was seen to be stained and fully intact but not peeled in the control group.

BCVA of the patients were evaluated by using logMAR (log of the minimum angle of resolution) unit. The cases determined to have cataracts in the anterior segment biomicroscopy of the eye during preoperative period were not included in the study. The patients who were determined to have cataracts at the postoperative 3rd month (n=8), primarily cataract surgery were performed. Secondly, BCVA and control test results were considered.

OCT scans and SLO-microperimetry tests were performed by using Spectral SLO/OCT device (OTI, Toronto, Canada). RETI-port Gamma Plus Electrophysiological Diagnostic Systems (Roland Consult, München, Germany) and contact lens electrode (ERG Jet, Fabrinal SA; Switzerland) were used for mfERG.

NCSS (Number Cruncher Statistical System) 2007&PASS (Power analysis and Sample Size) 2008 Statistical Software program (Utah,USA) was used for the statistical analysis. Significance was evaluated at the levels of $p < 0.05$ and $p < 0.01$.

RESULTS

The mean age of the study group was 67.4 ± 6.4 (53-74 years). The mean age of the control group was 70.9 ± 5.5 years (64-79 years).

In the double-peeling group, while the average preoperative LogMAR visual acuity was 0.60 ± 0.36 , postoperative logMAR visual acuity was found to be 0.32 ± 0.11 ($p=0.017$; $p < 0.05$). In the single-peeling group, while the average preoperative LogMAR visual acuity was 0.54 ± 0.24 , the average postoperative logMAR visual acuity was determined to be 0.29 ± 0.17 ($p=0.007$; $p < 0.01$). There is no statistically significant difference between the two groups ($p=0.617$; $p > 0.05$) **Table 1.**

In the double-peeling group, while the average preoperative CMT was $502.30 \pm 144.65 \mu$ (455), the average postoperative CMT was determined to be $353.70 \pm 28.77 \mu$ (343.5) ($p=0.005$). In the single-peeling group, while the average preoperative CMT was $412.0 \pm 46.30 \mu$ (401.5) the average postoperative CMT was found to be $284.10 \pm 72.81 \mu$ (277) ($p=0.005$). No statistically significant difference was determined between the two groups ($p=0.520$; $p > 0.05$). But greater postoperative CMT in the ILM-peeled group is remarkable **Table 2.**

In the double-peeling group, while the total average preoperative microperimetry score decreased from 8.2 (7.96 ± 2.21) dB to 7.9 (8.05 ± 1.82) dB postoperatively, the mean foveal score increased from 5 (4.80 ± 3.67) dB to 6 (5.80 ± 3.71) dB. In the single-peeling group, while the total average preoperative microperimetry score increased from 8.0 ($8.21 \pm$

Table 1: Preoperative and postoperative 3rd month BCVA.

LogMAR BCVA	Study Group (double-peeling)	Control Group (single-peeling)	⁺ p
	Average±SD (Median)	Average±SD (Median)	
Preoperative	0.60 ± 0.36 (0.40)	0.54 ± 0.24 (0.50)	0.816
Postoperative	0.32 ± 0.11 (0.40)	0.29 ± 0.17 (0.20)	0.337
⁺⁺ p	0.017*	0.007**	
Difference	0.28 ± 0.34 (0.15)	0.25 ± 0.18 (0.20)	0.617
*Mann Whitney U Test		⁺⁺ Wilcoxon Signed Ranks Test	*p<0.05 **p<0.01

Table 2: Preoperative and postoperative 3rd month CMT

CMT(μ)	Double-peeling	Single-peeling	⁺ p
	Average±SD (Median)	Average±SD (Median)	
Preoperative	502.30 ± 144.65 (455)	412.00 ± 46.30 (401.5)	0.173
Postoperative	353.70 ± 28.77 (343.5)	284.10 ± 72.81 (277)	0.058
⁺⁺ p	0.005**	0.005**	
Difference	148.60 ± 138.65 (120)	127.90 ± 50.66 (145.5)	0.520
*Mann Whitney U Test		⁺⁺ Wilcoxon Signed Ranks Test	**p<0.01

1.11) dB to 8.1 (8.19 ± 1.14) dB, the mean foveal score was determined to be 8.0 (7.00 ± 1.94) dB to 8.0 (7.60 ± 1.84) dB postoperatively. These changes in both of the groups were not found to be statistically significant (p=0.762; p=0.717; p>0.05 respectively).

Additionally, in the microperimetric evaluations of the cases with and without ILM peeling, absolute scotomes were seen to be improved after surgery. **Figure 1.**

While the patients in the double-peeling group did not regain foveal depression following, the foveal depression was recovered in 40% of the cases in the single-peeling group (p=0.087, p>0.05). **Figures 2-3.**

In the double-peeling group, while the average preoperative R1-N1 (N1 amplitude in ring 1) amplitude was 0.45 ± 0.10 (0.45 mV), the average postoperative R1-N1 amplitude was determined to be 0.31 ± 0.16 (0.33 mV) (p=0.044; p<0.05). In the ERM-peeled group, while the average preoperative R1-N1 amplitude was 0.43 ± 0.13 (0.41 mV), the average postoperative R1-N1 amplitude was found to be 0.33 ± 0.17 (0.32 mV) (p=0.012; p<0.05). There is no statistically significant difference between the two groups (p=0.622; p>0.05) **Table 3.** (R2-N1 [N1 amplitude in ring 2]) amplitude values can also be seen in this table).

In addition, changes in the average preoperative and postoperative R1-N1 latencies were not found to be statistically significant between the groups (p=0.507; p=0.623; p<0.05).

In the double-peeling group, while the average preoperative R1-P1 amplitude was 52.43 ± 17.59 (46.7), the aver-

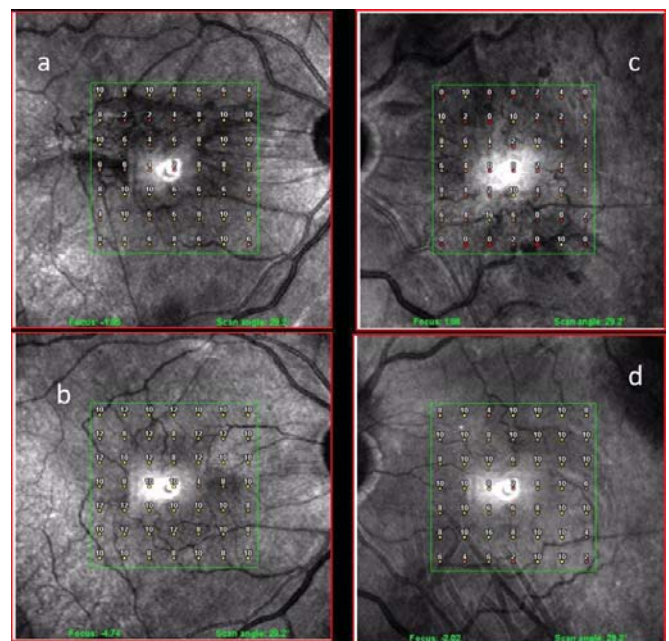


Figure 1: A: Preoperative microperimetry report of a patient in the study group. B: Postoperative 3rd month report of the same patient. C: Preoperative microperimetry report of an another patient. D: Postoperative 3rd month report of the same patient. Absolute scotomes were seen to be improved after surgery.

age postoperative R1-P1 amplitude was determined to be 39.43 ± 13.39 (38.6) (p=0.037; p<0.05). In the single-peeling group, while the average preoperative R1-P1 amplitude was 41.84 ± 17.58 (36.6), the average postoperative R1-P1 amplitude was found to be 45.36 ± 27.34 (39.2) (p=0.959;

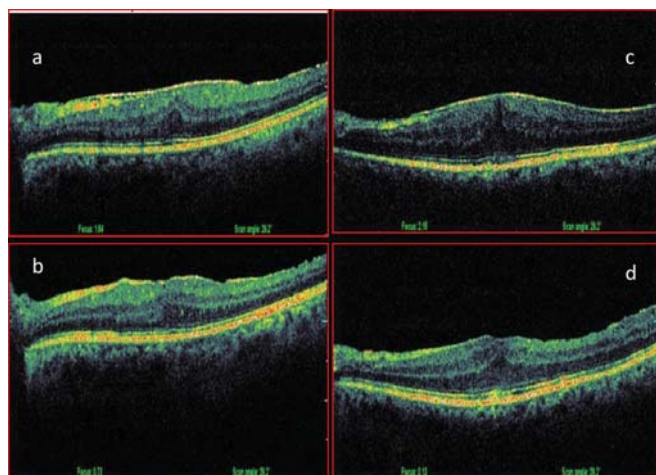


Figure 2: A: Preoperative OCT image of a patient in the ILM peeled group. B: Postoperative 1st year OCT image of the same patient. C: Preoperative OCT image of another patient in the ILM peeled group. D: Postoperative 1st year OCT image of the same patient. It can be seen that the foveal contour have not occurred yet in the 1st year of the surgery.

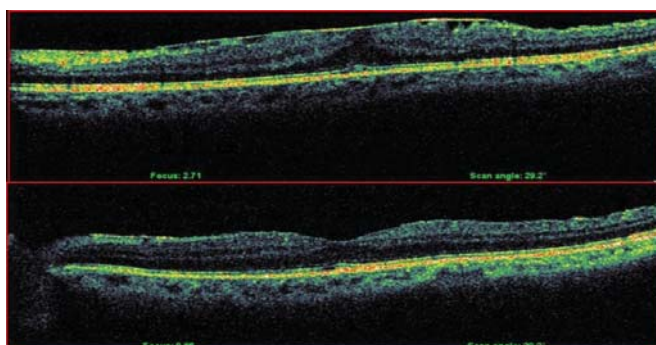


Figure 3: Preoperative and postoperative 3rd month OCT image of a patient in the ERM peeled group. It can be seen that the foveal contour is normal.

p>0.05). A statistically significant difference was found between the two groups (p=0.041; p<0.05). In the cases of the double-peeling group, decreases in the postoperative R1-P1 amplitude values (13.00 ± 16.60) compared to the preoperative R1-P1 amplitude values were significantly higher than the changes in the R1-P1 amplitude values of the cases in the single-peeling group (3.52 ± 16.35). **Table 4.** (R2-P1 (P1 amplitude in ring 2) amplitude values can also be seen in this table).

DISCUSSION

Reporting recurrence rates about 20% after standard surgical treatment in ERM surgery the surgeons tended to ILM peeling.⁶ Well then, how this procedure affects the retinal functions? There are many studies related with this issue in the literature. In some of these studies, it has been reported that ILM peeling has no unfavorable effect on the macula and in some of them, it has been stated that electrophysiological responses and visual field scores were deteriorated while the visual acuity was preserved.^{1,5-7}

Therefore, in the current study, it was aimed to find out what kind of differences were present between the cases with and without ILM peeling both functionally and anatomically. We found no statistically significant difference in visual acuities between the study and the control groups. This result is similar to many studies in the literature.^{1,5-6,11-15}

Vision impairment in the ILM peeled eyes has been reported in a study performed by Sivalingam et al. in 1990.¹⁰ In another study performed by Tari et al., a decrease was seen in the visual field sensitivities of 5 of 10 patients with ILM peeled.⁷ In our study, although there was no difference in general and foveal microperimetry scores statistically between two groups, we observed a decrease from 8.2 dB to 7.9 dB in double-peeling group while an increase from 8 dB to 8.1 dB in single-peeling group especially regarding median value of general scores.

Table 3: Preoperative and postoperative 3rd month R1-N1 and R2-N1 amplitudes (µV; R1=Ring 1; R2=Ring 2)

		Double-peeling	Single-peeling	+p
		Ave±SD (Median)	Ave±SD (Median)	
R1-N1 Amplitude (µV)	Preoperative	0.45 ± 0.10 (0,45)	0.43 ± 0.13 (0,41)	0.649
	Postoperative	0.31 ± 0.16 (0,33)	0.33 ± 0.17 (0,32)	0.939
	++p	0.044*	0.012*	
	Difference	0.14 ± 0.21 (0,12)	0.10 ± 0.12 (0,04)	0.622
R2-N1 Amplitude (µV)	Preoperative	0.24 ± 0.12 (0,21)	0.17 ± 0.08 (0,17)	0.288
	Postoperative	0.20 ± 0.07 (0,19)	0.20 ± 0.09 (0,19)	0.850
	++p	0.308	0.262	
	Difference	0.04 ± 0.14 (0,05)	0.03 ± 0.10 (0,05)	0.131

+Mann Whitney U Test ++Wilcoxon Signed Ranks Test *p<0.05

Table 4: Preoperative and postoperative 3rd month R1-P1 and R2-P1 amplitudes				
		Double-peeling	Single-peeling	+p
		Ave±SD (Median)	Ave±SD (Median)	
R1-P1 Amplitudes (nv/deg²)	Preoperative	52.43 ± 17.59 (46.7)	41.84 ± 17.58 (36.6)	0.112
	Postoperative	39.43 ± 13.39 (38.6)	45.36 ± 27.34 (39.2)	1.000
	++p	0.037*	0.959	
	Difference	13.00 ± 16.60 (7.90)	3.52 ± 16.35 (0.80)	0.041*
R2-P1 Amplitudes (nv/deg²)	Preoperative	36.34 ± 10.92 (35.5)	30.67 ± 13.89 (32.2)	0.364
	Postoperative	30.17 ± 11.75 (28.1)	32.07 ± 13.43 (30.6)	0.650
	++p	0.185	0.683	
	Difference	6.17 ± 14.08 (7.0)	1.40 ± 9.58 (1.45)	0.212
*Mann Whitney U Test		++Wilcoxon Signed Ranks Test		*p<0.05

ERM removal with ILM peeling was observed to be effective and safe in eyes with idiopathic macular ERM.^{16,17} ILM peeling is progressively become generalized in ERM surgery to reduce recurrences. Schechet et al. reported that the rate of recurrent ERM and need for repeat ERM surgery is lower in eyes where the ILM is removed with the ERM, whereas BCVA and CMT were similar with or without ILM removal.¹⁸ In harmony with this results Deltour et al. showed that ILM peeling procedure does not change the postoperative visual acuity but increases the number of microscotomas and also severity. Active ILM peeling in ERM surgery may be responsible for visual impairment related to its microtraumatic effects.¹⁹ A statistically significant decrease in CMT was found in both study and the control group. Many studies in the literature are supporting our results.^{1,7,11,15}

However, higher postoperative CMT in the double-peeling group compared to the single-peeling group are remarkable. When we consider the function of muller cells in the retina, this finding may have been developed due to the damage in the muller cells that occurred during ILM peeling procedure.

Another important result of our study was recovering of foveal contour in 40% of the cases in the single-peeling group at the end of 3rd month while foveal contour did not occur in any patient in the double-peeling group. In our opinion this is a very important finding. Most likely, a muller cell damage may have resulted in this condition. Ji Woong Lee et al.¹² support our results. They reported a 84.2% foveal depression occurrence rate in the ERM peeled subjects, while a 42.9% in the double peeled subjects.¹² The authors attributed this finding to the muller cell damage or ICG use. As we have not used ICG in our study, this difference between two groups may have resulted from the muller cells. Nonetheless, it must be stated that foveal contour status has no effect on the visual acuity; as it has been reported both in our study and the others in the literature.^{12,15}

Decreased preoperative microperimetry scores of ERM patients were reported in the literature.^{20,21} In a multicentric and randomized clinical trial on 60 people with ERM, the ILM-not peeling group had better outcomes than the ILM peeling group as measured by mean retinal sensitivity and number of microscotomas after a 12-month follow.²² But there is only one study comparing the microperimetric changes before and after ERM surgery.²¹ We observed that absolute scotomas were improved after surgery in both groups. We did not find any recent absolute scotomas following surgery. But we observed recent relative scotomas following surgery. This may be associated with the mechanical damage developed iatrogenically during membrane peeling procedure as stated by the other authors.²¹

In ERM cases, decrease in the preoperative P1 and N1 waves' amplitudes in mfERG testing was observed by many researchers.²²⁻²⁵ Moschos et al.²⁵ and Parisi et al.²⁴ who had performed single peeling, reported an early postoperative improvement in these amplitudes. Conversely, Ji Won Lim et al.¹ and Chryssanthi et al.¹⁵ who had performed double-peeling, reported an early postoperative decrease in the mfERG responses (P1 and N1 amplitudes). Also, in a study performed by Tari et al.⁷, the authors found a decrease in mfERG responses of 8 of 10 patients with ILM peeling. The authors attributed this condition to muller cell residues they observed in ILM specimens of 4 patients in their study. *When considered from this point of view, our study is the first study comparing ERM peeling and ILM peeling in terms of preoperative and postoperative mfERG responses in the literature.*

In our study, we found a decrease in postoperative N1 amplitudes compared to the preoperative values in both study and the control group.

Most dramatic result of our study is the difference between postoperative and preoperative P1 amplitudes of the subjects

in the study and the control groups. In the double-peeling group, a marked decrease in the postoperative P1 amplitudes were observed. While there was not a similar change in the P1 amplitudes of the single-peeling group. As is known, P1 wave is originating from muller cells and the inner retinal layers. Therefore, we attribute this condition to muller cell damage which may have been occurred during ILM peeling, as the other authors in the literature.^{7,26} This study also had several limitations. It is a retrospective with small number of patients and short follow-up period.

Meanwhile, several studies showed equivalent effectiveness and safety of ERM removal with and without ILM peeling. Therefore, whether or not ILM peeling should be performed during vitrectomy for ERM removal remains controversial.

In conclusion, though ILM peeling does not result in visual acuity impairment; it may be leading to an additional damage to the muller cells and the inner segments of the retina.

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