

Anatomic and functional results of idiopathic macular epiretinal membrane surgery

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Abstract

• **AIM:** To assess the impact of macular surgery on the functional and anatomic outcomes in patients with grade 2 epiretinal membrane (ERM), and the effect of internal limiting membrane (ILM) peeling on visual acuity and to analyze the long-term effect of pars plana vitrectomy (PPV) on intraocular pressure (IOP).

• **METHODS:** Pseudophakic eyes (62 eyes) diagnosed as idiopathic grade 2 ERM with at least 6mo postoperative follow-up were included in this retrospective study. The fellow eye was nonvitrectomized. Patients were divided into two groups: group 1 (29 eyes) treated with ERM and ILM peeling and group 2 (33 eyes) with only ERM peeling. Preoperative and postoperative best corrected visual acuity (BCVA), slit-lamp, and a dilated fundus examination was performed. IOP was measured with Goldman applanation tonometer before, day 1 and first week and each visit after surgery. The incidence of significant IOP elevation was compared between vitrectomized eyes and nonvitrectomized fellow eyes.

• **RESULTS:** Visual improvement was statistically significant and similar in both groups ($P=0.008$ in group 1, $P=0.002$ in group 2, $P=0.09$ inter-group). The amount of decrease in central macular thickness was statistically significant and similar in both groups ($P=0.005$ group 1, $P=0.008$ group 2, $P=0.37$ intergroup). At the final follow-up (14.1±9.6mo) the incidence of significant IOP elevation was 4% in vitrectomized eyes (three eyes) and 3% (two eyes) in the nonvitrectomized fellow eyes ($P=0.12$). Four eyes (12.1%) had recurrent ERM after a mean follow-up of 8.6±1.1mo in group 2, there was no recurrence in group 1 ($P=0.01$).

• **CONCLUSION:** Recurrence of ERM may be decreased by ILM peeling during ERM surgery. However, it seems that ILM peeling do not affect the functional outcome and 23-gauge PPV alone do not have a significant effect on IOP.

• **KEYWORDS:** epiretinal membrane; internal limiting membrane peeling; pars plana vitrectomy; intraocular pressure

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INTRODUCTION

An idiopathic macular epiretinal membrane (ERM) is a semitranslucent, nonvascular, fibrocellular membrane on the inner retinal surface along the internal limiting membrane (ILM)^[1]. It is frequently bilateral, and it commonly develops in patients older than 50 years old^[2-3]. Abnormal vitreomacular interface (VMI) and disturbance in posterior hyaloid membrane detachment are cardinal etiological factors in ERM^[4]. Multiple pathological changes in the vitreoretinal junctions have been detected in ERM formation. Retinal glial cells, fibrous astrocytes, Müller cells, macrophages, and retinal pigment epithelial (RPE) cells constitutes ERM formation^[5]. Patients with ERMs may suffer from some symptoms of visual disturbance such as metamorphopsia, micropsia, and vision loss^[5].

According to Gass^[6], translucent membranes without any retinal distortions are Grade 0; cellophane maculopathy (CM), or membranes with irregular wrinkling of the inner retina, represents Grade 1; and crinkled CM and opaque membranes with full-thickness retinal distortion are Grade 2; macular pucker (MP). Membrane contraction, which is secondary to the action of myofibroblasts, is an important etiological factor in disease progression^[5].

Removing the ERM using pars plana vitrectomy (PPV) commonly results in a significant regression of retinal wrinkling, with significant visual improvement^[7]. Retinal wrinkling can be regressed efficiently after ILM peeling; unfortunately, visual disturbance may not regressed after the ILM peeling^[8-9].

An unusual early postoperative complication after PPV is a temporary elevation of intraocular pressure (IOP) secondary to surgery-induced inflammatory reactions or use of viscoelastics, silicone oil tamponade, or intraocular gas tamponade^[10-12].

Previously, sustained IOP elevation causing open angle glaucoma (OAG) after PPV was presented^[13-15]. Chang^[16] was the first author claiming that approximately 20% of eyes treated with uneventful PPV could develop OAG in the long term; however, other researchers found no association between OAG or increased IOP and uneventful PPV^[17-19]. The studies on IOP elevation after PPV showed inconsistent outcomes with respect to development of ocular hypertension (OHT) and glaucoma^[20].

It was considered that PPV markedly raises intravitreal oxygen concentration, which causes nuclear sclerosis in phakic eyes, and oxidative damage in trabecular meshwork in pseudophakic or aphakic eyes^[21]. The purpose of the current study is to evaluate the effectiveness of the ERM surgery with or without ILM peeling on the visual and anatomic outcomes of patients with grade 2 ERM. Second aim of this study is to analyze any IOP change in the long-term after PPV.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the local ethical committee regarding the ethical standards of the institutional and national research and conducted in accordance with the 1964 Helsinki Declaration. A written informed consent was obtained from all subjects before the surgery.

This retrospective and comparative study was conducted to evaluate the effect of ERM surgery on the visual and anatomic outcomes of the patients undergoing ERM with or without ILM peeling. Medical charts of patients with a diagnosis of ERM and treated with PPV and intraocular air tamponade in our Retina Unit between January 2014 and January 2017 were retrospectively analyzed in this study.

The VMIs were assessed using spectral domain optical coherence tomography (SD-OCT; Optovue OCT V 5.1, RTVue 100-2; Optovue, Fremont, CA, USA). The ERM grades were also classified according to the Gass classification. Pseudophakic patients diagnosed with idiopathic grade 2 ERM and having more than 6mo of the follow-up were enrolled in the current study. In addition, the fellow eye was requested to be nonvitrectomized. Eyes with high myopia (\geq minus 6 D), grade 0 and grade 1 ERM, history of previous PPV, anterior segment inflammation, previous penetrating ocular trauma, diabetic retinopathy, and proliferative vitreoretinopathy, diagnosis of glaucoma (neovascular, traumatic, congenital, open angle, or narrow angle), suspected glaucoma, OHT, previous chronic systemic or topical intravitreal or periocular steroid treatment, were excluded from the study.

In comparison of the anatomic and visual outcomes, patients were separated into two groups. First group composed of the patients who underwent ERM surgery with ILM peeling, and second group composed of the patients who underwent ERM surgery alone. Baseline clinical and demographic

characteristics of the patients consisting of age, gender, duration of symptoms was recorded for each patient. Preoperative and postoperative best-corrected Snellen visual acuity (BCVA) test, slit-lamp biomicroscopy, Goldmann applanation tonometry and funduscopy were performed. The presence of ERM was confirmed by using SD-OCT.

IOP was measured before the surgery and on the first day, first week, and each visit after surgery. IOP was measured in the morning between 9 and 11 a.m. IOP values of the contralateral fellow eye served as a control group. The baseline IOP was defined as the presurgical mean IOP for two consecutive visits. Significant IOP elevation was defined as an increase ≥ 4 mm Hg in IOP or $IOP \geq 22$ mm Hg at least 2 postoperative visits after the first month of the surgery. We determine the IOP increase according to a cutoff of 4 mm Hg because the diurnal variation of IOP could range about 3.7 mm Hg in normal eyes without glaucoma^[22-23]. In addition, hypotony was defined as an $IOP \leq 8$ mm Hg. We compare the IOP values of operated eyes with nonoperated contralateral eyes (control group) from baseline to the last follow-up visit and also the incidence of significant IOP elevation between vitrectomized eyes and the control group.

Surgical Technique A single experienced surgeon (Unsal E) carried out all surgeries under peribulbar anesthesia. A three-port, 23-gauge PPV was performed to all patients. Following displacement of the conjunctiva to misalign the conjunctival and scleral incisions with oblique entries, a trocar was employed in every case. After applying core vitrectomy *via* triamcinolone acetonide (10 mg/mL), posterior hyaloid membrane was detached around the optic disc with the help of a vitrectomy probe, and then removal of the peripheral vitreous was done under the careful inspection of the peripheral retina. We carried out a fluid-air exchange and then stained macula with Trypan Blue dye (Vision Blue, 0.06%, DORC International). After about 1min, we cleaned the dye around the macula by using a vitrectomy probe. After that, we peeled ERM within a fovea-centered circular area of two-three optic disc diameters. After the ERM peeling, we stained ILM with brilliant blue (Oculblue plus, brilliant blue G solution, aurolab) and then peeled it within a fovea-centered circular area of two-three optic disc diameters.

ILM peeling was not a preoperatively planned application. If brilliant blue was available for the surgery in the operation day, ILM peeling was applied. In patients that brilliant blue was not available in the operation day, only ERM peeling was performed.

ILM peeled cases after staining with brilliant dye were included in group 1. Only ERM peeled cases after staining with Trypan Blue dye were included in group 2. Air was used as an intraocular tamponade to reduce the need for suturing of the

Table 1 Demographic characteristics

Parameters	Group 1	Group 2	<i>P</i>
Mean age (y)	70.5±8.8	69.8±9.9	0.77 ^a
Patients/eyes	29/29	33/33	
Female/male	16/13	18/15	0.68 ^b
Mean follow-up time (mo)	12.3±9.2	15.7±11.8	0.21 ^a
Preoperative phakia/pseudophakia	0/29	0/33	
PPV/phaco+PPV	29/0	33/0	
Pachymetry (µm)	573.2±33.4	566.4±39.1	0.11 ^a
History of trauma	0	0	
History of glaucoma	0	0	

PPV: Pars plana vitrectomy. ^aIndependent samples *t*-test. ^bChi-square test.

Table 2 Comparison of functional outcomes

Parameters	Group 1			Group 2			<i>P</i> ^b
	logMAR	<i>n</i>	<i>P</i>	logMAR	<i>n</i>	<i>P</i>	
Preop. BCVA	0.89±0.58			0.79±0.48			0.55
Postop. BCVA 3mo	0.64±0.33	29	0.01 ^a	0.63±0.36	33	0.009 ^a	0.42
Postop. BCVA 6mo	0.60±0.36	29	0.008 ^a	0.61±0.35	33	0.004 ^a	0.38
Postop. BCVA 9mo	0.54±0.34	16	0.023	0.55±0.38	20	0.034 ^a	0.55
Postop. BCVA 12mo	0.52±0.35	10	0.032	0.54±0.37	15	0.041 ^a	0.62
Postop. BCVA final	0.60±0.40	29	0.008 ^a	0.61±0.38	33	0.002 ^a	0.31
Visual improvement	-0.28±0.51			-0.17±0.30			0.09

^aIntragroup analysis paired samples *t*-test. ^bIntergroup analysis independent samples *t*-test. BCVA: Best corrected visual acuity. The post surgical final values refer to the final data values after an average follow-up of each patient. Visual improvement was calculated according preop-BCVA and postop-BCVA final.

sclerotomies. The trocars and infusion lines were removed, followed by the repositioning and inspection of the conjunctiva.

Following surgery, moxifloxacin (Vigamox; Alcon, USA) and prednisolone acetate eye drops (Allergan Pharmaceuticals, Ireland) were administered 4 times daily. While moxifloxacin (Vigamox; Alcon, USA) eye drops were continued for 3wk, prednisolone acetate eye drops (Allergan Pharmaceuticals, Ireland) were tapered and then stopped within 3wk, according to the condition of the patient. Postoperative visits were done on 1d, 1, 4wk, 3, and 6mo of the follow-up. All the results of complete ophthalmological examinations, SD-OCT images taken during pre- and postoperative visits, were reevaluated for each case. Postoperative complications were noted.

Statistical Analysis We used SPSS version 22.0 (USA) to analyses all data. Descriptive data were shown as minimum, maximum, and mean±SD. The distribution of data was evaluated by Kolmogorov-Smirnov test. Independent samples *t*-test were used for independent samples. Paired samples *t*-test was used for related samples. Chi-squared test is used to determine the differences between frequencies of independent groups. Pearson correlation analysis was used to define possible prognostic factors influencing the postoperative final

BCVA. A *P* value less than 0.05 was considered as statistically significant.

RESULTS

Sixty-two eyes of 62 patients fulfilled the inclusion criteria and were included in this study. Demographic characteristics are similar in both groups. The demographic characteristics of patients and the mean follow up time are shown in Table 1.

We compared two different groups in terms of functional and anatomic outcomes (Tables 2 and 3, respectively). Postoperative BCVA was significantly better than preoperative BCVA in both groups. Although visual improvement was higher in group 1, this difference was not significant (Table 2). Additionally, we found that central macular thickness (CMT) decreased significantly after surgery, the amount of decrease was similar in both groups (Table 3). A statistically significant positive correlation was observed between postoperative final BCVA scores and preoperative BCVA, a decrease of CMT (Table 4). Mean IOP values of vitrectomized eyes and fellow nonvitrectomized eyes from baseline to the last follow-up visit are summarized in Table 5. For the mean pachymetry values of different groups were similar, we did not consider a correction factor of IOP according to corneal thickness. Preoperative and

Table 3 Comparison of anatomical outcomes

Parameters	Group 1			Group 2			P ^b
	CMT	n	P	CMT	n	P	
Preop.	432.9±80.9			411.9±90.9			0.68
Postop. 3mo	372.4±71.3	29	0.01 ^a	366.5±72.3	33	0.01 ^a	0.51
Postop. 6mo	344.4±70.8	29	0.007 ^a	333.6±76.4	33	0.005 ^a	0.42
Postop. 9mo	324.5±66.3	16	0.016	319.6±72.6	20	0.011 ^a	0.54
Postop. 12mo	315.6±61.4	10	0.036	308.4±68.4	15	0.031 ^a	0.52
Postop. Final	330.9±72.6	29	0.005 ^a	323.5±81.0	33	0.008 ^a	0.76
Decrease	102.2±72.6			88.3±90.4			0.37

^aIntragroup analysis Paired Samples *t*-test. ^bIntergroup analysis Independent Samples *t*-test. CMT: Central macular thickness. The post surgical final values refer to the final data values after an average follow-up of each patient. Decrease of CMT was calculated according preop-CMT and postop-CMT final.

postoperative IOP values were similar between treated and untreated fellow eyes (Table 5).

At the final follow-up (14.1±9.6mo) the incidence of significant IOP elevation was 4% in vitrectomized eyes (3 eyes) and 3% (2 eyes) in the control group (Chi-square test, *P*=0.12). Two eyes in vitrectomized group had IOP elevation ≥4 mm Hg and IOP≥22 mm Hg (one had 27 mm Hg and one had 28 mm Hg) at the fifth months' follow-up after the surgery. We applied anti-glaucomatous therapy to control IOP in these patients. One of these three patients had IOP elevation ≥4 mm Hg in the fourth month after the surgery. We did not apply anti-glaucomatous therapy and we began to observe retinal nerve fiber layer for any decrease. Two eyes in the control group had IOP elevation ≥4 mm Hg and IOP≥22 mm Hg (one had 24 mm Hg and one had 25 mm Hg) at the 5mo follow-up. The eyes with significant IOP elevation had a pachymetry value of 560.2±12.5 μm, all of them had a grade 3-4 angle according to the Shaffer classification.

We did not observe any intraoperative complications. Postoperative topical steroid therapy was prescribed four times a day, tapered and then stopped within three weeks and there was not any IOP spike due to topical steroid therapy. We observe transient hypotony in fifteen eyes which were resolved in a week. Four eyes (12.1%) had recurrent ERM after a mean follow-up of 8.6±1.1mo in group 2, there was no recurrence in group 1 (Chi-square test, *P*=0.01). There was no need for reoperation of recurrent ERM because the visual acuity remained stable in these patients.

DISCUSSION

Idiopathic ERM is usually associated with abnormal posterior vitreous detachment (PVD) that causes breaks in the ILM^[24]. A previous study demonstrated that glial cells could proliferate and transform into other cell types after access to the inner retinal surface *via* defects in the ILM^[25]. PPV is the most preferred treatment of ERM, as it has significant visual improvement rates^[7].

Table 4 Possible prognostic factors influencing the postoperative final BCVA

Parameters	Postop. final BCVA
Follow-up	<i>r</i> =-0.278 <i>P</i> =0.236
Decrease of CMT	<i>r</i> = 0.744 <i>P</i> =0.035
Preop. BCVA	<i>r</i> =0.470 <i>P</i> =0.01

Pearson correlation analysis. BCVA: Best corrected visual acuity; CMT: Central macular thickness.

Table 5 Comparison of IOP values between vitrectomized eyes and fellow nonvitrectomized eyes

Parameters	Vitrectomized	Control group	<i>P</i>
Preop. IOP	15.8±2.8	15.6±2.7	0.77 ^a
Postop. 1d	11.4±3.2	15.4±2.6	0.01 ^a
Postop. 1mo	15.6±2.7	15.5±2.4	0.71 ^a
Postop. 3mo	15.9±2.9	16.0±2.6	0.76 ^a
Postop. 6mo	15.7±2.4	15.8±2.7	0.73 ^a

IOP: Intraocular pressure. ^aIndependent samples *t*-test.

The first purpose of the current study was to evaluate the effect of ILM peeling on functional results. Both groups had significant visual improvement after surgery. However, ILM peeling had no significant effect on postoperative BCVA (Table 2). Our results are consistent with the literature^[1,26]. Lee and Kim^[26] stated that ILM peeling had no effect on the visual outcome. Although they focused particularly on anatomical changes, their functional results are better than results from the present study^[26]. Because they included patients treated with combined phacoemulsification and ERM surgery, visual improvement values were expected. Additionally, Kwok *et al*^[27] reported a marked increase in BCVA in both ILM peeling and the non-ILM peeling groups after ERM surgery. Their visual improvement values were better than those from the

current study. However, patients with combined cataract and ERM surgery were also analyzed in their study^[27]. We thought that patients' characteristics could be another cause of their better results^[26-27]. Additionally, Donati *et al*^[28] reported that ERM surgery contributes to a continuous increase in BCVA within six months of follow-up leading to a progressive reduction of residual intraretinal edema and recomposition of retinal layers. Similarly, the visual acuity of our patients continued to improve in correlation with a decrease of CMT.

The recurrence rate of ERM is approximately 10% after surgery, and additional surgery may be required in 3% of patients^[26-27,29-30]. ILM peeling may decrease the recurrence rate by removing the scaffold for myofibroblast proliferation. However, its effect on recurrence rate is controversial^[1,27,31-32]. While Kim *et al*^[32] reported that additional ILM peeling in patients with complete ERM removal does not affect postoperative visual acuity or recurrence, Kwok *et al*^[27] presented a high recurrence rate (17%) in patients without ILM peeling. Similar to Kim *et al*^[32], Kwok *et al*^[27] did not perform additional surgery for these recurrences due to visual stability. Consistently, we observed a high recurrence rate (12%) in patients with no ILM peeling. However, there was no need for reoperation of recurrent ERM because visual acuity remained stable in those patients.

The second aim of the current study was to assess the effect of ILM peeling on anatomical results. We found that both groups had a significant decrease in CMT after surgery and that the amount of decrease between different groups was similar (Table 3). Our anatomical results are different from Lee and Kim^[26] While they reported higher CMT values in patients with ILM peeling, we found no significant difference^[26]. They performed indocyanine green (ICG)-assisted ILM peeling and suggested that macular thickening seen after surgery is more likely to be attributable to ILM peeling than to ICG use^[26]. Because we did not use ICG in this study, we do not have experience with ICG effects on macular thickness.

In the present study, we found that CMT decrease is associated with visual improvement. The third aim of the present study was to assess the long-term effect of PPV on IOP. We found that PPV does not significantly affect long-term IOP. There is no difference between patients treated with PPV and their untreated fellow eyes. It is well-known that increased IOP is the most important risk factor for glaucoma^[23]. The exact mechanism of late-onset elevation of IOP after vitrectomy has yet to be determined, and many factors have been discussed. Siegfried *et al*^[21] presented that there is no oxygen consumption by the vitreous or the lens in vitrectomized pseudophakic—therefore, the increased oxygen concentration of the anterior chamber could cause oxidative damage to the trabecular meshwork. This hypothesis was used by Chang^[16]. However,

their series included patients with previous vitrectomy (or scleral buckling), vitrectomies for retinal detachment, retained lens fragment, and dislocated intraocular lens. These complicated surgeries may already predispose patients toward glaucoma because of a high rate of complications, increased tissue trauma, and inflammation.

In the literature, there are different rates of ocular hypertension in heterogeneous groups of patients^[11-15]. Tognetto *et al*^[33] reported that incidence of IOP \geq 22 mm Hg or an increase of mm Hg from the baseline is 5.7% in vitrectomized eyes and 5.7% in nontreated fellow eyes. Patients in the study underwent 23-, 25-, or 27-gauge PPV \pm phacoemulsification to treat ERM; complicated surgeries were not included in their study. Therefore, their study group was fairly homogeneous, and their results suggest that PPV alone does not significantly affect IOP^[33]. Similarly, we found that the incidence of significant IOP elevation was 4% in vitrectomized eyes (three eyes) and 3% (two eyes) in the control group (Chi-squared test, $P=0.12$). All our patients only underwent 23-gauge PPV, and we did not perform any additional surgery. Thus, we feel that our results demonstrate the effects of the 23-gauge PPV on IOP in a better way than did the previous literature. We suggested that 23-gauge PPV alone does not have a significant effect on IOP.

Limitations of our study included retrospective design, no evaluations of the postoperative external limiting membrane and the inner and outer segment (IS/OS), and insufficient follow-up for evaluating the onset of OHT or primary OAG.

In conclusion, recurrence of ERM may be decreased by ILM peeling during ERM surgery. However, ILM peeling did not affect the functional outcome. Both procedures had a significant effect on CMT, and the amount of CMT decrease between different groups was similar. According to our study we thought that 23-gauge PPV alone did not have a significant affect on IOP.

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