MACULAR PUCKER

To Peel or Not to Peel the Internal Limiting Membrane? A Microperimetric Response

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Background: To compare functional and anatomical outcomes after idiopathic macular pucker removal between eyes that underwent internal limiting membrane (ILM) peeling and eyes that did not.

Methods: In this multicentric, randomized clinical trial, 60 eyes of 60 patients affected with idiopathic macular pucker were enrolled. Thirty eyes underwent 23-gauge pars plana vitrectomy associated with ILM peeling ("ILM peeling group"), whereas 30 eyes did not undergo ILM peeling ("ILM not peeling group"). Retinal sensitivity, frequency of microscotomas, and all the other microperimetric parameters were tested by MP1 microperimetry. Best-corrected visual acuity was investigated with the Early Treatment Diabetic Retinopathy Study chart. Anatomical outcomes were analyzed with spectral domain optical coherence tomography.

Results: After a 12-month follow-up, the mean retinal sensitivity in the 4° central area showed a greater and faster recovery in the ILM not peeling group than in the ILM peeling group ($P = 0.041$). The number of absolute microscotomas (0 dB) within the 12° central retinal area was significantly higher in the ILM peeling group than in the ILM not peeling group ($P = 0.044$).

Conclusion: The ILM not peeling group seems to show better outcomes than the ILM peeling group as measured by mean retinal sensitivity and number of microscotomas after a 12-month follow-up.

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Idiopathic epiretinal membrane (ERM) is a common disease affecting ~2% of individuals younger than 60 years of age and 12% in those older than 70 years.[1]

The pathogenesis of ERMs is not well known. Some authors hypothesize that ERM could develop as a result of microbreaks in the retina after posterior vitreous detachment, allowing for the migration of fibroblasts, glial cells, and astrocytes from the retina to the internal limiting membrane (ILM), where they proliferate.[2] However, the most recent hypothesis states that collapse of the liquefied vitreous body without sufficient dehiscence at the vitreoretinal interface can induce a split within the posterior vitreous cortex (vitreoschisis), leaving the outermost layer of the posterior vitreous cortex attached to the macula.[3]

Visual disturbance resulting from decreased best-corrected visual acuity (BCVA) with or without metamorphopsia because of retinal wrinkling and distortion is the main indication for ERM surgery.[4] Epiretinal membrane symptoms also include micropsia, macropsia, and monocular diplopia.[5]

Surgery for ERMs has been a common vitreoretinal procedure for many years.[6] Indeed, previous works have reported good results in patients with symptomatic

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ERM who underwent pars plana vitrectomy (PPV) and ERM removal, even if the recurrence rate of ERM after surgery was ~10% of vitrectomized eyes.[7–9] To reduce the risk of ERM recurrence, ILM peeling has been introduced in ERM surgery with good results.[10–13] However, being the ILM, the basal lamina connected to the end feet of the Müller cells, its removal may be responsible for mechanical and functional damage to these cells.[14–16] In fact, ILM peeling has been shown to lead to small and perceptible anatomical changes in the peeled area of the retina, causing the retina to have the appearance of a "dissociated optic nerve fiber layer".[17,18] However, why peeling also induces functional deterioration of the retina is still unclear.[18–20]

Microperimetry MP1 (Nidek Technologies, Padua, Italy) is a relatively new equipment providing objective and quantitative information about the whole macular function.[21] Moreover, it is increasingly being recognized as a useful clinical tool in the assessment of various retinal pathologies.[22–28]

In addition, retinal function is assessed using microperimetry in relation to the fundus, and thus spatial light increment sensitivity can be mapped.[29] Moreover, the auto-tracking system corrects for involuntary eye movements allowing for an exact point-by-point correlation between anatomical abnormalities and retinal sensitivity.[30,31] These central visual field functions are important in day-to-day activities such as those involving contrast and color sensitivity[32]; finally, reduced retinal sensitivity and the presence of paracentral microscotomas may cause visual discomfort despite good visual acuity, as reported by some patients after ERM surgery.[24]

The aim of this prospective clinical trial was to investigate the retinal sensitivity and the frequency of microscotomas in eyes that had undergone ILM peeling and in eyes that had not, during a 1-year follow-up.

Methods

Data from a prospective consecutive series were analyzed. All the patients were examined at "Retina Unit of G. B. Bietti IRCCS Foundation, Rome," "Retina Unit of San Giovanni Addolorata Hospital, Rome," and "Retina Unit of Pisa University" from April 2009 to September 2012. The study was performed in adherence to the tenets of the Declaration of Helsinki; all patients signed an informed consent form.

Patients and Clinical Examination

Sixty patients diagnosed with idiopathic fovea–attached type ERM[6] documented by spectral domain optical coherence tomography (SD-OCT) (OCT Spectralis; Heidelberg Engineering, Dossenheim, Germany) were enrolled.

Randomly, 30 patients underwent PPV associated with ILM peeling, whereas 30 did not undergo ILM peeling. In each Retina Unit, 10 patients underwent PPV associated with ILM peeling, and 10 patients did not undergo ILM peeling. The randomization process has been locally performed. Enrolled patients were randomized at a 1:1 ratio for PPV associated with ILM peeling or PPV without ILM peeling. The randomization sequence was computer generated. Follow-up visits were scheduled at 1, 7, 30 days and 3, 6, and 12 months after surgery.

Baseline and follow-up visits included slit-lamp examination, intraocular pressure measurement with Goldmann applanation tonometry, BCVA with Early Treatment Diabetic Retinopathy Study score at 4 m according to the Study protocol,[33] dilated fundus examination, foveal thickness, cube average thickness, and cube volume measurements by SD-OCT, and retinal sensitivity evaluated by Microperimetry MP1.

During the first month of follow-up, only BCVA and/or OCT scans were carried out. Microperimetry MP1 analysis was performed at baseline and at 3, 6, and 12 months of follow-up.

The inclusion criteria were: 1) diagnosis of idiopathic fovea–attached type ERM[6]; 2) presence of metamorphopsia judged on the basis of subjective symptoms and tested with the Amsler grid chart; 3) visual acuity loss; 4) integrity of subfoveal inner segment/outer segment junction (diameter centered on the fovea of 200 μm); 5) macular thickness >250 μm as measured by OCT; 6) all eyes were pseudophakic (at least 180 days before the enrollment); 7) no previous vitreoretinal surgery; and 8) willingness to adhere to the scheduled visits during the follow-up period.

The exclusion criteria were: 1) traumatic ERM; 2) ERM associated with retinal tears; 3) pseudohole type ERM[6]; 4) concomitant or previous retinal vascular diseases; 5) additional ocular comorbidity such as glaucoma; 6) dioptric media opacity such as corneal opacity; 7) previous surgically induced complications such as phacoemulsification complications; 8) previous vitreoretinal surgery (i.e., for retinal detachment or vitreous hemorrhages); 9) previous argon laser treatment for retinal breaks; 10) ocular axial length >25.00 mm or myopic >6.00 diopters; and 11) phakic eyes.

Functional Macular Mapping

MP1 testing parameters were a grid of 33 stimuli covering the central 12° (centered onto the fovea); stimulus size Goldmann III with 200 milliseconds

projection time; white monochromatic background at 4 apostilb; and a bright red cross of 4° in size was used as the fixation target. The starting stimulus light attenuation was set at 10 dB. A 4-2-1 double-staircase strategy was used with an automatic eye tracker that compensates for eye movements. The fellow eye was patched. Pretest training was performed, and a 5-minute mesopic visual adaptation was allowed before starting the test. All subjects underwent microperimetry with dilated pupil. The mean overall threshold value (in decibels) and 4° central area threshold value (in decibels) were evaluated for each patient at baseline and the final visit. If no threshold value was detected, the corresponding area was defined as absolute scotoma. The total number of absolute scotoma locations and the number of absolute scotoma locations in the 4° central area were taken into consideration for statistical analysis.

End Points

Primary end point was to analyze differences between groups in the mean 4° and 12° central retinal sensitivity and microscotomas points.

Secondary end points were to investigate the differences between groups in BCVA, OCT parameters, and other microperimetric parameters and to evaluate the trend until a 12-month follow-up in each group.

Definition of "Fovea-Attached Epiretinal Membrane"

It was based on the article of Hwang et al.[6] They performed a SD-OCT–based morphologic classification of idiopathic ERM, identifying two groups: ERMs involving fovea (fovea-attached type) and ERMs sparing fovea (pseudohole type). Within the first group, they spotted 3 different subgroups: 1A, ERM with outer retinal thickening and near normal inner retina; 1B, ERM with exaggerated tenting of the outer retinal layer in the foveal area; and 1C, ERM with prominent inner retinal thickening.

Surgical Procedure

Vitreoretinal surgeries were performed by three operators (G.R., G.G., and M.P.), one for Retina Unit. The operative procedure was based on a standard 3-port PPV using 23-gauge instruments that included removal of posterior hyaloids and ERM with intraocular forceps. If necessary, posterior vitreous detachment was induced by enhanced suction with the vitrectomy probe around the optic nerve disk. For patients who underwent ILM peeling, Brilliant Blue G (Geuder, Heidelberg, Germany) was used to stain the ILM. Internal limiting membrane peeling was performed either at the same time as or after the ERM removal using end-gripping forceps and a rhexis technique in all cases well up to three disk diameters centered on the foveola. A second stain with Brilliant Blue G was performed to check whether the ILM peeling was completed.

Statistical Analysis

Student's paired *t*-tests were used to evaluate changes in selected parameters at different follow-up times as compared with baseline, whereas Student's unpaired *t*-test and Mann–Whitney *U* test were used in assessing difference between groups for normal and skewed variables, respectively. The Kolmogorov–Smirnov test was used to assess normality of data.

A mixed analysis of variance between/within subjects was conducted to simultaneously explore:

1. The impact of surgical therapy duration until 12 months of follow-up ("effect of time")
2. The impact of treatment (peeling ILM vs. no peeling ILM; "effect of treatment")
3. The interaction between surgical therapy duration and treatment ("interaction effect of time and treatment").

Before analysis of variance, logarithmic transformations were applied for skewed variables having a non-Gaussian distribution according to the Kolmogorov–Smirnov test. Post hoc comparisons were performed using the Bonferroni correction in case of a significant analysis of variance result.

Pearson correlation coefficient was used to investigate a possible correlation between Δ location fixation and Δ mean retinal sensitivity.

Finally, to analyze possible differences related to participation of the three different Retinal Units (and surgeons), a comparative analysis of the final results obtained by each hospital has been performed.

The values of $P < 0.05$ were considered statistically significant. Data are presented as mean ± standard deviation.

Sample Size

Formal sample size was calculated to assess the change in macular sensitivity measured by MP1 microperimetry (which was the primary end point of our study) between the preinterventional and postinterventional periods, and between groups, if one existed. Treatment difference for the primary criterion was estimated with a 2-sided 95% confidence interval and a 5% noninferiority margin. We assumed a change of 10% of the maximum possible score as clinically relevant, and we therefore estimated Δ (the difference

between postinterventional and preinterventional score) at 1.8 ± 3.0. Using $\alpha = 0.05$ and $\beta = 0.90$, the sample size would enumerate 30 patients per group.

Results

Eighty-four patients affected by ERM were preenrolled. Twenty-four patients were excluded: eight for previously retinal vascular diseases treated with intravitreal injections; six for loss of integrity of the subfoveal inner segment/outer segment junction; one because of concomitant primary open angle glaucoma; two for corneal opacity that could interfere with the microperimetric examination; one for previous vitreous hemorrhage; one for undergoing previous retinal detachment to scleral buckling; two for previous vitreoretinal surgery related to phacoemulsification complications; and three for previous argon-laser treatment for retinal peripheral breaks.

Sixty eyes of 60 pseudophakic patients affected by idiopathic ERM were included in the statistical analysis. The mean age was 72.3 ± 8.3 years, and the outcomes from 32 men and 28 women were analyzed. Epiretinal membranes were classified as follows: 24 as 1A (13 in the "ILM peeling group" and 11 in the "ILM not peeling group"; $P > 0.05$); 19 as 1B (9 in the ILM peeling group and 10 in the ILM not peeling group; $P > 0.05$); and 17 as 1C (8 in the ILM peeling group and 9 in the ILM not peeling group; $P > 0.05$). Baseline sample clinical characteristics are described in Table 1. No differences between groups were detected, except for fixation stability inside the 2° central area ($P = 0.004$) (Table 1).

Mean retinal sensitivity in the 12° central area did not show statistically significant differences between groups in the postsurgical trend until 12 months of follow-up ($P = 0.058$) (Figure 1). However, analysis of variance showed a statistically significant interaction effect of time and treatment, meaning differences between groups in the manner and speed of postsurgical recovery (Figure 1). Moreover, a paired *t*-test showed significant differences between groups at 3-month and 12-month follow-ups (Figure 1).

A significant, different postsurgical behavior between groups was observed for the mean retinal sensitivity in the 4° central area ($P = 0.041$) (Figure 2). Analysis of variance showed a statistically significant interaction effect of time and treatment, demonstrating a better and faster recovery in retinal sensitivity in the ILM not peeling group than in the ILM peeling group (Figure 2), and the paired *t*-test showed significant differences between groups at each follow-up time point (Figure 2).

The mean time of microperimetry test was 502 ± 28 seconds, and no difference between groups was seen ($P = 0.321$). No differences between groups were seen in BCVA postsurgical trend ($P > 0.05$) (Figure 3).

The number of absolute microscotomas (0 dB) within the 12° central retinal area was significantly higher in the ILM peeling group than in the ILM not peeling group ($P = 0.044$) (Figure 4). The interaction effect of time and treatment showed a significantly different trend between groups during the follow-up period ($P = 0.047$), and the paired *t*-test demonstrated significant differences at each follow-up time point ($P < 0.05$) (Figure 4).

No differences between groups were found for other microperimetric parameters at each follow-up visit

Table 1. Baseline Characteristics of "ILM Peeling Group" and "ILM Not Peeling Group"

	ILM Peeling Group	ILM Not Peeling Group	*P*
BCVA, n ± SD	39.70 ± 10.70	40.10 ± 9.50	0.86
The 12° central retinal sensitivity, dB ± SD	15.10 ± 2.20	15.10 ± 2.80	0.95
The 4° central retinal sensitivity, dB ± SD	13.60 ± 2.10	13.60 ± 2.60	0.90
Absolute microscotomas' points in the 12° area, n ± SD	1.03 ± 1.22	1.20 ± 1.19	0.56
Absolute microscotomas' points in the 4° area, n ± SD	0.27 ± 0.64	0.20 ± 0.61	0.68
Fixation stability inside the 2° area, % ± SD	71.90 ± 14.70	79.50 ± 13.70	0.04
Fixation stability inside the 4° area, % ± SD	93.90 ± 4.50	94.30 ± 6.60	0.75
Location fixation, % ± SD	58.20 ± 21.10	68.60 ± 23.40	0.07
Foveal thickness, μm ± SD	464.20 ± 89.20	473.80 ± 75.70	0.66
Cube average thickness, μm ± SD	327.50 ± 45.70	336.80 ± 56.30	0.48
Cube volume, mm^3 ± SD	11.40 ± 1.40	11.70 ± 1.10	0.50

SD, standard deviation.

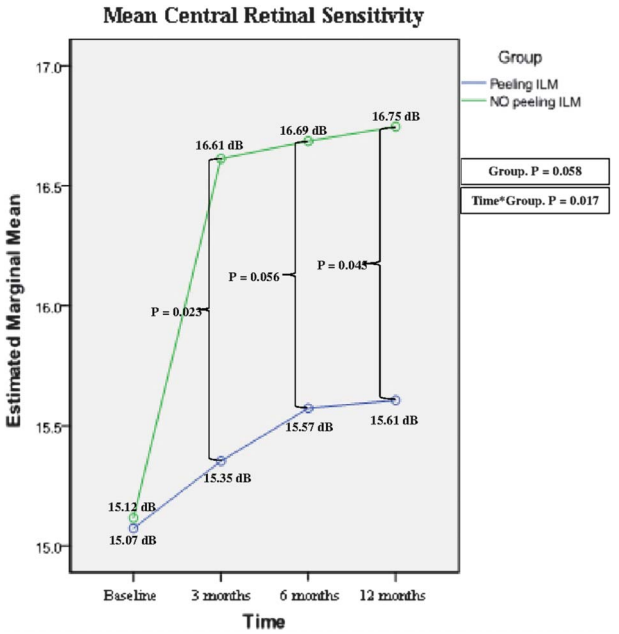

Fig. 1. Mean retinal sensitivity trend until 12 months of follow-up after ERM surgery.

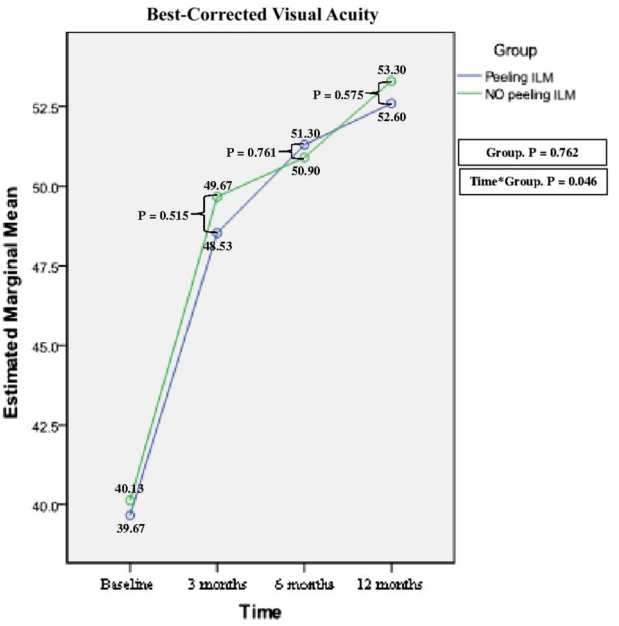

Fig. 3. Best-corrected visual acuity trend until 12 months of follow-up after ERM surgery.

(location fixation and fixation stability) ($P > 0.05$) (Table 2).

Pearson coefficient showed a significant correlation between Δ location fixation and Δ mean retinal sensitivity at a 12-month follow-up only within the ILM not peeling group (r = 0.366, $P = 0.047$).

Anatomical outcomes investigated by SD-OCT (foveal thickness, cube average thickness, and cube volume) did not show statistically significant differences between groups in the postsurgical trend until 12 months of follow-up ($P = 0.174$, =0.169, and =0.184, respectively) (Figure 5, A–C). However, the interaction effect of time and treatment showed faster reduction of retinal thickness and volume in the ILM not peeling group than in ILM peeling group (Figure 5, A–C).

Comparative analysis of the final results among the 3 Operative Units showed no statistically significant

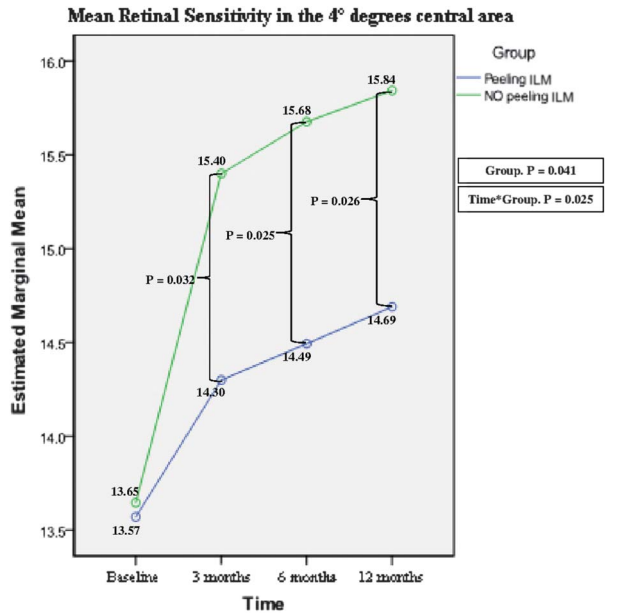

Fig. 2. Mean retinal sensitivity in the 4° central area trend until 12 months of follow-up after ERM surgery.

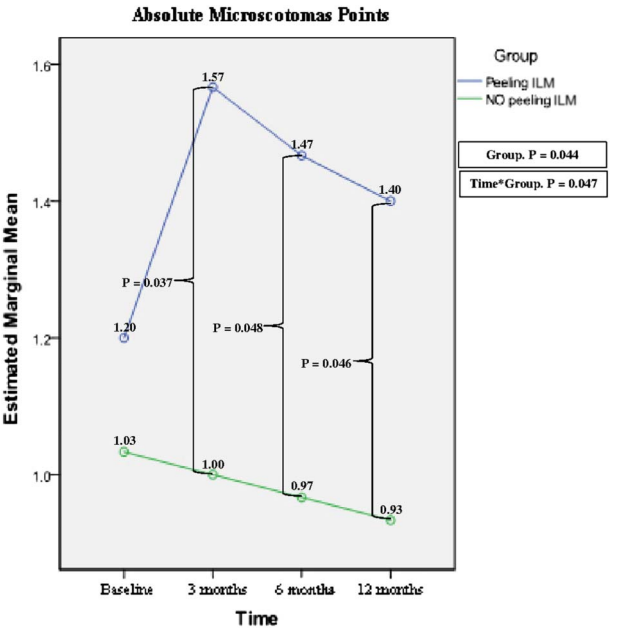

Fig. 4. Absolute microscotoma points' trend until 12 months of follow-up after ERM surgery.

Table 2. Comparison Between Groups at Each Follow-up Time During 12 Months of Follow-up and Time Trend (30 Eyes for Group)

ILM Peeling Group/ILM Not Peeling Group	3-Month Follow-up (*P*)	6-Month Follow-up (*P*)	12-Month Follow-up (*P*)	Time Trend
BCVA, n ± SD	48.53 ± 5.65/49.67 ± 7.60 (0.515)	51.30 ± 4.00/50.90 ± 5.93 (0.761)	52.60 ± 4.11/53.30 ± 5.41 (0.575)	Cubic
The 12° central retinal sensitivity, dB ± SD	15.35 ± 1.99/16.61 ± 2.19 (0.023)	15.57 ± 2.13/16.69 ± 2.29 (0.056)	15.61 ± 2.04/16.75 ± 2.25 (0.045)	Cubic
The 4° central retinal sensitivity, dB ± SD	14.30 ± 1.87/15.40 ± 2.02 (0.032)	14.49 ± 2.04/15.68 ± 1.95 (0.025)	14.69 ± 1.87/15.84 ± 2.04 (0.026)	Cubic
Absolute microscotomas' points in the 12° area, n ± SD	1.57 ± 1.14/1.00 ± 0.91 (0.037)	1.47 ± 1.07/0.97 ± 0.85 (0.048)	1.40 ± 1.00/0.93 ± 0.83 (0.046)	Quadratic
Absolute microscotomas' points in the 4° area, n ± SD	0.17 ± 0.53/0.13 ± 0.35 (0.774)	0.23 ± 0.57/0.20 ± 041 (0.795)	0.20 ± 0.49/0.20 ± 0.41 (1.000)	Cubic
Fixation stability inside the 2° area, % ± SD	77.87 ± 13.24/81.80 ± 13.33 (0.156)	77.20 ± 13.54/83.60 ± 12.94 (0.066)	77.53 ± 13.47/83.63 ± 12.71 (0.076)	Quadratic
Fixation stability inside the 4° area, % ± SD	95.17 ± 4.00/95.43 ± 4.79 (0.815)	95.07 ± 5.25/96.23 ± 4.13 (0.351)	95.47 ± 4.31/95.97 ± 4.20 (0.651)	Linear
Location fixation, % ± SD	75.13 ± 13.02/78.23 ± 14.59 (0.389)	74.27 ± 13.89/80.20 ± 15.87 (0.131)	76.20 ± 14.64/82.03 ± 16.01 (0.067)	Cubic
Foveal thickness, μm ± SD	400.90 ± 53.67/371.10 ± 47.19 (0.026)	386.03 ± 47.62/359.03 ± 48.24 (0.033)	376.90 ± 45.12/351.03 ± 40.24 (0.023)	Cubic
Cube average thickness, μm ± SD	307.87 ± 38.08/285.03 ± 41.94 (0.031)	299.37 ± 33.17/276.80 ± 51.10 (0.047)	289.50 ± 29.47/267.60 ± 44.90 (0.029)	Cubic
Cube volume, mm^3 ± SD	10.10 ± 1.02/9.55 ± 1.02 (0.031)	10.01 ± 0.92/9.47 ± 1.03 (0.031)	9.93 ± 0.90/9.35 ± 0.97 (0.031)	Cubic

SD, standard deviation.

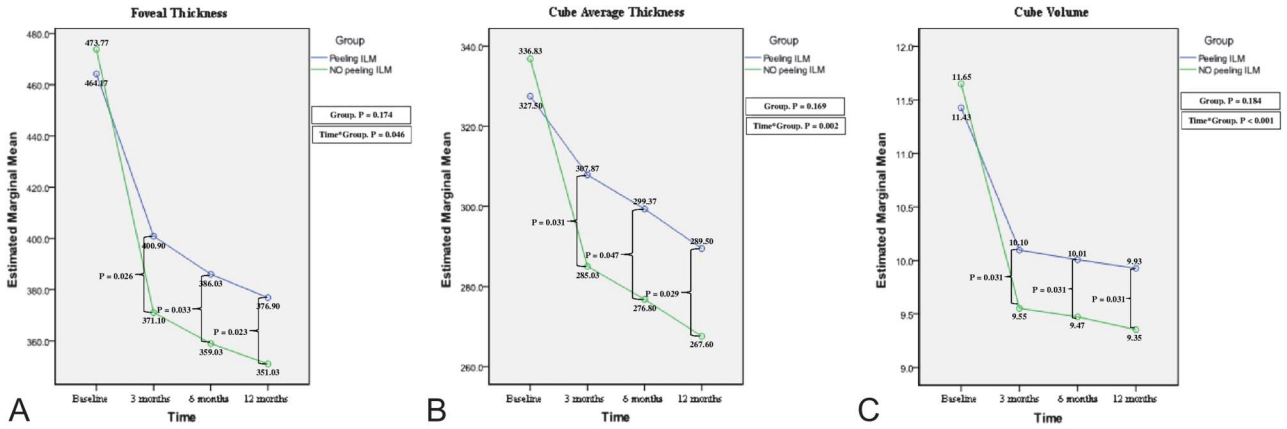

Fig. 5. Foveal thickness (**A**), cube average thickness (**B**), and cube volume (**C**) trends until 12 months of follow-up after ERM surgery, respectively.

differences for BCVA ($P = 0.108$), foveal thickness ($P = 0.070$), mean retinal sensitivity in the 4° central area ($P = 0.093$), and the number of absolute microscotomas points in the 4° and 12° central areas ($P = 0.781$ and $P = 0.203$, respectively). However, cube volume ($P = 0.016$), mean retinal sensitivity in the 12° central area ($P = 0.045$), fixation stability inside the 2° and 4° central areas ($P = 0.048$ and $P = 0.036$, respectively), and fixation location ($P = 0.045$) showed significant differences.

No ocular or systemic adverse events related to the surgical procedure that could influence the outcomes were reported during the follow-up.

Discussion

In this study, macular pucker surgery for ERM was successfully performed in both groups, improving visual acuity equally either group.

In both groups, patients also obtained significant postoperative improvement in retinal sensitivity as demonstrated by microperimetry MP1. However, either the 12° or 4° central area retinal sensitivity analysis showed different behavior between the groups in the postsurgical trend until 12 months of follow-up. In particular, recovery of the mean retinal sensitivity in the ILM not peeling group was earlier and better than that observed in the ILM peeling group (Figures 1 and 2).

A possible explanation could be related to the ILM function. Wollensak et al[34] observed a remarkably plastic biomechanical behavior of the retina providing a certain protective mechanism against tear formation. Moreover, their results showed that the mean strength of the central retina was reduced significantly by 53.6% after ILM removal regarding the unpeeled specimens, demonstrating that the ILM is the structure that mostly contributes to the biomechanical strength of the retina.[35] Performing ILM peeling, the surgeon removes not only the basement membrane of the Müller cells, but also the cell end feet, which are in contact with the nerve fibers.[36] Moreover, the Müller cell cone, an inverted cone-shaped zone of the specialized Müller cells that form the base of the fovea,[37] serves as a plug that binds the photoreceptor cells in the foveola and supports the foveola structurally.[38] The Müller cells also maintain the nerve fiber bundles close to each other[39] and are irregularly distributed.[40] Thus, Müller cells' end feet removal associated with ILM peeling results in substantial ultrastructural damage to the inner retinal surface, especially in regions where there is a greater concentration of Müller cells such as between nerve fiber bundles, which can be observed on fundus examination or with retinal imaging.[41] In fact, Clark et al[42] described the presence of postoperative swelling of the arcuate retinal nerve fiber layer few days after ILM peeling. Moreover, Alkabes et al[43] described "concentric macular dark spot" at 3 months after surgery in the area of ILM peeling using en face SD-OCT. These concentric macular dark spots are basically the en face tomographic feature of the dissociated optic nerve fiber layer, described by Tadayoni et al.[17]

These ultrastructural changes for the most part are subclinical and do not seem to have an effect on macular function as measured by visual acuity.[44] However, Terasaki et al[15] showed b-wave abnormalities after ILM peeling in their multifocal macular electroretinography study, suggesting that these findings are suggestive of the Muller cell damage. The authors hypothesize that b-wave abnormalities found by Terasaki et al could lead to different changes in retinal sensitivity between the ILM not peeling group and the ILM peeling group reported in this study.

Moreover, significant dissociation between BCVA and retinal sensitivity measured by microperimetric

MP1 has already been demonstrated.[22] Indeed, microperimetry is able to detect more subtle changes compared with visual acuity alone.[22] The different sensibility between these 2 functional tools could explain why no differences were seen between groups for the BCVA, but a significant different trend was detected for the mean retinal sensitivity until a 12-month follow-up (Figures 1–3).

Adverse effects of ILM peeling on retinal function have also been reported in other studies. The presence of long segments of ILM within the histopathologic specimen indicates a less favorable visual outcome in one study.[45] Visual field defects occurred after PPV for ERM with ILM peeling as a result of direct trauma to the nerve fibers during ILM peeling.[16] However, this is the first prospective work to study a direct comparison between ERM removal with or without ILM peeling using retinal sensitivity measured by microperimetry MP1 as a main parameter.

Also the presence of microscotomas' points (0 dB) is basic to evaluate the life quality of the patient because they may cause visual discomfort despite good visual acuity, as reported by some patients who underwent ILM peeling.[24]

In our study, the number of microscotomas was significantly bigger in the ILM peeling group than in the ILM not peeling group.

The cause of the development of microscotomas after peeling has still not been established. The direct trauma caused while using the forceps when gripping the ILM may be a possible cause. Anyway, operations were performed by experienced surgeons (G.R., G.G., and M.P.) accustomed to exercise caution when peeling off the ILM. The effect of dyes, which were used only for peeled eyes, cannot be completely excluded. However, this hypothesis seems unlike as the indocyanine green, the only dye that has been certainly demonstrated to have a toxic effect on ganglion cells, was not used. Indeed, Iriyama et al[46] demonstrated that Brilliant Blue G exerts no detectable detrimental effect on rat retinal ganglion cells, both in vitro and in vivo, after short time exposure and no significant toxic effect even after a longer time exposure. Awad et al studied the possible toxic effects of Brilliant Blue G on human pigment epithelial cells. After incubation for 5 minutes, the viability of the cells was between 100% and 114% relative to the control phosphate-buffered saline solution. They concluded that with an incubation time of 5 minutes, no statistically significant cell toxicity was found.[47] Microscotomas could be due to focal deterioration of the Müller cells, whose end feet are closely connected to the ILM and may be affected by ILM peeling.[20] Moreover, it is possible that the deterioration of other retinal cells is either directly because of the stretching caused by peeling or indirectly because of Müller cells deterioration.

Δ location fixation was correlated with Δ mean retinal sensitivity at the 12-month follow-up only within the ILM not peeling group ($P = 0.047$). This correlation was probably related to the greater increase in mean retinal sensitivity within the ILM not peeling group than in the ILM peeling group.

The difference between the ILM not peeling group and ILM peeling group in the postsurgical trend until 12 months of follow-up of SD-OCT parameters (foveal thickness, cube average thickness, and cube volume) was not significant, even if faster reduction was seen in the ILM not peeling group than in the ILM peeling group. Our results are consistent with those of Lee and Kim[44]: the mean postoperative central macular thickness was significantly higher in the ILM peeling group than in the ILM not peeling group ($P = 0.025$) in their work.

In both groups, no recurrences were seen, even if a longer follow-up should be necessary.

Also limitations of our prospective study should be mentioned. Strict a priori inclusion criteria (e.g., integrity of subfoveal inner segment/outer segment junction [diameter centered on the fovea of 200 μm]) allow enrolling only a portion of eyes that we see in the daily clinical practice. However, the authors have considered it appropriate to select these patients to reduce bias related to nonhomogeneous sample. Moreover, all the phakic eyes were excluded. Indeed, Richter-Mueksch et al[23] demonstrated a high rate of occurrence of cataract few months after ERM surgery, a possible important confounding factor for retinal sensitivity evaluation during 12 months of follow-up.

Another potential limiting factor of microperimetric evaluation is represented by some technical problems such as patient inexperience and fixation loss. For such reasons, patients underwent a short training session before each repeat testing during the follow-up to minimize potential learning artifacts. Moreover, patient fatigue is an important limitation of microperimetry (the mean time of test is >8 minutes).

Finally, the lack of histopathologic studies on extracted tissue specimens may be a possible limiting factor because the ILM and the ERM may be indistinguishable clinically, and varying amounts of ILM have been reported incidentally in ERM specimens. Therefore, we cannot exclude the possibility that some ILMs might have been peeled in some patients enrolled in this study, although only ERM peeling was performed.

In conclusion, although this study showed no deleterious effect of ILM peeling on the final visual

acuity, there may have been mechanical damage to the Müller cells and the structure of the macula. This damage, detectable by microperimetry retinal sensitivity analysis, may influence daily activities, as previously demonstrated.[32] Furthermore, macular pucker affects the entire macular region, although BCVA can assess the foveal function mainly without evaluating the whole macular status. Therefore, microperimetry mean retinal sensitivity represents an important complementary tool to investigate functional recovery after vitreoretinal surgery for macular pucker, showing a greater mean increase within the ILM not peeling group than in the ILM peeling group. These findings could be really important to manage this kind of patients, influencing the surgical plan. Indeed, ILM peeling in ERM surgery should be considered only in selected cases, for example, when the ILM is so tenaciously adherent to the ERM that the removal of the ERM alone is difficult. Additional ILM peeling may not be necessary when complete ERM removal without ILM peeling is possible.

Key words: microperimetry, retinal sensitivity, ERM removal, ILM peeling, microscotomas.

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