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Original Article

Idiopathic Epiretinal Membranes: Visual Outcomes and Prognostic Factors

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Abstract

Objectives: To evaluate the associations between anatomical changes and visual outcomes in patients with idiopathic epiretinal membrane (ERM).

Materials and Methods: We performed a prospective study of 130 consecutive idiopathic ERM patients and report their visual outcomes and the factors associated with visual outcome and anatomical changes.

Results: Of 130 eyes of 130 patients, 87 eyes underwent surgery, while the remaining 43 eyes were observed. At 6-month follow-up, the best-corrected visual acuity (BCVA) increased in the whole population. Mean Early Treatment Diabetic Retinopathy Study letter score changed from 51 to 65 in the surgical group and from 67 to 68 in the non-surgical group. The surgical group had improvement in BCVA at all ERM stages and grades of disorganization of the retinal inner layers (DRIL) ($p<0.01$). In multivariable analysis of the surgical group, factors associated with BCVA of ETDRS 60 letters or more were no or mild DRIL and the absence of ellipsoid zone disruption at baseline ($p=0.002$ and $p=0.034$, respectively) and this statistically significant positive correlation was still maintained at 12-month follow-up

Conclusion: Baseline DRIL grade and presence of ellipsoid zone disruption were the most informative prognostic factors in patients with idiopathic ERMs. Patients with severe DRIL and/or advanced ERMs had improved vision after ERM removal.

Keywords: Idiopathic epiretinal membranes, disorganization of the retinal inner layers, visual outcome, prognostic factors

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Introduction

Epiretinal membranes (ERMs) are one of the common causes of visual impairment, with a reported prevalence of 6-7% of the population.[1,2] The prevalence of ERMs increases significantly by age group, especially in older adults (0.5% for 40 to 49 years, 2.6% for 50 to 59 years, 7.2-9.4% for 60 to 69 years, 11.6-15.1% for 70 to 79 years, and 9.3-11.3% for 80 years and older).[1,2] ERMs lead to deformation of the retinal architecture and may distort the distribution of photoreceptors, causing various visual complaints such as metamorphopsia and ultimately loss of visual acuity. ERMs can be associated with several vitreoretinal diseases such as retinal vasculitis, diabetic retinopathy, retinal venous occlusive disease, retinal detachment, retinal injury, previous retinal surgery. As a minority of idiopathic ERM cases become symptomatic, only a small proportion of affected patients require surgical removal.[1]

Multiple prognostic factors determining visual outcomes in ERM after pars plana vitrectomy (PPV) and ERM peeling have been evaluated, including preoperative visual acuity, symptom duration, patient age, central macular thickness, preoperative integrity of foveal photoreceptors, the status of the cone outer segment tips, and irregularity of the inferior border of the inner plexiform layer.[3,4,5,6,7,8,9,10,11,12] Spectral-domain optical coherence tomography (SD-OCT) has driven a transformative change in the study of ERMs to better identify anatomical characteristics, including central macular thickness (CMT), intraretinal cystic space, ellipsoid zone disruption, cotton ball sign, ectopic inner foveal layer, ERM stages, and recently, disorganization of the retinal inner layers (DRIL).[13,14]

The purpose of this study was to evaluate the associations between anatomical changes visualized by SD-OCT and visual outcomes in patients with idiopathic ERM.

Materials and Methods

A prospective study was conducted at Chiang Mai University Hospital, Thailand including all patients diagnosed with ERM and seen by retinal specialists at the Retinal Service Clinic between January 1, 2014 and December 31, 2018. The study was approved by the Ethics Committee of Chiangmai University Hospital and conformed to the Declaration of Helsinki.

Study Participants

The study inclusion criteria were: (1) age 18 years or older; (2) idiopathic ERMs; (3) no previous ocular surgery except uncomplicated cataract surgery more than 6 months ago; and (4) at least 6 months of follow-up after ERM diagnosis. In patients with bilateral idiopathic ERM, the more severely affected eye was included.

Exclusion criteria were: (1) Other concomitant ocular diseases that are usually associated with ERMs (i.e., diabetic retinopathy, age-related macular degeneration, retinal vascular disease, retinal inflammatory disease or infection); (2) secondary ERMs or ERMs associated with other vitreoretinal diseases; (3) macular hole; (4) vitreomacular traction; (5) any other ocular condition compromising visual acuity except the presence of cataract (i.e., amblyopia, glaucoma); and (6) need for intraocular surgery, especially cataract surgery, during study period.

After the patients were diagnosed, demographic data including their age, sex, laterality, underlying diseases, subjective visual symptoms, history of previous ocular surgery, and best-corrected visual acuity (BCVA) at baseline were recorded. Then the patients were divided into two groups by treatment option (surgery or observation), which was determined according to patient preference and the retinal specialist's recommendation based on factors such as visual acuity, complaints of distortion, and ERM grade. All patients signed an informed consent form prior to participation. Subsequent investigations and BCVA assessment were performed at 6-month and 12-month follow-up.

Surgical Procedure

The surgeries were performed by 5 surgeons (P.K., D.P., J.C., N.W., and V.C.) with more than 10 years of experience in vitreoretinal surgery. A 3-port 23-gauge transconjunctival sutureless vitrectomy was performed using the CONSTELLATION Vision System (Alcon Laboratories, Inc, Fort Worth, Texas, USA). In all eyes, a central vitrectomy was performed and the posterior vitreous humor was separated from the retina. After vitrectomy the ERM and internal limiting membrane were removed using end-gripping forceps (Alcon, Fort Worth, TX, USA) with the assistance of Brilliant Blue G dye (0.05% w/v, Aurolab, India) or triamcinolone (40 mg/mL, Triesence; Alcon, Fort Worth, Texas, USA). The ERM and internal limiting membrane were removed from the central macular area up to the arcades.

Optical Coherence Tomography Analysis

All subjects underwent SD-OCT scans centered on the fovea (Spectralis; Heidelberg Engineering, Heidelberg, Germany) with 25 section images and automatic real-time mean =9 at baseline, 6-month, and 12-month follow-up.

ERMs were defined as discrete, irregular, and hyperreflective lines above the inner retinal surface. Retinal thickness was analyzed and measured by the automated thickness map function. Continuous ectopic inner foveal layer was defined as the presence of a continuous hyporeflective or hyperreflective band that extends from the inner nuclear layer (INL) and inner plexiform layer (IPL) across the foveal region and is visible in all OCT scans.[15] Disruption of the ellipsoid zone was defined as a discontinuous ellipsoid band in the foveal region. The presence of a round or diffuse hyperreflective area between the ellipsoid zone and the cone outer segment tip line at the center of the fovea was defined as the "cotton ball sign" (Figure 1).[16]

The presence and severity of DRIL were assessed within the central 2,000 µm based on distinguishability (score 0 for distinguishable, 1 for indistinguishable) and boundary regularity (score 0 for regular, 1 for irregular) between the ganglion cell-inner plexiform layer complex (GC-IPL) and INL and between the INL and outer plexiform layer (OPL), resulting in a score

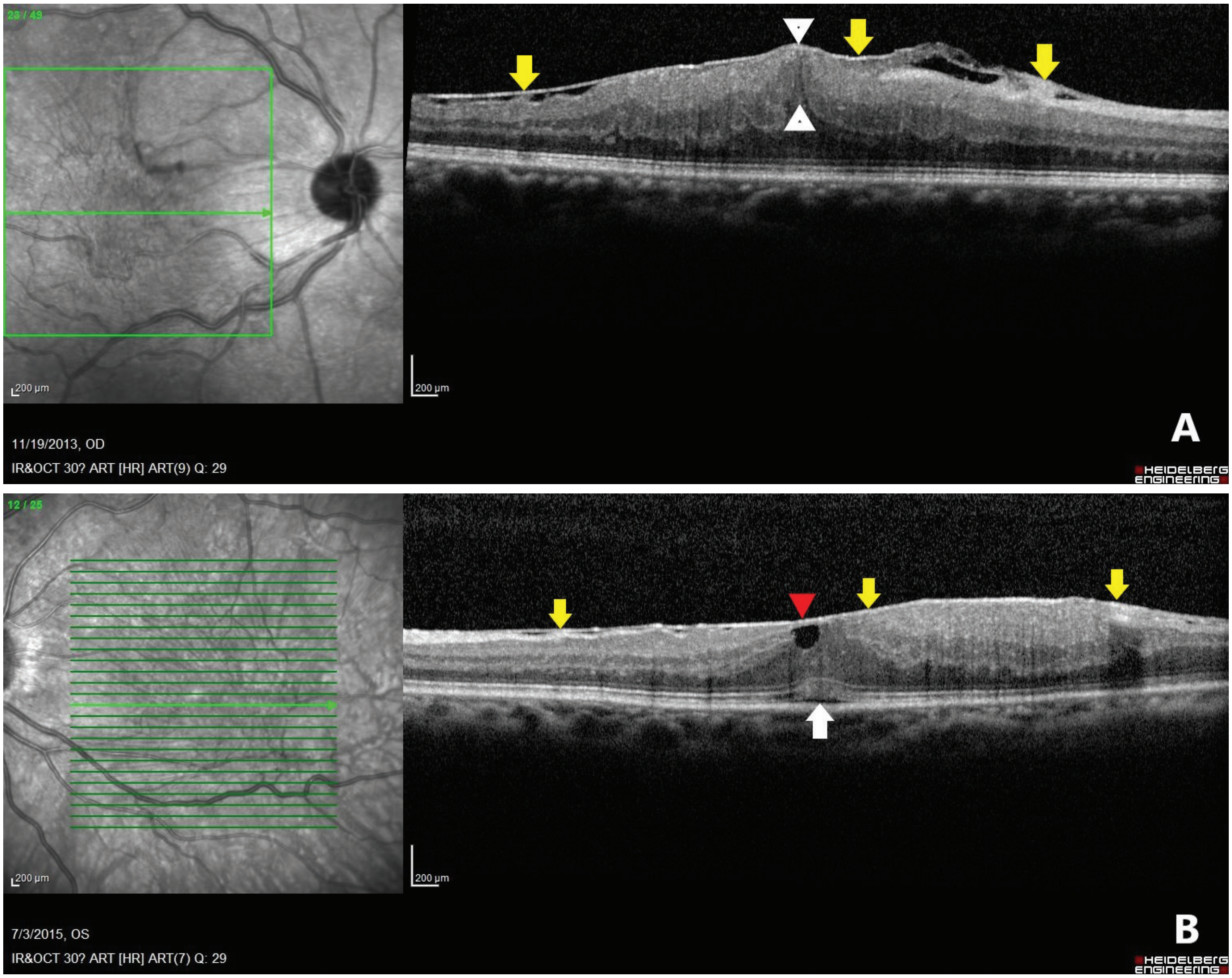

Figure 1. Morphologic characteristics of epiretinal membranes. Figure 1A shows stage 3 epiretinal membranes (yellow arrows) and continuous identified ectopic inner foveal layers (white arrow head), which appears as a continuous hyporeflective or hyperreflective band extending from the inner nuclear layer and inner plexiform layer across the foveal region. Figure 1B shows stage 3 epiretinal membranes (yellow arrows), cotton ball sign (diffuse hyperreflective area between the ellipsoid zone and the cone outer segment tip line at the center of the fovea; white arrow) and intraretinal cyst (hyporeflective intraretinal cystoid space; red arrow head)

ranging from 0-4 points. DRIL was classified into 3 grades: presence of no DRIL was considered grade 0 (0 points); presence of mild DRIL was considered grade 1 (1-3 points); presence of severe DRIL was considered grade 2 (4 points).[14]

ERM staging was also done in this study in order to describe disease severity. Stage 1 was defined as the presence of a mild ERM with negligible morphologic or anatomic disruption, with all retinal layers and foveal depression clearly identifiable; stage 2 was defined as the presence of ERM associated with progressive retinal distortion and loss of foveal depression, but all retinal layers were clearly identifiable; stage 3 was defined as the presence of ERMs with continuous ectopic inner foveal layers anomalously crossing the central foveal area, absence of foveal depression, but all retinal layers clearly identifiable; and stage 4 was defined as an ERM complicated by significant retinal thickening and marked anatomic disruption of the macula, with retinal layers that were significantly distorted, disorganized, and not clearly identifiable with OCT.[13]

Outcome Measures

The main outcome measure was visual outcome in the idiopathic ERM patients at 6 months. Secondary outcomes were associated factors and correlations between visual outcome and anatomical changes at 6 months. Visual acuity was tested using the Snellen acuity chart and converted to Early Treatment Diabetic Retinopathy Study (ETDRS) letter scores for all calculations and statistical analyses.

Statistical Analysis

All the analyses were carried out using the SPSS version 24.0 (IBM Corp, Armonk, NY). Descriptive statistics were first calculated for all variables of interest. Mean and standard deviation values were calculated. Parametric and nonparametric tests (independent t-test, Mann-Whitney U test) were used to compare quantitative variables, and the chi-square test was used to test for correlation with confounders. Univariate and multivariate logistic regression was used to identify factors associated with BCVA. Differences were reported with 95% confidence intervals (CI). A p value <.05 was considered statistically significant.

Results

One hundred and ninety-one patients were diagnosed with idiopathic ERMs, of which 61 were excluded due to the presence of one or more exclusion criteria. The remaining 130 patients (130 eyes) were enrolled; 45 (35%) were men, 85 (65%) were women, and the mean age was 67 years. Demographic and baseline characteristics are shown in Table 1. Mean BCVA (approximate ETDRS letter score) was 56±17, 66±13, and 69±12 at baseline, 6-month, and 1-year follow-up, respectively, with a mean follow-up period of 9.8±5.5 months.

Anatomical Appearance and Changes in the Surgical and Non-Surgical Groups

Of the 130 eyes with ERMs, 87 eyes underwent surgery, while the remaining 43 eyes were observed as the control (non-surgical) group. Baseline anatomical apppearance in terms of ERM staging and DRIL grading was analyzed in both groups. We observed that patients with more severe ERM and DRIL more frequently underwent surgery (Table 2).

Comparisons of baseline characteristics between the surgical and non-surgical group in terms of mean baseline ETDRS letter scores and CMT revealed significant differences between the groups. The surgical group had lower mean baseline ETDRS letter score (51±14 vs. 67±17) and higher mean baseline CMT (503.3±92.6 µm vs. 400.6±103.9 µm) than the non-surgical group ($p<0.01$ for both). In addition, mean ERM stage and DRIL grade in the surgical group (2.9±0.8 and 1.4±0.5, respectively) were higher than those in the non-surgical group (2.2±1.0 and 0.7±0.7, respectively) ($p<0.01$).

At 6 months, the overall mean CMT decreased significantly from 469.31±107.6 µm to 408.7±81.5 µm ($p<0.01$). However, subgroup analysis showed that mean CMT only decreased in the surgical group, from 503.3±92.6 µm to 406.5±70.1 µm ($p<0.01$), while it increased slightly from baseline in the non-surgical group (from 400.6±103.9 µm to 412.4±99.2 µm, $p=0.127$). Evaluation of the anatomical changes according to ERM stages and DRIL grades at 6-month follow-up are shown in Table 3 and Figure 2.

Table 1. Demographic data and baseline characteristics of patients with idiopathic epiretinal membranes

Characteristics	Results
Age, years, mean ± SD (range)	67±23 (44-90)
Male:female, n (%)	45:85 (35:65%)
Laterality, OD, n (%)	72 (55.4)
Systemic co-morbidity, n (%)	
Hypertension	55 (42.3)
Diabetes mellitus*	19 (14.6)
Pseudophakia, n (%)	36 (27.7)
Metamorphopsia, n (%)	15 (11.5)
BCVA, approximate ETDRS, mean ± SD	56.22±16.56
Central macular thickness, µm, mean ± SD	469.31±107.61
Ellipsoid zone disruption, n (%)	8 (6.2)
Continuous ectopic inner foveal layers, n (%)	74 (56.9)
Cotton ball sign, n (%)	15 (11.5)
Intraretinal cystic space, n (%)	36 (27.7)
Epiretinal membrane (ERM) stage, n (%)	
1	17 (13.1)
2	33 (25.4)
3	52 (40.0)
4	28 (21.5)
Disorganization of retinal inner layers (DRIL) grade, n (%)	
0 (none)	20 (15.4)
1 (mild)	63 (48.5)
2 (severe)	47 (36.2)
Treatment, n (%)	
Monitoring/observation	43 (33.1)
Surgery	87 (66.9)

BCVA: Best-corrected visual acuity, ETDRS: Early treatment diabetic retinopathy study, *No patient had diabetic retinopathy, SD: Standart deviation

Table 2. Baseline anatomical appearance of patients with idiopathic epiretinal membrane

		Total (eyes)	Surgical group (eyes)	Non-surgical group (eyes)	P value
ERM stage	1	17	5 (29%)	12 (71%)	0.02
	2	33	18 (55%)	15 (45%)	0.46
	3	52	42 (81%)	10 (19%)	<0.01
	4	28	22 (79%)	6 (21%)	<0.01
DRIL grade	0 (none)	20	2 (10%)	18 (90%)	<0.01
	1 (mild)	63	45 (71%)	18 (29%)	<0.01
	2 (severe)	47	40 (85%)	7 (15%)	<0.01

ERM: Epiretinal membrane, DRIL: Disorganization of the retinal inner layers

Visual Acuity Changes in the Surgical and Non-Surgical Groups

BCVA at 6-month follow-up increased in the whole ERM population, with no differences between the surgical and non-surgical groups (mean ETDRS letter score: 64.94 in the surgical group and 67.95 in the non-surgical group; p=0.234). However, a gain of 15 letters or more was seen in over half of patients in the surgical group (47/87 eyes, 54%) versus only 9% of patients in the non-surgical group (4/43 eyes) (p<0.01, odds ratio [OR]: 11.46, 95% CI: 3.77-34.83). This result increased over time to

Table 3. Anatomical changes at 6-month follow-up

Anatomical changes at 6-month follow-up		Surgical group (87 eyes)	Non-surgical group (43 eyes)
ERM stage	Improved	34 (39%)	0 (0%)
	Stable	51 (59%)	36 (84%)
	Worse	2 (2%)	7 (16%)
DRIL grade	Improved	39 (45%)	1 (2%)
	Stable	46 (53%)	36 (84%)
	Worse	2 (2%)	6 (14%)

ERM: Epiretinal membrane, DRIL: Disorganization of the retinal inner layers

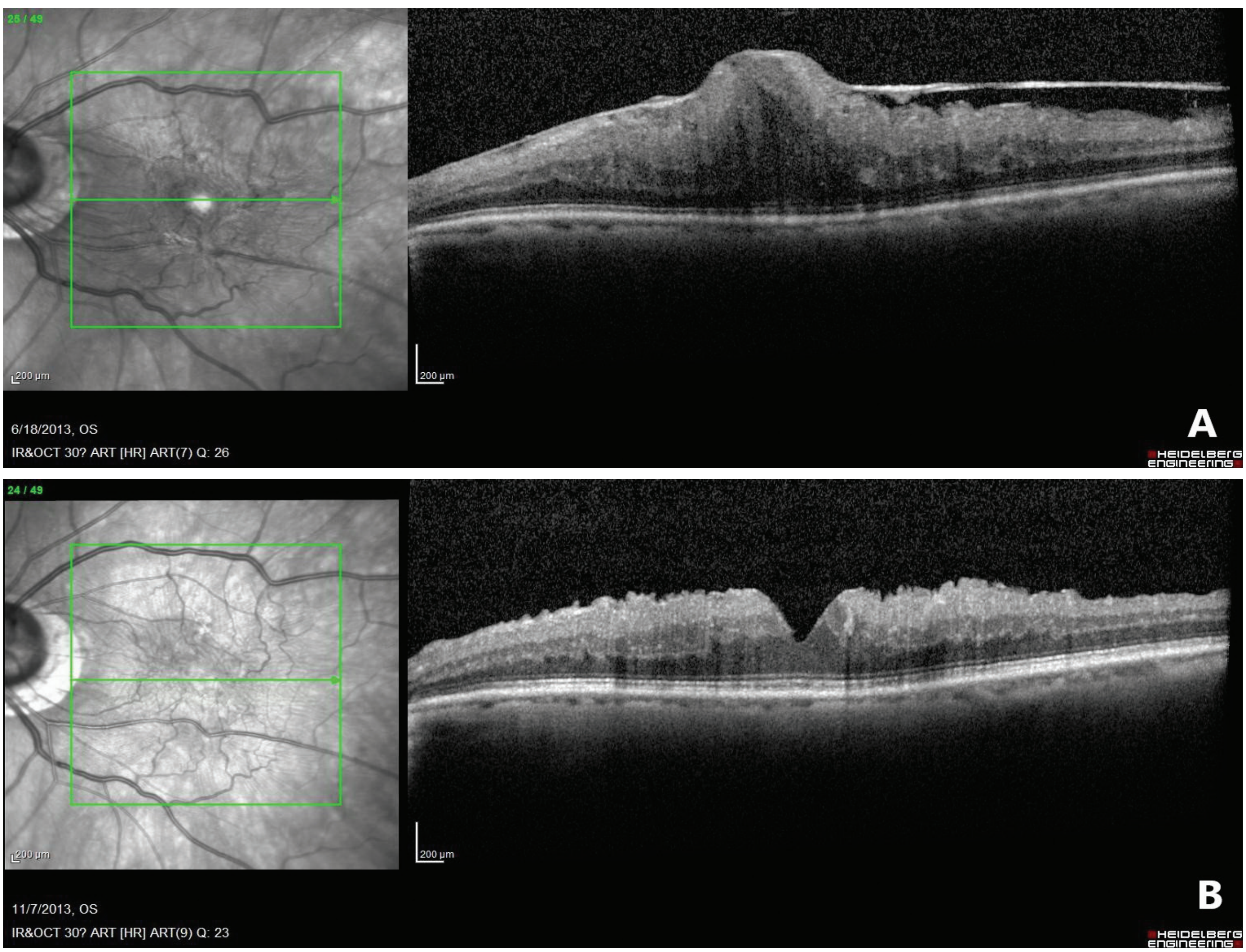

Figure 2. Anatomical changes evaluated by optical coherence tomography. Figure 2A shows stage 4 epiretinal membranes (ERMs), retinal thickening, and anatomic disruption of the macula with loss of foveal depression and significantly distorted and disorganized retinal layers. Disorganization of the retinal inner layers (DRIL) grade 2 was also considered in this morphologic characteristic. Figure 2B shows postoperative regression of ERM stage and DRIL grade at 6-month follow-up, with partial regression of the ectopic inner foveal layer and some remaining disorganization of the retinal layers

30/58 eyes (52%) in the surgical group and 4/34 eyes (12%) in the non-surgical group at the 12-month follow-up evaluation ($p<0.01$, OR: 8.04, 95% CI: 2.51-25.72).

ERM stage, DRIL grade, and their relationship with BCVA changes are shown in Table 4. The surgical group showed improvement in BCVA at all stages and grades ($p<0.01$), while there were no significant differences in BCVA in the non-surgical group. In a subgroup analysis of the surgical group, patients with good baseline visual acuity (20/60 or better; 22 patients) had a visual acuity improvement of 4.18 letters on average, while those with poor baseline visual acuity (20/200 or less; 15 patients) had a mean visual acuity improvement of 23.0 letters.

Factors Associated with Visual Outcome

The analysis of potential factors correlating with visual outcomes is shown in Table 5 and Table 6. In univariate analysis of the whole group (Table 5), we found several factors were positively associated with BCVA of ETDRS 60 letters or more at 6-month follow-up. However, in surgical subgroup univariate analysis (Table 6), we found only baseline visual acuity of ETDRS 55 letters or more, absence of ellipsoid zone disruption, and no or mild DRIL were positively associated with BCVA of ETDRS 60 letters or more at 6 months, whereas only no or mild DRIL was associated with gaining 15 letters or more. Furthermore, patients with severe DRIL experienced an improvement of 10 letters and a larger increase in CMT (>450 μm) was associated with a BCVA gain of 15 letters or more ($p<0.01$).

In multivariable analysis of the surgical group, the factors associated with a BCVA of ETDRS 60 letters or more at 6-month follow-up were no or mild DRIL and absence of ellipsoid zone disruption at baseline ($p=0.002$, OR: 5.676, 95% CI: 1.896-16.991 and $p=0.034$, OR: 11.745, 95% CI: 1.204-114.578, respectively). This statistically significant positive correlation was still maintained at 12-month follow-up (baseline no or mild DRIL; $p<0.01$, OR: 6.821, 95% CI: 2.190-21.244 and

Table 4. Correlation between visual acuity changes from baseline to 6-month follow-up and epiretinal membrane stage and disorganization of the retinal inner layers grade

Anatomical changes		Surgical group (n=87)	Non-surgical group (n=43)	P value
ERM stage	1-2 (n=50)	58.43 → 68.48 (p<0.01)	70.70 → 72.07 (p=0.519)	0.212
	3 (n=52)	52.02 → 67.52 (p<0.01)	65.30 → 65.70 (p=0.898)	0.527
	4 (n=28)	40.91 → 56.32 (p<0.01)	52.83 → 52.83 (p=1.00)	0.630
DRIL grade	0-1 (no/mild) (n=83)	55.94 → 69.55 (p<0.01)	68.89 → 70.69 (p=0.336)	0.594
	2 (severe) (n=47)	45.00 → 59.53 (p<0.01)	57.00 →53.57 (p=0.304)	0.311

ERM: Epiretinal membrane, DRIL: Disorganization of the retinal inner layers

Table 5. Anatomical and clinical characteristics of epiretinal membranes and visual acuity at 6-month follow-up

Factors	ETDRS >60 letters (n=94)	ETDRS <60 letters (n=36)	P value (Odds ratio, 95% CI)
Mean baseline BCVA	60.8	44.25	<0.01
Baseline ETDRS >45 letters	84 (89%)	24 (67%)	<0.01 (4.20. 1.62-10.9)
Baseline ETDRS >55 letters	70 (74%)	10 (28%)	<0.01 (7.60. 3.20-18.0)
Ellipsoid zone disruption	1 (1%)	7 (19%)	<0.01 (22.45. 2.65-190.10)
Ectopic inner foveal layer	45 (48%)	29 (81%)	<0.01 (4.51. 1.80-11.31)
CMT <450 μm	48 (51%)	10 (28%)	0.019 (2.71. 1.18-9.22)
ERM stage 1-2 - Surgical group - Non-surgical group	42 (45%) 18 (19%) 24 (26%)	8 (22%) 5 (14%) 3 (8%)	0.019 (2.828. 1.167-6.848) 0.307 (0.45. 0.10-2.13)
ERM stage 3-4 - Surgical group - Non-surgical group	52 (55%) 43 (46%) 9 (9%)	28 (78%) 21 (58%) 7 (20%)	0.019 (2.828. 1.167-6.848) 0.559 (1.593. 0.52-4.87)
DRIL grade: none/mild - Surgical group - Non-surgical group	71 (76%) 41 (44%) 30 (32%)	12 (34%) 6 (17%) 6 (17%)	<0.01 (6.174.2.672-11.264) 0.617 (1.367. 0.40-4.66)
DRIL grade: severe - Surgical group - Non-surgical group	23 (24%) 20 (21%) 3 (3%)	24 (67%) 20 (56%) 4 (11%)	<0.01 (6.174.2.672-11.264) 0.727 (1.33. 0.26-6.74)

BCVA: Best-corrected visual acuity, ETDRS: Early Treatment Diabetic Retinopathy Study, CMT: Central macular thickness, ERM: Epiretinal membrane, DRIL: Disorganization of the retinal inner layers, CI: Confidence interval

Table 6. Anatomical and clinical characteristics of epiretinal membrane patients in the surgical group and their association with ETDRS letter score of 60 and gain of 15 letters at 6-month follow-up

Factors	ETDRS letter score		P value (odds ratio, 95% CI)	Letter gain		P value (odds ratio, 95% CI)
	>60 (n=61)	<60 (n=26)		>15 (n=47)	<15 (n=40)	
Mean baseline BCVA	53.67	44.42	0.159	47.34	55.10	0,289
Baseline ETDRS >45 letters	51 (83.6%)	17 (65.4%)	0.088	34 (72.3%)	34 (85.0%)	0,154
Baseline ETDRS >55 letters	37 (60.7%)	7 (26.9%)	<0.01 (4.185, 1.528-11.459)	21 (44.7%)	23 (57.5%)	0.233
Ellipsoid zone disruption	1 (1.6%)	6 (23.1)	<0.01 (18.00, 2.042-158.701)	2 (4.3%)	5 (12.5%)	0.159
Ectopic inner foveal layer	39 (63.9%)	22 (84.6%)	0.054	31 (66.0%)	30 (75.0%)	0.358
CMT <450 µm	21 (34.4%)	6 (23.1%)	0.295	14 (29.8%)	13 (32.5%)	0.785
ERM stage 1-2	18 (29.5%)	5 (19.2%)	0.32	11 (23.4%)	12 (30.0%)	0.487
ERM stage 3-4	43 (70.5%)	21 (80.8%)		36 (76.6%)	28 (70.0%)	
DRIL grade: none/mild	41 (67.2%)	6 (23.1%)	<0.01 (6.833, 2.374-19.672)	30 (63.8%)	17 (42.5%)	**0.047 (2.388, 1.006-5.666)**
DRIL grade: severe	20 (32.8%)	20 (76.9%)		17 (36.2%)	23 (57.5%)	

BCVA: Best-corrected visual acuity, ETDRS: Early Treatment Diabetic Retinopathy Study, CMT: Central macular thickness, ERM: Epiretinal membrane, DRIL: Disorganization of the retinal inner layers, CI: Confidence interval

no presence of ellipsoid zone disruption; p=0.023, OR: 12.925, 95% CI: 1.767-121.351).

No serious intraoperative or postoperative complications were registered over the follow-up period in the surgical group or the non-surgical group. However, 8 of 87 patients (9%) had decreased visual acuity after surgery. The factor associated with worsening visual acuity was stage 1 or 2 ERMs (p=0.028, OR: 5.648, 95% CI: 1.229-25.950). We found that 4 of these 8 patients had good baseline visual acuity (20/60 or better) and lost less than 5 letters in the follow-up period. The other 4 patients had a visual acuity loss of more than 10 letters (3 patients had severe DRIL at baseline and no regression after surgery, 1 patient had severe ellipsoid zone disruption).

Discussion

ERMs can cause decreased visual acuity as well as other visual disturbances such as micropsia and metamorphopsia that are often slowly progressive. The natural history of ERM from the Blue Mountain Study showed that without treatment, only 30% of patients had progressed at 5 years, while the others regressed or remained stable.[17] Therefore, the surgical management of ERMs is recommended for patients with severe complaints and those with poor visual acuity. PPV and membrane peeling are considered standard treatment for ERM patients with visual acuity of 20/50 or less, or for those with intolerable symptoms. In contrast, there is no consensus on the management of ERM patients with good visual acuity (better than 20/50 or 20/60) and those with severe ERMs (poor preoperative visual acuity, or severely disorganized retinal layers, or very thick macula). In ERM patients with BCVA better than 20/50, non-surgical follow-up is often recommended since the majority of the patients prefer to keep their satisfactory visual acuity and avoid unnecessary complications of PPV such as retinal detachment, endophthalmitis, and accelerated cataract formation.[18] Several studies have reported favorable success rates in visual improvement and low risk of complications from PPV and membrane peeling in patients with idiopathic ERMs.[4,10,19,20,21,22,23,24,25,26,27,28,29] It is possible that early PPV could result in the preservation of better visual acuity and less irreversible damage to the retina than the usual follow-up regimen, which basically results in performing PPV when visual impairment and/or more advanced anatomical changes have occurred.[30,31,32] In severe ERM patients, PPV is controversial because photoreceptor cells may be severely disrupted, resulting in permanent visual loss.

Our study demonstrates that PPV can improve anatomic appearance and vision significantly in all stages and all grades of ERM, though the greatest benefit was noted in more severe cases. We emphasize that all patients who are symptomatic, have loss of vision, and would like to improve their vision should undergo surgery earlier for better long-term visual preservation after a thorough discussion of the potential benefits and risks of surgery without unintentional bias (Table 4). Although several reports suggested that surgery can also cause retinal damage, including swelling of the arcuate nerve fiber layer[33], dissociated optic nerve fiber layer defect[34], secondary paracentral macular hole[35], and microcysts in the INL of the retina[36], none of these were observed in the present study. Another factor in support of early surgery is that it results in better postoperative visual acuity when there is good preoperative vision.[20,31,37,38]

Multiple studies have evaluated SD-OCT parameters as visual prognosticators in ERM surgery.[9,10,11,12,16,21,39,40,41,42,43,44,45,46,47] Various prognostic factors have been identified, including baseline visual acuity, degree of preoperative metamorphopsia, microstructural factors, CMT, ellipsoid zone disruption, and the inner-retinal layer irregularity index.[9,10,11,12,21,22,45,46,48,49,50,51,52,53,54] However, there is no consensus on the best marker. The present study showed that baseline visual acuity, presence of ellipsoid zone disruption, and DRIL grade were all relevant, but in the multivariate analysis, baseline DRIL grade and presence of ellipsoid zone disruption were identified as the most important markers.

Baseline visual acuity was strongly associated with visual prognosis, but this association was obviously predictable. Most patients in the non-surgical group with good visual acuity at baseline remained stable. Patients with good baseline visual acuity who underwent surgery also had good visual acuity at follow-up, whereas those with poor baseline visual acuity remained suboptimal but exhibited improvement. These findings are similar to previous studies.[20,24,29,45]

The OCT feature termed DRIL was firstly characterized by Sun et al.[55] as the horizontal extent in microns for which any boundaries between the GC-IPL, INL, and OPL could not be identified. Particularly, DRIL was found to be associated with visual acuity after the resolution of center-involving diabetic macular edema and improvement in DRIL was predictive of better visual outcomes.[56,57,58] Similarly, DRIL has been identified as an important biomarker for functional outcome in patients with ERMs. Recently, Zur et al.[14] reported that DRIL grading correlated with functional and anatomical measures and could play a role as a biomarker to predict the visual outcome after surgery in a patient with idiopathic ERMs. The authors reported that visual and anatomic outcomes of patients with severe DRIL were limited and that these patients were further prone to develop intraoperative and postoperative complications. However, this study did not include a control group and the prognosis of patients with severe DRIL without surgery was not reported. Our study reveals that visual outcomes in patients with severe DRIL after surgery were better (though limited) than in the observation group. All patients with severe DRIL and improvement of more than 15 letters were in the surgical group. There have been many mechanisms proposed to explain the association of DRIL with visual acuity, including the presence of disorganization or destruction of cells within inner retinal layers (bipolar, amacrine, or horizontal cells) causing a disruption of pathways that transmit visual information[55], or prolonged tractional forces leading to irregularity of the inner retinal layers that may progress and cause deformation or disconnection of synaptic junctions between photoreceptors and ganglion cells.[14] In addition, cellular damage to Müller cells and inner retinal cells is believed to influence the visual prognosis in eyes with ERM.

Cho et al.[12] reported that after ERM removal, tractional forces are reduced, but the recovery period for restoring natural retinal structure and function can be variable. We found that 6 months after surgery, the desired visual outcomes were not completely achieved even after apparently successful removal. The visual outcome in some patients was not associated with their ERM stage. To explain this phenomenon, future randomized controlled clinical trials are needed in order to investigate other factors affecting visual outcome apart from ERM morphology.

Study Limitations

This study had several limitations. Firstly, the surgical techniques varied, as some procedures were Brilliant Blue G-assisted and the internal limiting membrane peeling size depended on the surgeon's discretion. Secondly, the postoperative follow-up period of 6 months was relatively short. Moreover, visual outcomes after surgery might be underestimated since a majority of our patients remained phakic after PPV and their cataract progression might influence their vision. Nonetheless, we believe that at the first 6 months, the influence of cataract on visual outcome is minimal. Cataract surgery at the sole surgeon's discretion could also affect the results of this study because visual acuity may also improve from cataract surgery (not ERM removal). We attempted to minimize this effect by excluding all patients who developed visually significant cataracts and needed cataract surgery during the study period.

Conclusion

In conclusion, we identified baseline DRIL grade and the presence of ellipsoid zone disruption as the most informative prognostic factors in patients with idiopathic ERMs, independent from surgical intervention. Furthermore, we demonstrate that patients with severe DRIL and/or advanced ERMs could improve their vision after ERM removal.

Ethics

Ethics Committee Approval: Ethics Committee approval number OPT-2561-05442 Chiangmai University.

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Authorship Contributions

Surgical and Medical Practices: P.K., D.P., J.C., N.W., V.C., Concept: P.K., M.S., D.P., J.C., N.W., V.C., Design: P.K., K.P., Data Collection or Processing: M.S., Analysis or Interpretation: M.S., J.C., Literature Search: P.K., M.S., K.P., A.R., Writing: P.K., M.S., K.P., A.R.

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