Research Square

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Long-term natural history of idiopathic epiretinal membranes: an optical coherence tomography-based study

Yolradee Winuntamalakul
Navamindradhiraj University
Kornwipa Hemarat
Navamindradhiraj University
Yodpong Chantarasorn
Navamindradhiraj University
Plern Sutra
Navamindradhiraj University
Itsara Pokawattana
itsara@nmu.ac.th

Navamindradhiraj University

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Abstract

Background

The progression of idiopathic epiretinal membranes (ERMs) is highly variable, and long-term clinical data are essential for management decisions. This study aimed to evaluate the natural history of idiopathic ERM and identify predictors of progression using optical coherence tomography (OCT).

Methods

This retrospective cohort study included patients with idiopathic ERMs who had at least one year of follow-up. Best-corrected visual acuity (BCVA), lens status, OCT findings and management information were reviewed. OCT parameters included ellipsoid zone (EZ) disruption, the cotton ball sign, intraretinal (IR) cysts, and central subfield thickness (CST). Idiopathic ERMs and their variants are classified into four types, and isolated idiopathic ERMs are further divided into four stages.

Results

A total of 192 eyes were included, 162 of which were followed under observation, while 30 underwent surgery. The mean follow-up period was 3.7 ± 1.9 years. The percentages of ERM progression in stages 1 to 4 were 33.8%, 39.1%, 15.2%, and 0%, respectively. In stage 1, BCVA significantly worsened from 0.30 ± 0.18 to 0.38 ± 0.19 ($P < 0.001$), while changes in other stages were not significant. BCVA deterioration was strongly associated with surgery risk (OR: 24.87, 95% CI: 3.59–172.56, $P = 0.001$). CST changes were significantly linked to progression risk (OR: 1.02, 95% CI: 1.01–1.02, $P < 0.001$). Other OCT parameters were not significantly associated with surgery or progression.

Conclusions

Idiopathic ERMs generally remain stable across stages over a long-term period. BCVA and CST changes are key predictors of disease progression and surgery.

Introduction

The epiretinal membrane (ERM) is avascular, semitranslucent, fibrocellular proliferation on the inner retinal surface. ERM is classified as idiopathic or secondary to trauma, surgery, or other retinal pathologies. The global ERM incidence is 9.1% [1], with variation among ethnicities: Chinese (39%), Hispanic (29.3%), Caucasian (27.5%), and Black (26.2%) [2].

ERM may be asymptomatic or cause visual disturbances such as blurred vision or metamorphopsia. The Blue Mountains Eye Study [3] reported a 5.3% incidence in individuals without ERM, with progression,

regression, and stability rates of 28.6%, 25.7%, and 38.8%, respectively.

Optical coherence tomography (OCT) plays a vital role in the diagnosis, staging and monitoring of ERMs. OCT findings: Central macular thickness, membrane configuration, ellipsoid zone (EZ) disruption, and macular choroidal thickness can predict visual prognosis [4–8].

This study investigated ERM progression, analyzed OCT findings, and identified factors influencing visual outcomes. This research provides valuable insights into the management and treatment of patients with ERM, contributing to improved care strategies in the future.

Methods

This retrospective cohort study reviewed the medical records of ERM patients at Vajira Hospital from 2017 to 2022, with approval from the Institutional Review Board of the Faculty of Medicine at Vajira Hospital and adherence to the Declaration of Helsinki.

Patient selection

The inclusion criteria were idiopathic ERM diagnosis, OCT performed, and ≥ 1 year of follow-up. The exclusion criteria were secondary ERMs, underlying retinal conditions affecting vision, prior retinal surgery, or incomplete medical records.

Data collection

The collected data included demographic information (gender, age, and laterality), best-corrected visual acuity (BCVA) measured in logMAR, lens status at baseline and follow-up duration. The follow-up period ended at surgery or at the last OCT.

OCT analysis

OCT images were obtained at baseline and at the last visit via spectral-domain OCT (Heidelberg Engineering, Heidelberg, Germany) with a raster scan protocol. Central subfield thickness (CST) was measured within the 1 mm foveal zone via automated software analysis.

The ERM appeared as a hyperreflective layer over the internal limiting membrane (ILM) with possible retinal wrinkling. ERMs may be followed by other pathologies, including foveoschisis, lamellar macular hole (LMH), or macular pseudohole (MPH).

OCT definitions

Foveoschisis: separation (“schisis”) between foveal retinal layers, typically the outer nuclear layer (ONL) and outer plexiform layer (OPL), at the level of Henle’s fiber layer [9].

LMH: irregular foveal contour, defect in the inner fovea (may not have actual loss of tissue), intraretinal schisis (typically between the OPL and ONL), and intact photoreceptors according to the International Vitreomacular Traction Study group [10].

MPH: invaginated foveal edges, concomitant central opening with steep macular contour to central fovea with near-normal central foveal thickness, absence of retinal tissue [10].

ERM stage was classified into 4 stages. Stage 1: ERM with the presence of a foveal pit. Stage 2: ERM with the loss of foveal depression. Stage 3: ERM with continuous ectopic inner foveal layers. Stage 4: ERM with continuous ectopic inner foveal layers with retinal layer disruption or disorganized retinal inner layers (DRILs) [11]. Stage classification was applied only to eyes with isolated idiopathic ERM.

EZ disruption: disruption of the inner segment/outer segment (IS/OS) zone.

Cotton ball sign: a round, hyperreflective lesion between the IS/OS junction and the cone outer segment tip lines at the foveal center [12].

Intraretinal (IR) cyst: a round, hyporeflective cystic-like lesion with well-defined boundaries within the retinal layers [13].

Disorganization of the retinal inner layers (DRILs): unidentifiable boundaries between the inner plexiform layer (IPL), inner nuclear layer (INL), and OPL [14]. According to the DREAM study [15], 0 indicates no DRIL, 1–3 indicates mild DRIL, and 4 indicates severe DRIL.

Outcome Measures

Outcome Measures
Patients were classified into surgical or observation groups. Subgroups (regression, stable, progression) were defined by a ≥ 10% increase in CST or worsening of the ERM stage as progression. Regression was defined as a decrease in CST ≤ 10% or an improvement in the ERM stage. Eyes that did not meet criteria for progression or regression were classified as stable.

The primary outcome was parameter changes that predict progression or need surgery on the basis of OCT. The secondary outcome was the BCVA change between groups.

Statistical analysis

SPSS version 29.0 (IBM Corp., Armonk, NY, USA) was used. Continuous data are presented as the means ± standard deviations (SDs), whereas categorical data are reported as frequencies (percentages). Comparisons of continuous variables were performed via paired t-tests for parametric data and

Wilcoxon signed-rank tests for nonparametric data. Categorical variables were analyzed via the chi-square test. Univariate and multivariate logistic regression analyses were conducted to evaluate the associations between OCT parameters and disease progression or the need for surgery. A P-value of < 0.05 was considered to indicate statistical significance.

Results

Among the 192 eyes (150 patients), the mean age was 69.5 ± 8.0 years. A total of 131 eyes (68.2%) were female. The mean baseline BCVA was 0.35 ± 0.2 logMAR. There were 161 eyes with isolated idiopathic ERMs (83.9%), 10 eyes of ERMs with foveoschisis (5.2%), 16 of ERMs with LMH (8.3%), and 5 of ERMs with MPH (2.6%). For idiopathic ERMs, 74 eyes (38.5%) were in stage 1, 46 eyes (24.0%) were in stage 2, 33 eyes (17.2%) were in stage 3, and 8 eyes (4.2%) were in stage 4. The mean follow-up period was 3.7 ± 1.9 years. A total of 162 eyes were observed, while 30 eyes underwent surgery. The baseline characteristics are shown in Table 1.

Table 1
Baseline characteristics of patients with idiopathic epiretinal membrane

Characteristics	Result
No. eyes/patients	192/150
Age (years)	69.45 ± 8.03
Gender	
Male	61 (31.8)
Female	131 (68.2)
Laterality	
Right eye	104 (54.2)
Left eye	88 (45.8)
Lens status	
Phakic	125 (65.1)
Pseudophakic	67 (34.9)
OCT finding	
EZ disruption	
No	183 (95.3)
Yes	9 (4.7)
Cotton ball sign	
No	176 (91.7)
Yes	16 (8.3)
IR cysts	
No	165 (85.9)
Yes	27 (14.1)
CST (μm)	355.53 ± 69.38
Types of ERM	
Isolated ERM	161 (83.9)
Stage 1	74 (38.5)

ERM = epiretinal membrane; EZ = ellipsoid zone; IR cysts = intraretinal cysts; LMH = lamellar macular hole; MPH = macular pseudohole

Characteristics	Result
Stage 2	46 (24)
Stage 3	33 (17.2)
Stage 4	8 (4.2)
ERM with foveoschisis	10 (5.2)
ERM with LMH	16 (8.3)
ERM with MPH	5 (2.6)
Treatment	
Observe	162 (84.4)
Surgery	30 (15.6)
Data are presented as the mean ± SD for continuous measures and n (%) for categorical measures.	
ERM = epiretinal membrane; EZ = ellipsoid zone; IR cysts = intraretinal cysts; LMH = lamellar macular hole; MPH = macular pseudohole	

The logMAR BCVA for each type of ERM at baseline and at the last visit is shown in Table 2. The baseline logMAR BCVA in the isolated ERMs was 0.35 ± 0.20 and decreased significantly to 0.41 ± 0.19 at the last visit ($P < 0.001$). BCVA of stage 1 ERMs significantly changed from 0.30 ± 0.18 at baseline to 0.38 ± 0.19 at the last visit ($P < 0.001$). For ERMs with LMH, the BCVA worsened from 0.36 ± 0.23 at baseline to 0.48 ± 0.29 at the final visit, reaching statistical significance. However, no statistically significant differences in BCVA were observed for isolated ERMs at other stages, ERMs with foveoschisis, or ERMs with MPH.

Table 2 BCVA logMAR during follow-up period			
	BCVA logMAR		
Types of ERM	Baseline	Last visit	P-value
Isolated ERM†	0.35 ± 0.20	0.41 ± 0.19	< 0.001*
Stage 1†	0.30 ± 0.18	0.38 ± 0.19	< 0.001*
Stage 2‡	0.40 ± 0.19	0.43 ± 0.21	0.245
Stage 3†	0.38 ± 0.19	0.41 ± 0.16	0.383
Stage 4‡	0.39 ± 0.24	0.45 ± 0.21	0.551
ERM with foveoschisis†	0.37 ± 0.23	0.37 ± 0.23	0.943
ERM with LMH‡	0.36 ± 0.23	0.48 ± 0.29	0.014*
ERM with MPH†	0.26 ± 0.09	0.38 ± 0.04	0.063
Data are presented as the mean ± SD.			
* Statistically significant			
† Data were analyzed with Wilcoxon signed-rank test.			
‡ Data were analyzed with paired t-test.			
ERM = epiretinal membrane; LMH = lamellar macular hole; MPH = macular pseudohole			

In our series, 162 eyes (84.4%) were observed and 30 eyes (15.6%) underwent surgery. No significant differences in surgery rates were found across ERM variants (P = 0.432) or stages (P = 0.093), although the surgery rate was highest in eyes with MPHs (40.0%) and stage 4 ERMs (37.5%) (Table 3). Isolated ERMs were observed in 14 eyes (8.7%) with regression, 99 eyes (61.5%) with stable ERMs, and 48 (29.8%) with progression. ERM progression and surgical intervention are shown in Tables 3 and 4. Regarding ERM variants, morphological changes were observed in 30.0% of eyes with foveoschisis, 18.8% with LMH, and 20.0% with MPH.

Table 3
Management of idiopathic ERM categorized by type

Types of ERM	**Observe (n = 162)**	**Surgery (n = 30)**
Isolated ERM	136 (84.5)	25 (15.5)
Stage 1	67 (90.5)	7 (9.5)
Stage 2	38 (82.6)	8 (17.4)
Stage 3	26 (78.8)	7 (21.2)
Stage 4	5 (62.5)	3 (37.5)
ERM with foveoschisis	9 (90)	1 (10)
ERM with LMH	14 (87.5)	2 (12.5)
ERM with MPH	3 (60)	2 (40)
Data are presented as n (%).		
Data were analyzed with Chi-square.		
ERM = epiretinal membrane; LMH = lamellar macular hole; MPH = macular pseudohole		

Table 4 Progression of idiopathic ERM categorized by stage

Isolated ERM stage	Regression	Stable	Progression
	n = 14 (8.7)	n = 99 (61.5)	n = 48 (29.8)
Stage 1	5 (6.8)	44 (59.5)	25 (33.8)
Stage 2	5 (10.9)	23 (50)	18 (39.1)
Stage 3	2 (6.1)	26 (78.8)	5 (15.2)
Stage 4	2 (25)	6 (75)	0 (0)
Data are presented as n (%).			
Data were analyzed with Chi-square.			
ERM = epiretinal membrane			

The changes in BCVA were 0.04 ± 0.17 in the observation group and 0.19 ± 0.22 in the surgery group. A statistically significant association was observed between an increased risk of surgery and a odds ratio (OR) of 24.87 (95% CI: 3.585–172.563, P = 0.001). An increase in BCVA was associated with disease progression, with a odds ratio (OR) of 1.02 (95% CI: 0.998–1.011, P = 0.191), but this association did not reach statistical significance. The changes in the CST were 31.40 ± 60.20 μm in the surgery group and 8.83 ± 39.26 μm in the observation group, which did not reach statistical significance (95% CI: 0.998–1.011, P = 0.191). However, the changes in the CST between the regression/stable and progression

groups were − 1.94 ± 23.32 μm and 53.60 ± 49.98 μm, respectively, which reached statistical significance. Other OCT parameters, including EZ disruption, the cotton ball sign, and the presence of an IR cyst, did not significantly affect surgical outcomes or disease progression (Tables 5, 6).

Table 5 OCT finding and management over follow-up period

Finding	Observe	Surgery	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
EZ disruption						
Yes	7 (77.8)	2 (22.2)	1.45 (0.35, 6.1)	0.61	0.97 (0.22, 4.37)	0.972
No	155 (84.7)	28 (15.3)	0.69 (0.16, 2.89)		1.03 (0.23, 4.62)	
Cotton ball sign						
Yes	12 (75)	4 (25)	1.69 (0.59, 4.85)	0.327	1.85 (0.62, 5.45)	0.268
No	150 (85.2)	26 (14.8)	0.59 (0.21, 1.69)		0.54 (0.18, 1.60)	
IR cysts						
Yes	23 (85.2)	4 (14.8)	0.94 (0.33, 2.69)	0.909	1.42 (0.48, 4.18)	0.527
No	139 (84.2)	26 (15.8)	1.06 (0.37, 3.05)		0.71 (0.24, 2.08)	
CST change (μm)	8.83 ± 39.26	31.40 ± 60.20	1.01 (1.00, 1.01)	0.016	1.00 (1.00, 1.01)	0.191
BCVA logMAR change	0.04 ± 0.17	0.19 ± 0.22	29.78 (5.02, 176.89)	< 0.001	24.87 (3.59, 172.56)	0.001*
Adjusted for lens status and other covariances.						
* Statistically significant						
Data are presented as the mean ± SD for continuous measures and n (%) for categorical measures.						
EZ = ellipsoid zone; IR cysts = intraretinal cysts; CST = Central subfield thickness; BCVA = Best corrected visual acuity						

Table 6 OCT finding and disease progression over follow-up period

Finding	No progression	Progression	Crude OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
EZ disruption						
Yes	2 (33.3)	4 (66.7)	2.35 (0.84, 6.54)	0.102	2.68 (0.90, 7.99)	0.077
No	111 (71.6)	44 (28.4)	0.43 (0.15, 1.19)		0.37 (0.13, 1.11)	
Cotton ball sign						
Yes	9 (69.2)	4 (30.8)	1.04 (0.37, 2.88)	0.948	1.19 (0.40, 3.54)	0.754
No	104 (70.3)	44 (29.7)	1.00 (0.35, 2.69)		0.84 (0.28, 2.50)	
IR cysts						
Yes	8 (57.1)	6 (42.9)	1.50 (0.64, 3.53)	0.353	1.64 (0.69, 3.94)	0.265
No	105 (71.4)	42 (28.6)	0.67 (0.28, 1.57)		0.61 (0.25, 1.46)	
CST change (μm)	-1.94 ± 23.32	53.6 ± 49.98	1.01 (1.01, 1.02)	< 0.001	1.02 (1.01, 1.02)	< 0.001*
BCVA logMAR change	0.05 ± 0.19	0.08 ± 0.20	1.54 (0.35, 6.68)	0.566	0.35 (0.08, 1.64)	0.184
Adjusted for lens status and other covariances.						
* Statistically significant						
Data are presented as the mean ± SD for continuous measures and n (%) for categorical measures.						
EZ = ellipsoid zone; IR cysts = intraretinal cysts; CST = Central subfield thickness; BCVA = Best corrected visual acuity						

Discussion

This study demonstrated that most ERMs were stable, with 29.8% progressing over the follow-up period. CST increase was the only significant OCT predictor. Other OCT parameters were not predictive.

Among all patients with ERMs, 15.6% underwent surgery and 15.5% of those with isolated ERMs required surgical management. The likelihood of surgical intervention correlated with disease severity, as 37.5% of stage 4 ERMs required surgery, whereas only 9.5% of stage 1 cases did. BCVA deterioration was most significant in isolated ERMs, especially in stage 1, and in ERMs with LMH, whereas other ERM subtypes represented only a slight decline in visual acuity. Additionally, an increased risk of surgery was significantly associated with BCVA changes.

According to the Blue Mountains Eye Study [3], ERM progression was observed in 28.6% of cases and most cases remained stable. Similarly, our study found an ERM progression rate of 29.8%. Our study revealed that up to 37.5% of patients with stage 4 ERM underwent surgery, indicating that poor vision and more advanced disease stages are factors in determining the need for surgical intervention.

We found that ERMs combined with foveoschisis and MPH resulted in a slight decrease in VA over time, but the difference did not reach statistical significance. However, ERMs with LMH had a significant decline in VA at the last follow-up visit. Additionally, most patients with ERMs combined with foveoschisis, LMHs, and MPHs were observed. A previous study showed that LMH and MPH are often stable over long periods, with LMH typically resulting in greater visual function impairment than MPH [16–18].

A previous study demonstrated that increased CST, the presence of DRIL, and decreased VA are associated with progression to surgery [5, 8, 19]. A thicker CST or the presence of DRIL indicates a more advanced stages of ERMs, which correlates with an increased need for surgical treatment.

According to Luu et al. [19], EZ disruption is a predictive factor for surgical intervention. However, we found that the presence of EZ disruption was not significantly associated with disease progression or the need for surgery, which may be due to the limited number of patients with EZ disruption in the study, potentially affecting the statistical significance.

Consistent with previous findings, our study demonstrated that an increase in the CST change was significantly associated with disease progression. The odds ratio of surgery in our study was also significantly greater in patients with worsening BCVA.

We highlight the crucial role of OCT in monitoring ERMs. Changes in BCVA and CST can help guide patient prognosis, the need for surgical intervention, and overall management decisions.

Our study has several limitations. First, the study was retrospective in nature. Second, various physicians participated while all were retinal specialists, and their individual expertise may have influenced the decision to perform surgery. Finally, the small sample size, particularly in terms of subtype, limits the statistical power to detect differences. A prospective study with a larger sample size is needed to better understand visual prognosis, surgery rate, and predictive factors from OCT, which could help identify factors associated with ERM progression, enabling closer monitoring and providing better disease outcome predictions.

Conclusion

Idiopathic ERMs are generally stable over time; however, changes in CST and BCVA are key indicators of disease progression and the need for surgical intervention. OCT monitoring remains critical for ERM management.

Abbreviations

ERM	Epiretinal membrane
OCT	Optical coherence tomography
BCVA	Best-corrected visual acuity
EZ	Ellipsoid zone
IR cysts	Intraretinal cysts
CST	Central subfield thickness
LMH	Lamellar macular hole
MPH	Macular pseudohole
DRILs	Disorganized retinal inner layers
IS/OS	Inner segment/outer segment
ILM	Internal limiting membrane
ONL	Outer nuclear layer
OPL	Outer plexiform layer
IPL	Inner plexiform layer
INL	Inner nuclear layer

Declarations

Ethics approval and consent to participate This study was approved by the Institutional Review Board of the Faculty of Medicine Vajira Hospital, Navamindradhiraj University (COA No. 124/2566). Due to the retrospective nature of the study, the requirement for informed consent was waived by the Institutional Review Board of the Faculty of Medicine Vajira Hospital. All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki).

Consent for publication Not applicable.

Availability of data and materials The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests The authors declare that they have no competing interests.

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Authors' contributions YW: Data collection, analysis and interpretation of data, and drafting of the manuscript. IP: Study design, supervision, data interpretation, and critically revised of the manuscript. KH, YC, PS: Data interpretation and clinical review. All authors read and approved the final manuscript.

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