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Postoperative Epiretinal Membrane After Rhegmatogenous Retinal Detachment Repair: Temporal Characteristics and Early OCT Predictors

Mehmet Onen

mehmetonen@hotmail.com

Ankara Bilkent City Hospital

Ece Ozdemir Zeydanli

Ankara Bilkent City Hospital

Muzaffer Sahin

Ankara Bilkent City Hospital

Huseyin Ozcan

Ankara Bilkent City Hospital

Ozgul Tanıs

Ankara Bilkent City Hospital

Elif Sahin Ozturk

Ankara Bilkent City Hospital

Feyza Dicle Isik

Mus Bulanik State Hospital

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Original Article
Title Page

Postoperative Epiretinal Membrane After Rhegmatogenous Retinal Detachment Repair: Temporal Characteristics and Early OCT Predictors

Running Title

Timing and OCT Predictors of Post-RRD ERM

Authors

1. Mehmet Onen, MD[1]
   ORCID: 0000-0001-8797-9634
   E mail: mehmetonen@hotmail.com
2. Ece Ozdemir Zeydanli , MD[1]
   ORCID: 0000-0001-6479-2228
   E Mail: ece.ozdmir@gmail.com
3. Muzaffer Sahin, MD[1]
   ORCID: 0000-0003-2160-2126
   E mail: drsahinm89@gmail.com
4. Huseyin Ozcan MD[1]
   ORCID:0009-0008-4260-0211
   Email:hsyn.zcn.98@gmail.com
5. Ozgul Tanıs MD[1]
   ORCID: 0000-0002-3617-0250
   Email: ozgul008@gmail.com
6. Elif Sahin Ozturk MD[1]
   ORCID: 0009-0004-8183-9672
   Email: elif108885@gmail.com
7. Feyza Dicle Isik MD[2]
   ORCID:0000-0003-4992-5103
   Email:feyzadicleisik@gmail.com

Affiliations

[1] Department of Ophthalmology, Ankara Bilkent City Hospital, Ankara , Turkey

[2] Department of Ophthalmology, Mus Bulanik State Hospital, Mus, Turkey

Corresponding Author

Mehmet ONEN, MD

Department of Ophthalmology , Ankara Bilkent City Hospital

Universiteler Caddesi 1604 Cad. N o:9 Cankaya Ankara, 06800 , Turkey

Mobil Telephone: +90-5326529468

E-mail: mehmetonen@hotmail.com

ORCID: **0000-0001-8797-9634**

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Ethics Approval

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Ethics Committee of **Ankara Bilkent City Hospital** (Approval No: **1/1040/2025**, Date: **26 February 2025**).

Informed Consent:The requirement for informed consent was waived because of the retrospective nature of the study. Patient confidentiality was maintained throughout the study.

Clinical Trial Registration: Not applicable.

Abstract

Purpose

To characterize the temporal pattern of epiretinal membrane (ERM) development following pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD) and to determine whether early postoperative optical coherence tomography (OCT) findings predict subsequent ERM formation.

Design

Retrospective, longitudinal cohort study.

Participants

Two hundred thirty consecutive eyes undergoing primary PPV, with or without scleral buckling, for RRD.

Methods

This retrospective longitudinal cohort study included 230 consecutive eyes undergoing primary PPV, with or without scleral buckling, for RRD. Patients underwent standardized OCT examinations at 1, 3, 6, and ≥12 months postoperatively. Time to first OCT-confirmed ERM was determined, and demographic, ocular, and surgical characteristics were compared between eyes with and without ERM. In eyes free of ERM at the 1-month visit with complete OCT data (n=133), multivariable logistic regression evaluated the predictive value of early OCT biomarkers, including intraretinal cysts (IRC), disorganization of the retinal inner layers, ellipsoid zone disruption, and subfoveal choroidal thickness, after adjustment for relevant clinical variables.

Results

ERM developed in 46 of 230 eyes (20.0%), and 23 eyes (50.0%) subsequently underwent membrane peeling. Median time to ERM detection was 5.5 months (IQR, 3.0–9.8), with 41.3% of cases detected within 3 months and 60.9% within 6 months; however, 21.7% were first identified beyond 12 months, with the latest case occurring 38 months after surgery. Conventional demographic and surgical characteristics showed limited predictive value. In contrast, IRC on the 1-month postoperative OCT was independently associated with subsequent ERM development (OR, 3.33; 95% CI, 1.25–8.82; *P*=0.016), whereas other OCT biomarkers were not independently predictive.

Conclusions

Postoperative ERM following PPV for RRD demonstrates a prolonged temporal profile, with most cases developing within 6 months but a clinically meaningful proportion arising beyond the first postoperative year. Early postoperative intraretinal cysts represent the strongest independent predictor of subsequent ERM formation, supporting the concept that postoperative ERM is a biologically heterogeneous process and highlighting the potential value of early OCT-based risk stratification and extended postoperative surveillance.

Keywords: *Rhegmatogenous retinal detachment; Epiretinal membrane; Optical coherence tomography; Intraretinal cysts; Vitrectomy; Predictive biomarkers.*

Abbreviations: ERM (epiretinal membrane)**; PPV** (pars plana vitrectomy); **RRD** (rhegmatogenous retinal detachment); **OCT**(optical coherence tomography; **IRC** (Intraretinal cysts).

Introduction

Rhegmatogenous retinal detachment (RRD) is a vision-threatening condition that requires timely surgical intervention to restore retinal anatomy and preserve visual function. Advances

in pars plana vitrectomy (PPV), scleral buckling (SB), and combined surgical techniques have increased primary retinal reattachment rates to more than 90% in contemporary series.[1] Nevertheless, successful anatomical repair does not always translate into optimal visual recovery, and postoperative abnormalities of the vitreoretinal interface remain an important cause of persistent visual impairment despite retinal reattachment.[2-4]

Among these postoperative changes, epiretinal membrane (ERM) formation is one of the most frequent structural complications following RRD repair. Postoperative ERM is thought to arise from proliferation and migration of retinal pigment epithelial cells, Müller cells, astrocytes, and other glial elements onto the retinal surface, followed by extracellular matrix deposition and myofibroblastic contraction.[5,6] Clinically significant ERM may result in metamorphopsia, reduced visual acuity, and secondary membrane peeling surgery, thereby limiting functional outcomes even after anatomically successful retinal detachment repair.

Previous studies have reported highly variable postoperative ERM incidences, ranging from approximately 3% to over 50%, reflecting differences in patient selection, surgical techniques, duration of follow-up, imaging modality, and ERM diagnostic criteria.[2,3,7,8] Several clinical and surgical factors including giant retinal tears, extensive retinal detachment, vitreous hemorrhage, silicone oil tamponade, drainage retinotomy, extensive laser photocoagulation, proliferative vitreoretinopathy, and postoperative retinal redetachment have been associated with increased ERM risk, whereas meticulous removal of the posterior vitreous cortex and intraoperative triamcinolone-assisted visualization have been suggested to reduce membrane formation.[2,7,8] Despite these observations, the predictive value of conventional clinical and surgical characteristics remains inconsistent across studies, limiting their usefulness for individualized postoperative risk assessment.

More importantly, most published studies have evaluated postoperative ERM as a dichotomous endpoint at a predefined follow-up visit rather than as a dynamic postoperative process.[9,10] Consequently, relatively little is known about the temporal evolution of ERM formation, including when membranes first become detectable after surgery, whether late-onset ERM represents a clinically relevant phenomenon, and whether early postoperative retinal alterations visible on optical coherence tomography (OCT) precede clinically apparent membrane development.(11) These questions have become increasingly relevant with the widespread use of high-resolution spectral-domain OCT, which enables detection of subtle retinal structural changes long before clinically significant ERM develops.

A better understanding of both the timing and the earliest imaging features of postoperative ERM could improve postoperative surveillance strategies, facilitate earlier identification of eyes at increased risk, and provide insight into the biological mechanisms underlying membrane formation after retinal detachment repair.[9-11]

Therefore, the present study aimed to characterize the temporal pattern of ERM development following primary PPV for RRD using a standardized longitudinal OCT follow-up protocol and to determine whether early postoperative OCT biomarkers, together with conventional demographic, clinical, and surgical characteristics, predict subsequent ERM formation.

Materials and Methods

Study Design and Participants

This retrospective longitudinal cohort study included consecutive patients who underwent primary pars plana vitrectomy (PPV), with or without scleral buckling, for rhegmatogenous retinal detachment (RRD) at a tertiary vitreoretinal center. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board. Because of

the retrospective design, the requirement for informed consent was waived. Eligible eyes had postoperative spectral-domain optical coherence tomography (SD-OCT) follow-up and sufficient clinical records for analysis. Eyes with pre-existing epiretinal membrane (ERM), previous vitreoretinal surgery, tractional or exudative retinal detachment, advanced ocular comorbidity affecting the macula, or inadequate OCT image quality were excluded. Follow-up duration varied among patients according to routine clinical practice.

Surgical Technique

All procedures were performed by a single experienced vitreoretinal surgeon using a standardized surgical protocol. Core vitrectomy was followed by meticulous confirmation of complete posterior vitreous detachment with triamcinolone acetonide when required. Residual premacular vitreous cortex was carefully removed. Additional procedures, including scleral buckling, retinotomy, endolaser photocoagulation, cryotherapy, tamponade selection, and internal limiting membrane peeling, were performed according to intraoperative findings and surgeon preference.

Clinical and OCT Assessment

Baseline demographic, ocular, and surgical variables were extracted from the medical records. Best-corrected visual acuity (BCVA), lens status, macular status, proliferative vitreoretinopathy, retinal break characteristics, tamponade type, and postoperative outcomes were recorded. SD-OCT examinations were routinely obtained at approximately 1, 3, 6, and ≥12 months postoperatively. OCT images were independently reviewed by two retinal specialists masked to clinical outcomes, with disagreements resolved by consensus. Evaluated biomarkers included intraretinal cysts (IRC), disorganization of the retinal inner layers (DRIL), ellipsoid zone disruption, external limiting membrane status, subfoveal choroidal thickness, and

postoperative ERM. ERM was defined as a hyperreflective fibrocellular membrane on the inner retinal surface associated with distortion of the retinal contour.

Outcome Measures

The primary outcome was development of OCT-confirmed postoperative ERM. Secondary outcomes included the timing of ERM development and the requirement for subsequent membrane peeling surgery. Time to ERM was defined as the interval between retinal detachment repair and the first OCT examination demonstrating ERM.

Statistical Analysis

Data distribution was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean ± standard deviation or median (interquartile range), as appropriate, and categorical variables as frequencies and percentages. Between-group comparisons were performed using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Univariable logistic regression was performed to identify variables associated with postoperative ERM. Variables with $P<0.10$ in univariable analysis together with clinically relevant covariates were entered into a multivariable logistic regression model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Analyses were performed using complete-case data. A two-sided P value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics (version 22; IBM Corp., Armonk, NY, USA).

Results

Study Cohort

A total of 230 eyes undergoing primary pars plana vitrectomy for rhegmatogenous retinal detachment were included. Postoperative ERM developed in 46 eyes (20.0%), whereas 184

eyes remained free of ERM during follow-up. Membrane peeling was subsequently performed in 23 eyes (50.0% of ERM cases). Baseline demographic, ocular, and surgical characteristics according to ERM status are summarized in Table 1.

Incidence and Temporal Pattern of ERM Development

The median interval from surgery to OCT-confirmed ERM detection was 5.5 months (interquartile range, 3.0–9.8 months). Nineteen eyes (41.3%) developed ERM within 3 months, 28 (60.9%) within 6 months, and 36 (78.3%) within 12 months. Ten eyes (21.7%) developed ERM after 12 months, with the latest diagnosis occurring 38 months after surgery. These findings indicate that postoperative ERM continued to occur beyond the first postoperative year. The temporal distribution of ERM development is summarized in Table 2 and illustrated in Figure 1.

Severity of Postoperative ERM

The severity of postoperative ERM at initial diagnosis was graded according to the Govetto classification. Most membranes were classified as early-stage disease, whereas advanced stages were less frequent. The distribution of ERM severity is shown in Figure 2.

Early Postoperative OCT Biomarkers

Early postoperative OCT biomarkers were compared between eyes that subsequently developed ERM and those that did not. Intraretinal cysts at the 1-month visit were significantly more frequent among eyes that later developed ERM, whereas differences in DRIL, ellipsoid zone disruption, and subfoveal choroidal thickness were not independently associated after adjustment. Detailed biomarker comparisons are presented in Table 3. The temporal relationship between intraretinal cysts and subsequent ERM development is illustrated in Figure 3.

Multivariable Logistic Regression Analysis

Variables meeting prespecified selection criteria were entered into the multivariable logistic regression model. Intraretinal cysts detected at the 1-month postoperative visit remained the only independent predictor of subsequent ERM development (OR 3.33, 95% CI 1.25–8.82; P=0.016). Macula-off status, proliferative vitreoretinopathy, and the total number of vitrectomy procedures were not independently associated with ERM development. Full model results are presented in Table 4 and Figure 4.

Discussion

This study provides a comprehensive longitudinal assessment of postoperative epiretinal membrane (ERM) development following pars plana vitrectomy (PPV) for rhegmatogenous retinal detachment (RRD). Unlike previous reports that primarily evaluated postoperative ERM prevalence or individual risk factors, our study was specifically designed to characterize both the temporal evolution of ERM formation and the predictive value of early postoperative OCT findings using a standardized imaging protocol. The use of a large single-surgeon cohort minimized variability in surgical technique, while serial OCT examinations enabled accurate determination of ERM onset rather than simple cross-sectional detection. The principal message emerging from our findings is that postoperative ERM appears to represent a prolonged and biologically heterogeneous process extending beyond the early postoperative period, and that an intraretinal cyst (IRC) identified one month after surgery may represent the earliest clinically detectable imaging marker of subsequent membrane formation.

The overall incidence of postoperative ERM in our cohort was 20%, which is lower than that reported in several previous series.(2,6-8) Although differences in study design, patient characteristics, and follow-up duration undoubtedly contribute to this variability, we believe that our surgical protocol also played an important role. Systematic triamcinolone-assisted

confirmation of complete posterior vitreous detachment and meticulous removal of residual premacular vitreous cortex, particularly in eyes with vitreoschisis, may have reduced the scaffold required for subsequent glial and fibrocellular proliferation.[12-14] This interpretation is biologically plausible given the recognized role of residual cortical vitreous in vitreoretinal interface pathology and may explain why our incidence remained comparatively low despite the limited use of prophylactic internal limiting membrane peeling.[15]

Beyond the overall incidence, perhaps the most clinically relevant finding was the temporal pattern of ERM development. As expected, most ERMs developed during the first six postoperative months, supporting the widely accepted concept that acute wound healing, retinal pigment epithelial cell dispersion, Müller cell activation, and postoperative inflammation drive early membrane formation after retinal detachment repair.[5,6] However, our prolonged follow-up demonstrated that more than one-fifth of ERMs first appeared after one postoperative year, with the latest case detected 38 months after surgery. This observation differs from previous studies with follow-up restricted to 12 months and suggests that the natural history of postoperative ERM extends well beyond the period traditionally considered clinically relevant.[9] Rather than representing a single pathological process, postoperative ERM may comprise at least two partially overlapping phenotypes: an early-onset form related predominantly to acute surgical wound healing and a late-onset form resulting from gradual vitreoretinal interface remodeling, persistent low-grade inflammation, delayed glial proliferation, or even superimposed age-related idiopathic ERM.[11] Although these mechanisms remain speculative, this conceptual framework better explains the prolonged right-tailed distribution observed in our cohort and has practical implications for postoperative surveillance. Restricting OCT follow-up to the first postoperative year may fail to identify a clinically meaningful subset of patients who develop ERM considerably later.

The identification of IRC on the one-month postoperative OCT as the only independent predictor of subsequent ERM represents the most important clinical finding of the present study. Notably, conventional demographic, ocular, and surgical variables added little predictive value once early OCT findings were considered. Moreover, the predictive effect of IRC was strongest during the earliest postoperative period and diminished at later examinations, suggesting that transient early retinal changes rather than persistent structural abnormalities may reflect the biological events initiating membrane formation. Although subfoveal choroidal thickness demonstrated a similar directional association, the evidence was considerably weaker and should be interpreted cautiously because of the limited number of events. Collectively, these observations support the hypothesis that postoperative inflammation and disruption of retinal homeostasis, rather than surgical complexity alone, are major determinants of subsequent ERM development.[16] Nevertheless, the modest explanatory power of our multivariable models indicates that IRC should currently be regarded as a promising imaging biomarker rather than a definitive predictive tool. Future prospective studies integrating OCT biomarkers with molecular indicators of intraocular inflammation may substantially improve postoperative risk stratification.

Our findings are supported by a recent systematic review and meta-analysis demonstrating that both intraretinal cysts and epiretinal membrane are associated with poorer visual outcomes following macula-off RRD repair.[17] Although that study evaluated visual prognosis rather than ERM development, the consistent association of IRC with both unfavorable visual recovery and subsequent ERM formation in our cohort suggests that IRC may represent an early imaging marker of persistent retinal injury and postoperative tissue remodeling. This concept is further supported by Shah et al., who demonstrated a strong association between postoperative cystoid macular edema (CME) and ERM after RRD repair, with ERM occurring significantly more frequently in eyes that developed CME than in those without CME.[18] Furthermore,

postoperative ERM remained an independent predictor of CME in multivariable analysis, highlighting the close biological interplay between these two postoperative complications. Together with our findings, these data suggest that intraretinal cystic changes likely reflect sustained retinal inflammation, Müller cell activation, and disruption of the blood–retinal barrier, creating a microenvironment that promotes fibrocellular proliferation and subsequent ERM formation.[19,20]

Several findings that were not statistically significant also merit consideration. We did not identify independent associations between postoperative ERM and several classical risk factors reported previously, including diabetes mellitus, proliferative vitreoretinopathy (PVR), macular status, giant retinal tears, or posterior retinotomy.[21-24] Importantly, however, the direction of these associations remained consistent with the existing literature, suggesting that limited statistical power rather than biological absence of effect may explain these negative findings. The lack of association between clinically evident PVR and postoperative ERM deserves particular attention. Because all visible PVR membranes and any suspicious premacular membranes were routinely identified using dual-dye staining and removed during the primary procedure, our postoperative outcome primarily reflects true de novo ERM formation after surgical clearance rather than persistence or progression of pre-existing proliferative tissue. Similarly, the absence of an association with posterior retinotomy may reflect the consistently atraumatic internal drainage technique employed throughout the study, minimizing retinal pigment epithelium dispersion and secondary proliferative stimulation.

Several limitations should be acknowledged when interpreting these findings. First, the retrospective design precludes causal inference and introduces the possibility of residual confounding. Second, approximately one-third of patients had less than 12 months of follow-up, which may have resulted in underestimation of late-onset ERM despite the longer

observation period compared with most previous reports. Third, although serial OCT review confirmed true new-onset ERM in the majority of affected eyes, exact onset timing remained uncertain in a small subset lacking early postoperative imaging. Finally, the relatively limited number of ERM events reduced statistical power for evaluating established clinical risk factors and constrained the complexity of multivariable modeling. Consequently, while the association between early postoperative IRC and subsequent ERM appears robust, it should be regarded as hypothesis-generating until validated prospectively in larger multicenter cohorts.

In conclusion, postoperative ERM following PPV for RRD should not be regarded as a uniformly early postoperative complication but rather as a prolonged and biologically heterogeneous process. Although most membranes develop within the first six postoperative months, a clinically important proportion arise well beyond one year after surgery. Early postoperative OCT, particularly the identification of intraretinal cysts, appears to provide valuable prognostic information beyond conventional clinical and surgical characteristics and may facilitate individualized postoperative surveillance. Confirmation of these findings in prospective studies incorporating longer follow-up and biological markers of postoperative inflammation will be essential before OCT-based risk stratification can be incorporated into routine clinical practice.

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of the local ethics committee (approval date: February 26, 2025; approval number: TABED 1/1040/2025). The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Consent for publication: Written informed consent for publication of clinical data and retinal images was obtained from the patients or their legal guardians.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Table 1. Baseline Demographic, Ocular, and Surgical Characteristics According to Postoperative ERM Status

Continuous variables are presented as mean ± SD; categorical variables are presented as No. (%). P values were calculated using the independent-samples t test for continuous variables and the χ^2 test or Fisher exact test for categorical variables. Statistically significant values (P < .05) are shown in bold.

[a] *The association between tamponade type and ERM was driven by a small subgroup (n = 5) receiving 5000-cSt silicone oil; after exclusion of this subgroup, the association was no longer significant (P = 0.762).*

Abbreviations: BCVA, best-corrected visual acuity; ERM, epiretinal membrane; ILM, internal limiting membrane; logMAR, logarithm of the minimum angle of resolution; PPV, pars plana vitrectomy; PVD, posterior vitreous detachment; PVR, proliferative vitreoretinopathy; RD, retinal detachment; SB, scleral buckling; SD, standard deviation.

Table 2. Temporal Distribution of OCT-Detected Epiretinal Membrane Development Following Primary Vitrectomy for Rhegmatogenous Retinal Detachment

Time to ERM detection was calculated from the date of surgery to the first postoperative OCT visit at which ERM was documented (n = 46 eyes with ERM).

Abbreviations: ERM, epiretinal membrane; OCT, optical coherence tomography.

Table 3. Association Between Early Postoperative OCT Biomarkers and Subsequent ERM Development

Values indicate the proportion (or mean ± SD for SFCT) of eyes that subsequently developed ERM, stratified by presence vs absence of the biomarker at each postoperative visit. P values were calculated using the χ^2 test or Fisher exact test for categorical comparisons and the independent-samples t test for SFCT. Statistically significant values ($P < .05$) are shown in bold.

Abbreviations: DRIL, disorganization of the retinal inner layers; ERM, epiretinal membrane; EZ/ISOS, ellipsoid zone/inner segment-outer segment junction; OCT, optical coherence tomography; SD, standard deviation; SFCT, subfoveal choroidal thickness.

Table 4. Multivariable Logistic Regression Analysis Identifying Independent Predictors of Postoperative ERM Development

Model based on 133 eyes without ERM at the 1-month visit with complete 1-month OCT data available; 28 subsequent ERM events. Model likelihood ratio $\chi^2 = 7.81$ (df = 4), $P = 0.09$;

Nagelkerke $R^2 = 0.089$; Cox-Snell $R^2 = 0.057$; area under the receiver operating characteristic curve = 0.661. Statistically significant values ($P < .05$) are shown in bold.

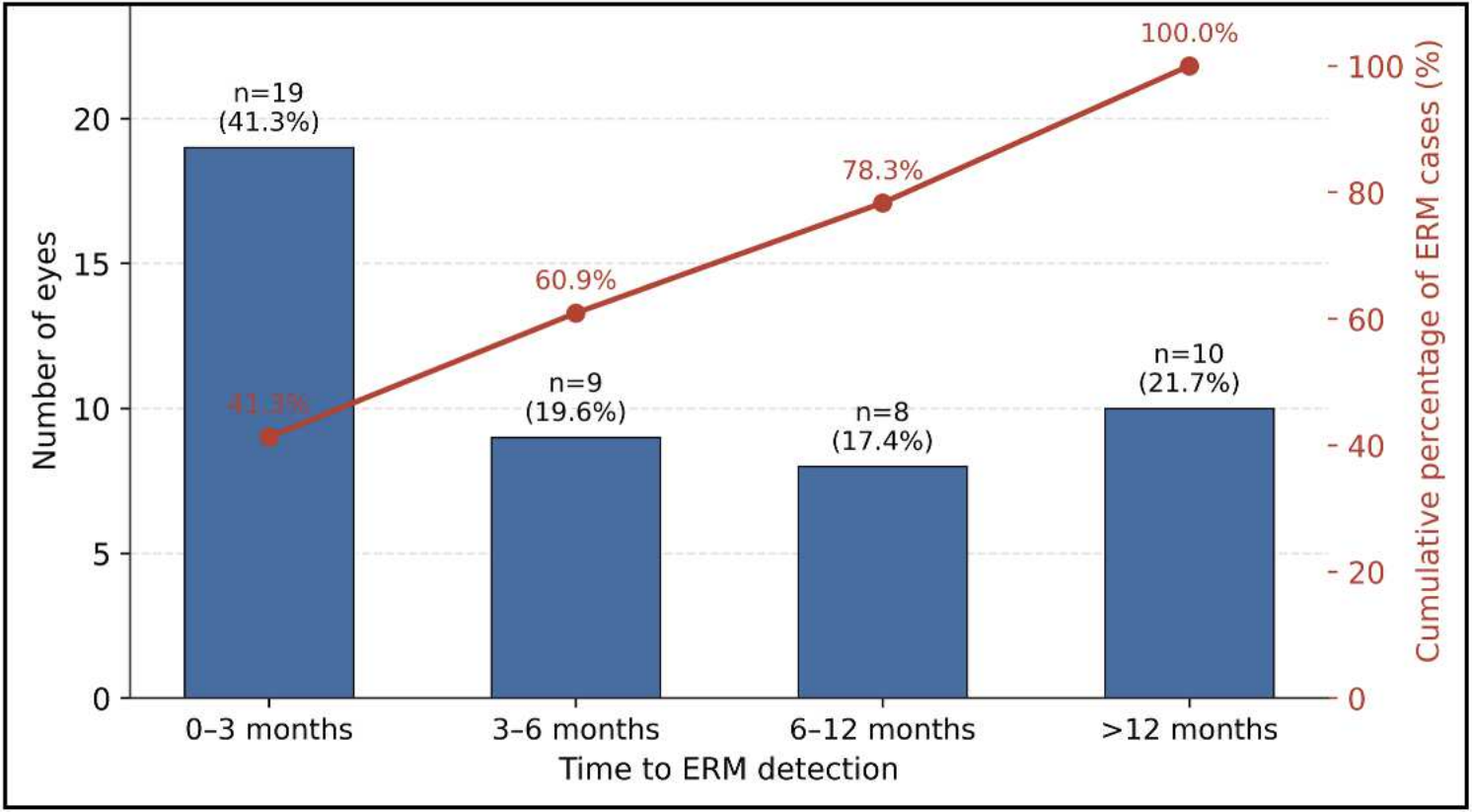
Abbreviations: CI, confidence interval; ERM, epiretinal membrane; OCT, optical coherence tomography; OR, odds ratio; PVR, proliferative vitreoretinopathy.

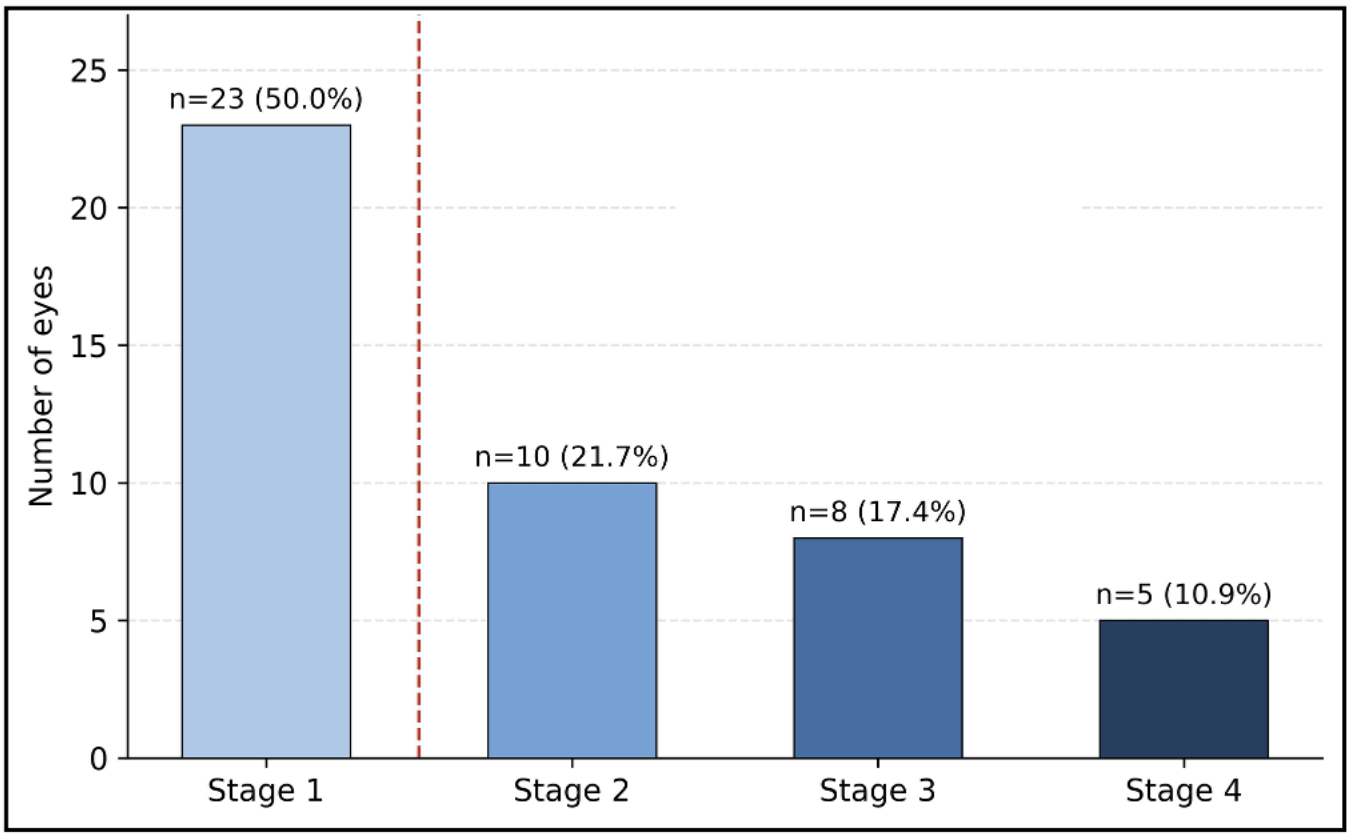
Figure 1. Time Course of Epiretinal Membrane Detection After Rhegmatogenous Retinal Detachment Repair

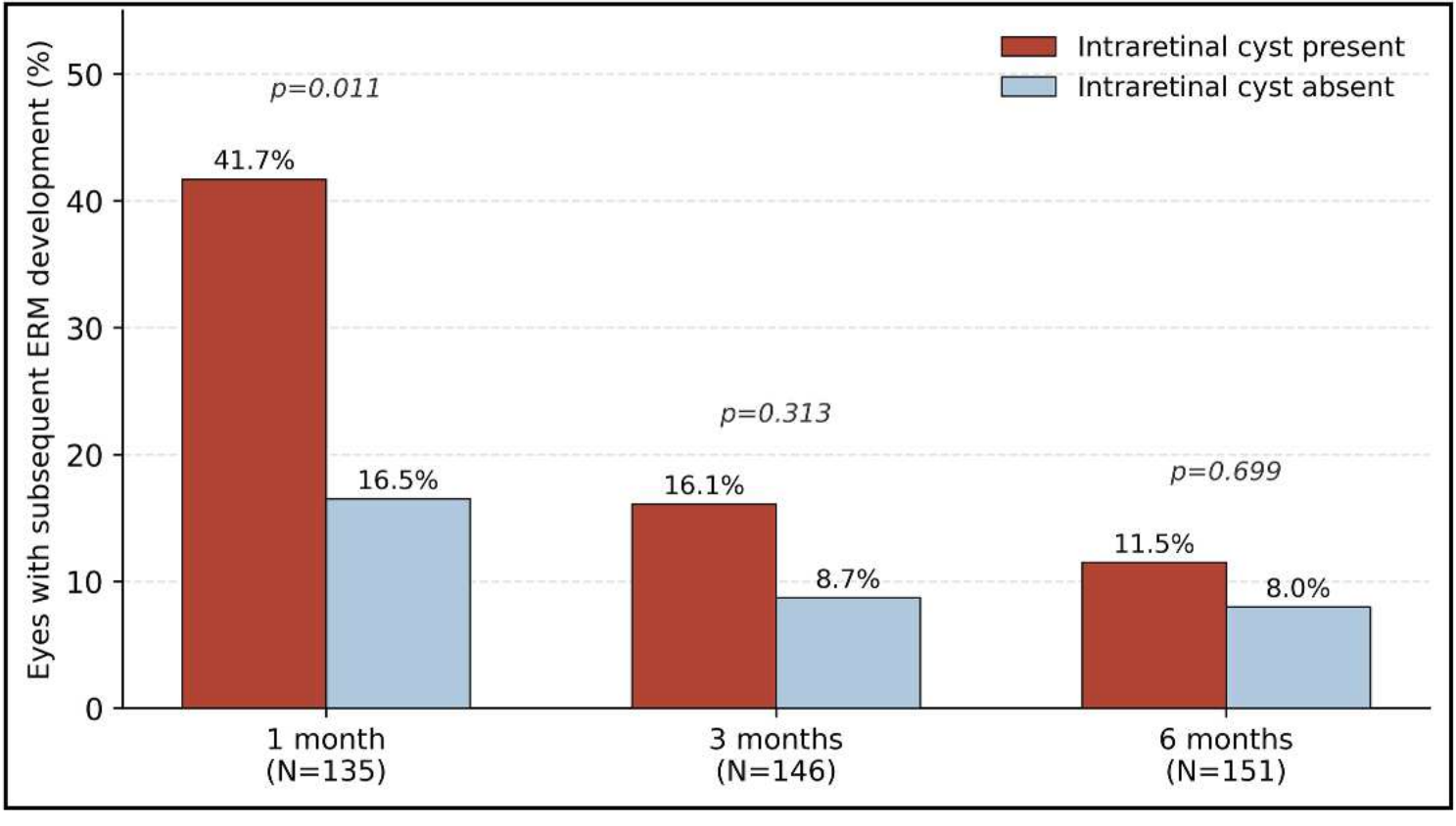
Figure 2. Distribution of Epiretinal Membrane Severity according to the Govetto Classification

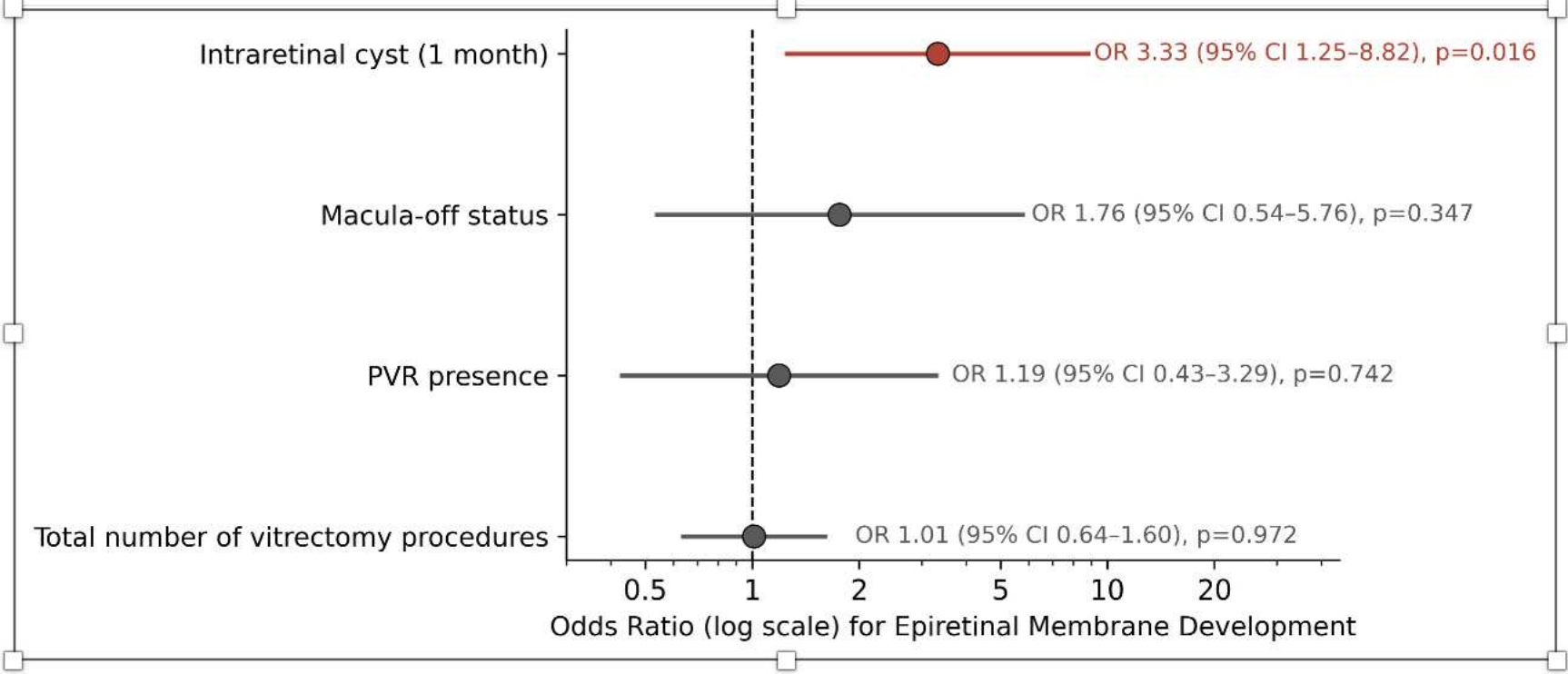
Figure 3. Association Between Intraretinal Cysts on Potoperative OCT and Subsequent Epiretinal Membrane Development

Figure 4. Multivariable Logistic Regression Model for Epiretinal Membrane Development


n=19
(41.3%)
n=9
(19.6%)
n=8
(17.4%)
n=10
(21.7%)
41.3%
60.9%
78.3%
100.0%
Number of eyes
Cumulative percentage of ERM cases (%)
0
5
10
15
20
0
20
40
60
80
100
0–3 months
3–6 months
6–12 months
>12 months
Time to ERM detection


Number of eyes
25
20
15
10
5
0
n=23 (50.0%)
n=10 (21.7%)
n=8 (17.4%)
n=5 (10.9%)
Stage 1
Stage 2
Stage 3
Stage 4


Intraretinal cyst present
Intraretinal cyst absent
Eyes with subsequent ERM development (%)
0
10
20
30
40
50
p=0.011
41.7%
16.5%
p=0.313
16.1%
8.7%
p=0.699
11.5%
8.0%
1 month
(N=135)
3 months
(N=146)
6 months
(N=151)


Intraretinal cyst (1 month)
OR 3.33 (95% CI 1.25–8.82), p=0.016
Macula-off status
OR 1.76 (95% CI 0.54–5.76), p=0.347
PVR presence
OR 1.19 (95% CI 0.43–3.29), p=0.742
Total number of vitrectomy procedures
OR 1.01 (95% CI 0.64–1.60), p=0.972
0.5
1
2
5
10
20
Odds Ratio (log scale) for Epiretinal Membrane Development

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.docx
- Table2.docx
- Table3.docx
- Table4.docx