Original Manuscript

ASRS American Society of Retina Specialists

Journal of VitreoRetinal Diseases
2025, Vol. 9(4) 438–444

DOI: 10.1177/24741264251337107
journals.sagepub.com/home/jvrd
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Timing of Epiretinal Membrane Surgery After Uncomplicated Retinal Detachment Repair

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Abstract

Purpose: To evaluate the features and outcomes of postoperative epiretinal membranes (ERMs) after retinal detachment (RD) repair based on the timing of macular peeling (MP). **Methods:** This retrospective consecutive case series comprised patients who had rhegmatogenous RD repair, developed an ERM, and had MP within 1 year. **Results:** Of the ERMs, 91% (50/55) were diagnosed between 1 month and 3 months after RD repair. When MP was performed less than 6 months after RD repair (n = 37), the final logMAR visual acuity (VA) was 0.31; this was statistically better than when MP was performed 6 months after RD repair or later (0.63, n = 18) (P = .005). In the 6-months or later MP cohort, 61% (11/18) had cataract surgery between the RD repair and MP while 7 patients were pseudophakic at RD presentation. Of the ERMs, 65%, 24%, and 11% were stage 4, stage 3, and stage 2, respectively; the final logMAR VA was 0.43, 0.38, and 0.30, respectively. There was no significant difference in the final VA or macular status between the stages. Overall, the mean logMAR VA before MP was 0.87, which improved to a final VA of 0.41 after MP ($P < .001$). **Conclusions:** ERMs formed after RD repair were most likely to be stage 4; however, this did not affect the final VA. The final VA was significantly better when MP was performed less than 6 months after RD repair. This is relevant because retina surgeons may be delaying MP until after cataract surgery.

Keywords

rhegmatogenous retinal detachment, epiretinal membrane, internal limiting membrane, membrane peel, macular surgery, visual acuity, macular pucker, surgical timing

Introduction

An epiretinal membrane (ERM) can occur after primary rhegmatogenous retinal detachment (RRD) repair. The reported rates of ERM formation after RRD repair vary greatly, ranging from 4.6% to 49%.[1–6] This significant variation may be related to differences in the study design, patient characteristics, and surgical technique.

ERM formation is thought to be secondary to liberation of retinal pigment epithelium cells from a retinal break with subsequent proliferation on the macular surface.[3,7,8] The internal limiting membrane (ILM) can act as a scaffold for cell proliferation, and it has been reported that ILM peeling at the time of RRD repair is effective in reducing postoperative ERM formation.[1,8–13] However, ILM peeling can alter the inner retinal layers and damage the Müller cell structure, reducing retinal sensitivity.[14–16]

In 2017, Govetto et al[17] created a classification system for grading ERM severity (grade 1 through 4) based on optical coherence tomography (OCT) features. In this classification system, higher grade ERMs were associated with worsening visual acuity (VA). Pars plana vitrectomy (PPV) with membrane peeling (MP) with or without ILM peeling can be performed for visually significant ERMs. In addition, ERMs that form after RD repair have been reported to be more severe than idiopathic ERMs.[18]

The appropriate timing of PPV with MP for ERM after RRD repair is not well studied. Given that the majority of ERMs after RDs are typically more severe, a delay in performing PPV with MP may induce permanent changes to the macula (ellipsoid zone [EZ] loss, microcystic changes, and ectopic inner foveal layers), resulting in permanent visual impairment. This study sought to determine the optimal timing of PPV with MP after RD repair. To our knowledge, our study is the first to the describe visual outcomes in cases of postoperative ERMs based on the timing of PPV with MP and the ERM grade.

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Methods

This retrospective consecutive case series was performed at a single private practice center. It comprised patients who had primary RRD repair between June 1, 2015, and June 1, 2022, at Illinois Retina Associates, Chicago, IL, USA. Institutional review board approval was obtained. This study adhered to the tenets of the Declaration of Helsinki.

All types of RRD repair (PPV with scleral bucking, PPV only, and scleral buckling only) were included in the study. There were no cases of ERM formation with subsequent MP after pneumatic retinopexy. Those who developed OCT-proven ERM after RD repair and had subsequent MP within 1 year were included. All patients had combined ERM and ILM peeling. No patient had combined phacoemulsification and vitrectomy. OCT was performed using the Spectralis device (Heidelberg Engineering) and the Cirrus device (Carl Zeiss Meditec AG). OCT was not routinely obtained at the time of the RRD diagnosis, similar to the protocol in previous studies.

Exclusion criteria included proliferative vitreoretinopathy (PVR) grade C or D at the time of RD, a diagnosis of ERM at the time of RD, the need for oil placement, formation of PVR postoperatively leading to a subsequent RD, epiretinal proliferation, and cystoid macular edema necessitating topical or injection therapy after RD.

Data collected included age, sex, laterality, lens status, VA, the duration of symptoms before the RRD diagnosis, a history of ocular trauma, the RRD characteristics and macular status, the type and technique of surgery for primary RRD repair, the total number of vitrectomies performed during the study period, the time to the ERM diagnosis, the grade of the ERM at diagnosis, the time to PPV with MP, the length of follow-up, and the timing of cataract surgery.

The primary outcome measures were the visual outcomes from the time of RD repair to MP and the grade of the developing ERM. A single retina specialist used OCT images to grade ERMs from 1 through 4 using the standard criteria. The secondary outcome was to determine whether the macular status at the time of the RD affected ERM formation or staging. Images were analyzed using Fiji software (US National Institutes of Health). Scale bars within the images were used to convert pixel measurements to metric measurements.

Statistical analysis was performed using a paired or unpaired *t* test, analysis of variance, or the χ^2 test based on the statistical hypothesis and groups being analyzed. Statistical significance was set at $P < .05$. Mean values are ± SD

Results

The study included 55 eyes. The mean age at the RRD diagnosis was 62.7 ± 10.0 years, and 64% of patients were men. Table 1 shows the demographics and clinical characteristics of the entire cohort. The symptom duration before the RRD diagnosis was 18 days (range, 1-150). Nine eyes (16%) had evidence of mild PVR at RRD presentation; none of them required retinectomy or oil placement.

Table 1. Demographics and Clinical Characteristics for the Entire Cohort (N = 55).

Demographic/Characteristic	Value
Patients (n)	55
Eyes (n)	55
Men, n (%)	35 (64)
RRD in right eye, n (%)	34 (62)
Mean age (y) at RRD diagnosis ± SD	62.7 ± 10.0
Lens status at RRD diagnosis, n (%)	
Phakic	33 (60)
Pseudophakic	22 (40)
Lens status at final follow-up, n (%)	
Phakic	6 (11)
Pseudophakic	49 (89)
Macula-off RRD, n (%)	34 (62)
Macula-on RRD, n (%)	21 (38)
RRD repair surgery type, n (%)	
PPV only	30 (55%)
PPV + SB	21 (38%)
SB only	4 (7%)

Abbreviations: PPV, pars plana vitrectomy; PVR, proliferative vitreoretinopathy; RRD, rhegmatogenous retinal detachment; SB, scleral buckling.

Of the patients, 34 (62%) presented with a macula-off RRD and 21 (38%) presented with a macula-on RRD. The most frequently used technique for RRD repair was PPV alone followed by PPV with scleral buckling, and then scleral buckling only (Table 1). During the study period, 2598 PPV or PPV with scleral buckling procedures were performed for primary RRD repair; 51 eyes (1.96%) that had those procedures developed a visually significant ERM postoperatively that required PPV with MP. In addition, 292 scleral buckling–only surgeries were performed for primary RRD repair; 4 eyes (1.37%) that had that procedure developed a visually significant ERM postoperatively that required PPV with MP. The median time from RD repair to MP was 150 days (mean, 162; range, 44-357).

Fifteen patients (27%) developed an ERM within 1 month after RRD repair. Of these, 3 (20%) had a stage 2 ERM, 1 (7%) had a stage 3 ERM, and 11 (73%) had a stage 4 ERM. Fifty patients (91%) developed an ERM within 3 months after RRD repair. Of these, 4 (8%) had a stage 2 ERM, 12 (24%) had a stage 3 ERM, and 34 (68%) had a stage 4 ERM. In the overall cohort, 6 eyes (11%) had a stage 2 ERM, 13 eyes (24%) had a stage 3 ERM, and 36 eyes (65%) had a stage 4 ERM.

In the overall cohort, the mean logMAR VA just before MP was 0.87 (Snellen equivalent, 20/150). There was a statistically significant improvement in the mean final logMAR VA after MP (0.41; Snellen equivalent, 20/52) ($P < .001$). Table 2 shows the clinical characteristics stratified by MP timing. When MP was completed within 6 months after RRD repair, the final logMAR VA was 0.31 (Snellen equivalent, 20/41), which was significantly better than the final logMAR VA of 0.63 (Snellen equivalent, 20/85) if the MP was completed 6 months after RRD repair or later ($P = .005$) (Figure 1).

Table 2. Clinical Characteristics Stratified by Membrane Peeling Timing.

Characteristic	Macular Peeling		*P* Value
	<6 Months After RRD Repair (n = 37)	≥6 Months After RRD Repair (n = 18)	
Macula-off RRD, n (%)	22 (59)	12 (67)	
Macula-on RRD, n (%)	15 (41)	6 (33)	.770
PVR at RRD diagnosis, n (%)	5 (14)	4 (22)	.453
Mean macula-off RRD symptom duration (d)	21.2	21.3	.500
Mean time to ERM diagnosis (d)	82.7	130.0	.076
Mean VA			
At time of RRD			.290
LogMAR	0.84	0.98	
Snellen equivalent	20/138	20/191	
At visit before MP			.006[a]
LogMAR	0.78	1.06	
Snellen equivalent	20/121	20/230	
At final visit			.007[a]
LogMAR	0.31	0.63	
Snellen equivalent	20/41	20/85	
At time of RRD: macula-off RRD only			.500
LogMAR	1.29	1.29	
Snellen equivalent	20/390	20/388	
Before MP: macula-off RRD only			.057
LogMAR	0.85	1.08	
Snellen equivalent	20/141	20/243	
Final: macula-off RRD only			.030[a]
LogMAR	0.34	0.70	
Snellen equivalent	20/44	20/100	
Pseudophakic at final follow-up, n (%)	32 (86)	18 (100)	.160

Abbreviations: ERM, epiretinal membrane; MP, membrane peeling; PVR, proliferative vitreoretinopathy; RRD, rhegmatogenous retinal detachment; VA, visual acuity.
[a]Statistically significant.

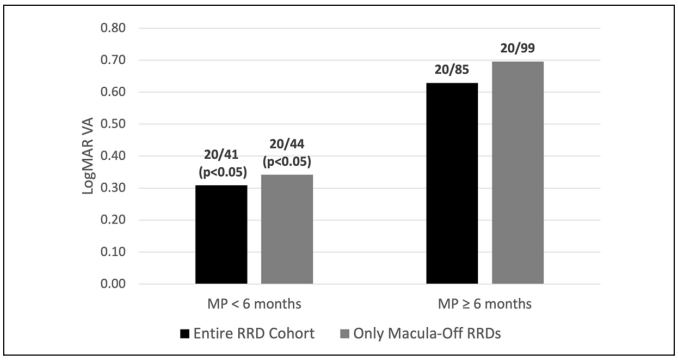

Figure 1. Final logMAR VA and Snellen VA stratified by MP timing.
Abbreviations: MP, membrane peeling; RRD, rhegmatogenous retinal detachment; VA, visual acuity.

Table 3 shows the preoperative anatomic characteristics stratified based on timing of MP surgery. In both groups (MP performed <6 months after RD repair; MP performed ≥6 months after RD repair), the most common ERM grade was stage 4 followed by stage 2 and then stage 1; no eye had a stage 1 ERM. Of the patients who had MP 6 months after RRD repair or later, 61% (11/18) had cataract surgery between the RRD repair and MP. The other 7 patients were pseudophakic at the time of the RD. The final logMAR VA of cases with stage 4 ERMs was 0.43 (Snellen equivalent, 20/50^{-}), of cases with stage 3 ERMs was 0.38 (Snellen equivalent, 20/40^{-}), and of cases with stage 2 ERMs was 0.30 (Snellen equivalent, 20/40) (Figure 2). There was no significant difference in the final VA or macular status between the ERM stages. There was no significant difference in the macular status at RRD diagnosis, PVR at RRD diagnosis, mean macula-off RRD symptom duration, and mean logMAR VA at RRD diagnosis between patients who had MP performed less 6 months after RD repair and those who had MP performed 6 months after RD repair or later (Table 2).

The mean time to MP was 177 days, 146 days, and 233 days if an ERM formed within 1 month, between 1 month and 3 months, or between 3 months and 6 months after RRD repair, respectively (Figure 3). ERM formation within the first month was statistically significantly faster when perfluoropropane (C_3F_8) was used as a tamponade agent than when sulfur hexafluoride (SF_6) was used ($P = .03$); however, there was no statistically significant difference after 1 month. The formation of ERM within the first month was statistically significantly faster

Table 3. Preoperative Anatomic Characteristics Stratified Based on the Timing of Membrane Peeling Surgery.

Characteristic	<6 Months (n = 37)	≥6 Months (n = 18)	*P* Value
ERM grade, n (%)			.63
1	0	0	
2	3 (8)	3 (16)	
3	9 (24)	4 (22)	
4	25 (68)	11 (61)	
Mean CFT (μm)	552	618	.12
EIFL present, n (%)	35 (94)	15 (83)	.17
EZ disruption, n (%)	13 (68)	7 (39)	.79
Inner retinal CME, n (%)	23 (85)	13 (72)	.46
SRF, n (%)	3 (8)	0	1
Cotton-ball sign, n (%)	1 (2.7)	2 (11)	1
Mean EIFL thickness (μm)	326	390	.24

Abbreviations: CFT, central foveal thickness; CME, cystoid macular edema; EIFL, ectopic inner foveal layers; EZ, ellipsoid zone; SRF, subretinal fluid.

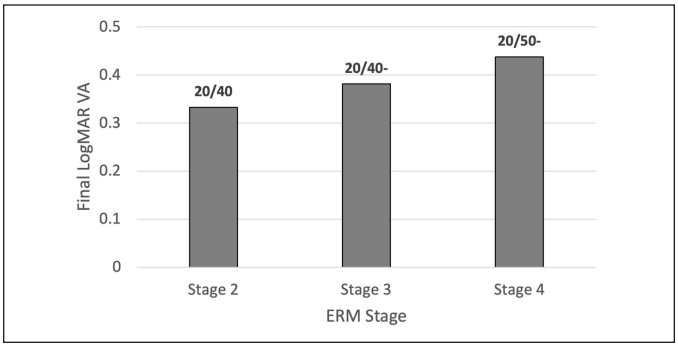

Figure 2. Final logMAR and Snellen VA stratified by ERM stage.
Abbreviations: ERM, epiretinal membrane; VA, visual acuity.

when PPV with scleral buckling was performed than with PPV only ($P = .02$); however, there was no statistically significant difference after 1 month. If a drainage retinotomy was made during PPV or PPV with scleral buckling, ERM formation was statistically significantly faster within the first month than when no drainage retinotomy was made ($P = .02$); however, the difference was not statistically significant after 1 month. There was no statistically significant difference between macular status, PPV gauge (23 vs 25), or duration of symptoms before RRD repair (≥2 weeks vs < 2 weeks) and the time to ERM formation ($P > .05$).

OCT images were analyzed a mean of 38.4 months from the date of surgery to the final follow-up. Table 4 shows the preoperative and postoperative ERM OCT analysis. The central foveal thickness (CFT) was the only preoperative variable that was correlated with the final VA ($P = .008$). The CFT and ectopic inner foveal layer thickness were the only anatomic variables that showed significant improvement postoperatively. The preoperative anatomic characteristics did not differ significantly based on the timing of MP (Table 3).

Conclusions

To our knowledge, our study is the first to characterize the visual outcomes of ERM formation after RRD repair based on MP timing and ERM staging. We report the characteristics, timing, and outcomes of 55 ERM cases after RRD repair (including PPV only, PPV with scleral buckling, and scleral buckling only) that subsequently had PPV with MP.

We found that when MP was completed within 6 months after RRD repair (37 patients), the final logMAR VA was 0.31 (Snellen equivalent, 20/41), which was significantly better than the final logMAR VA of 0.63 (Snellen equivalent, 20/85) if the MP was completed 6 months after RRD repair or later (18 patients) ($P = .005$). Furthermore, all eyes that had MP 6 months or later were pseudophakic at the final follow-up. In the entire cohort, 49 eyes (89%) were pseudophakic at the final follow-up, indicating that lens status was not a significant factor in the differences in the final VA. Of the patients who had MP 6 months after RRD repair or later, 61% (11/18) had cataract surgery between the RRD repair and MP, implying that the surgeon may be delaying PPV with MP until after cataract surgery.

The ERMs were stage 4 in 65% of cases (36/55), stage 3 in 24% (13/55), and stage 2 in 11% (6/55). The final logMAR VA in cases of stage 4 ERM was 0.43 (Snellen equivalent, 20/50^{-}), stage 3 ERMs was 0.38 (Snellen equivalent, 20/40^{-}), and stage 2 ERMs was 0.30 (Snellen equivalent, 20/40). Although eyes with progressively higher ERM grades had a slightly worse final VA, the difference was not statistically significant, implying that the decision to perform MP earlier should not be significantly influenced by the ERM grade.

The reported incidence of ERM formation after RRD repair ranges from 4.6% to 49%.[1–6] This significant variation may be related to differences in study design, patient characteristics, and surgical technique. In our study, the incidence was lower than previously reported rates. In our study, 2598 PPV or PPV with scleral buckling procedures were performed for primary RRD repair between 2015 and 2021; 51 eyes (1.96%) having these surgeries developed a visually significant ERM postoperatively and required PPV with MP. Also, 292 scleral buckling–only surgeries were performed for primary RRD repair between 2015 and 2021; 4 eyes (1.37%) having this surgery developed a visually significant ERM postoperatively and required PPV with MP.

Risk factors for postoperative ERMs include drainage retinotomy, a preoperative vitreous hemorrhage, a larger area of peripheral pathology, multiple retinal breaks, and the use of silicone oil for tamponade. In addition, a longer duration of macular detachment has been associated with postoperative ERMs. These factors, as well as 360-degree endolaser application, have also been associated with increasing ERM severity.[4,6,18]

The time to ERM detection after RRD repair varies in the literature but appears on average to be between 1 month and 4 months.[1,2] This timing is consistent with our study's findings, in which 50 patients (91%) developed an ERM within 3 months after RRD repair. Thirty-four (62%) of the initial RRDs that led

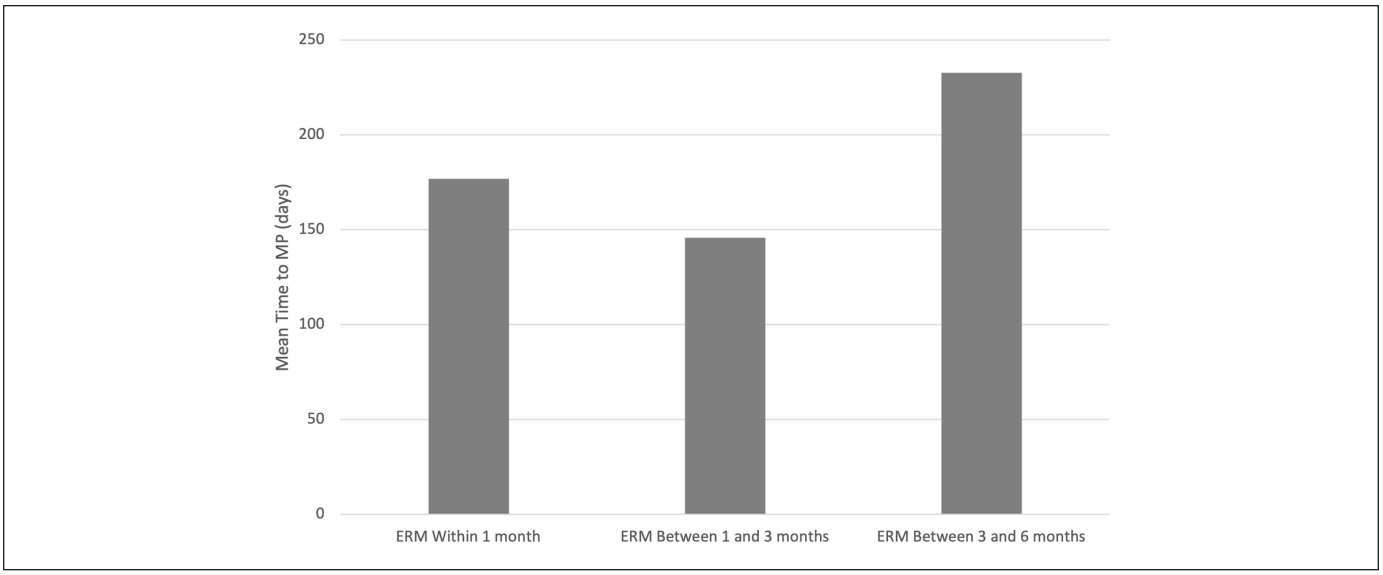

Figure 3. Mean time to MP based on time to ERM formation.
Abbreviations: ERM, epiretinal membrane; MP, membrane peeling.

Table 4. Preoperative and Postoperative Epiretinal Membrane Optical Coherence Tomography Analysis (N = 55).

Characteristics	Preoperative	Postoperative	*P* Value[a]	*P* Value[b]
ERM grade, n (%)			<.001[c]	0.75
1	0	16 (29)		
2	6 (11)	18 (32.7)		
3	13 (24)	19 (34.5)		
4	36 (65)	1 (1.8)		
Mean CFT (μm) ± SD	574 ± 150	349 ± 63	<.001[c]	.008[c]
EIFL present, n (%)	46 (94)	20 (36.4)	.27	.26
EZ disruption, n (%)	20 (36.4)	4 (7.4)	.14	.270
Inner retinal CME, n (%)	36 (67)	11 (20.4)	.30	.41
SRF, n (%)	3 (5.6)	0	1	.97
Cotton-ball sign, n (%)	3 (5.6)	1 (1.9)	1	.92
Mean EIFL thickness (μm) ± SD	347 ± 180	146 ± 80	<.001[c]	.12

Abbreviations: CFT, central foveal thickness; CME, cystoid macular edema; EIFL, ectopic inner foveal layers; EZ, ellipsoid zone; SRF, subretinal fluid.
[a]Comparing preoperative to postoperative values.
[b]Associated with final best-corrected visual acuity.
[c]Statistically significant.

to a visually significant ERM requiring MP were macula-off, and this may suggest that macula-off RRDs and ERMs after RD repair are associated. However, this is confounded by the fact that most RRDs were macula-off in our study. Thus, future studies comparing the rates of MP for ERM after macula-on RRDs vs macula-off RRDs would be helpful. ERM formation was statistically significantly faster with the use of C_3F_8, creation of a drainage retinotomy, and PPV with scleral buckling within the first month than with the use of SF_6, no drainage retinotomy, and PPV. There was no statistically significant difference in the time to ERM formation between the macular status, PPV gauge (23 vs 25), and duration of symptoms before RRD repair (≥2 weeks vs <2 weeks) ($P > .05$).

The timing of MP for visually significant ERMs after RRD is often determined on a case-by-case basis. The literature on when ERMs should be peeled is limited. However, there is now more effort to understand the timing of ERM removal, as evidenced by new studies including the DRCR Retina Network (clinical trial ID NCT05145491). A delay in ERM removal likely creates further cell damage, resulting in worse VAs. This is particularly relevant in our cohort of eyes that have already had retinal pathology in the form of an RD, many of which were macula-off. In our study, patients who had MP within 6 months of the initial RRD repair had significantly better final best-corrected VA (BCVA) than those who had MP after 6 months. Many patients who had MP 6 months or later had cataract surgery between RRD repair

and MP, implying the surgeon may be delaying the MP until after cataract surgery. Given our findings, we recommend that vitreoretinal surgeons consider expediting PPV with MP in eyes with ERM formation after RRD, regardless of the ERM grade and assuming that the cataract is not significantly obscuring the view of the fundus.

In our cohort, the presence and thickness of the ectopic inner foveal layers are similar to those reported in recent studies.[19] Postoperatively, we observed significant reductions in the ectopic inner foveal layer thickness, CFT, and ERM grade, suggesting significant anatomic recovery after membrane peeling procedures. However, only CFT was found to be correlated with the postoperative BCVA and the timing of MP did not affect the postoperative anatomic outcomes. These findings are consistent with those in recent studies of membrane peeling for ERMs after RRD.[17,20] Although outer retinal parameters such as EZ integrity and the cotton-ball sign have proven visually significant in previous studies, our study showed no statistically significant changes with respect to the outer retina. Given that the anatomic recovery of the ectopic inner foveal layer or ERM grade in our study did not correlate with functional recovery postoperatively, further studies to elucidate the role of inner retinal anatomic changes on functional visual outcomes are needed.

In the future, studies of even earlier intervention and more precise timing of PPV with MP for ERMs after RD should be performed. It is possible that these ERMs have to be evaluated by the surgeon with similar scrutiny as a macula-off RD in terms of timing. The literature has shown that macula-off RDs have the best outcomes when RD repair is performed within a certain timeframe.[21] Similarly, further studies could create detailed recommendations regarding when to operate on these severe ERMs after RD repair (possibly within weeks of their appearance).

Limitations of our study include its retrospective nature and the difficulty of comparing surgical groups because of the sample size, in particular with scleral buckling alone. In addition, multivariate analysis was considered and attempted; however, a thorough multivariate analysis with all variables could not be completed because of the sample size. Although this study was performed at a single private practice center, the surgeries were done by multiple retina surgeons in the practice; therefore, the surgeons' familiarity with various techniques and clinical experience likely influenced the outcomes.

Authors' Note

Presented at the annual meeting of the Association for Research and Vision in Ophthalmology, April 23–27, 2023, New Orleans, LA, USA, and the annual meeting of the American Society of Retina Specialists, July 17–20, 2024, Stockholm, Sweden.

Ethical Approval

This study was institutional review board approved and conducted in accordance with the tenets of the Declaration of Helsinki.

Statement of Informed Consent

The institutional review board waived the requirement for informed consent.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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