

Incidence and Impact of Outer Retinal Folds After Pars Plana Vitrectomy for Primary Rhegmatogenous Retinal Detachment Repair

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Abstract

Purpose: To determine the incidence, risk factors, and visual impact of outer retinal fold formation after pars plana vitrectomy (PPV) for macula-involving rhegmatogenous retinal detachment (RRD). **Methods:** A retrospective cohort study was performed of patients who had PPV with or without scleral buckling between 2011 and 2021 at a single tertiary referral center. Inclusion criteria were macular optical coherence tomography (OCT) performed within 6 weeks of PPV. Eyes with silicone oil tamponade or redetachment within 12 weeks of repair were excluded. Demographics, ocular characteristics, surgical technique, visual acuity (VA), and OCT data were analyzed. **Results:** This study included 154 eyes. Outer retinal folds developed in 19.2% of eyes that had OCT within 6 weeks of PPV. The mean time to resolution of an outer retinal fold was 131.9 days. Although eyes with outer retinal folds had worse preoperative vision, there was no difference in the final VA between the groups (preoperative: 20/1099 vs 20/230; $P = .003$) (12 months postoperative: 20/49 vs 20/46; $P = .73$). There was a trend toward more superior RRD in patients with outer retinal folds ($P = .10$). **Conclusions:** In this study, the incidence of outer retinal folds after PPV for macula-involving RRDs was lower than previously reported. Outer retinal folds that developed soon after surgery resolved quickly, and their presence or absence was not associated with the final VA.

Keywords

optical coherence tomography, outer retinal folds, pars plana vitrectomy, rhegmatogenous retinal detachment

Introduction

Primary rhegmatogenous retinal detachment (RRD) affects approximately 6 to 18 per 100 000 people annually,^{1–3} and the incidence is increasing.^{3,4} Various techniques are used to repair detachments, including scleral buckling, pars plana vitrectomy (PPV), and pneumatic retinopexy. The goal of selecting the appropriate repair technique is to optimize the patients' postoperative visual function. One major consideration is the single-surgery anatomic success rate because patients who require additional surgeries often have decreased final visual acuities (VAs).⁵ We and others have previously shown that PPV alone has a single-surgery success rate of 83% to 95%,^{6–12} which is comparable to the rates for PPV with scleral buckling (84% to 91%)^{7,11,12} and scleral buckling alone (82% to 94%).^{7,11–13} Multiple independent studies reported significantly lower single-surgery anatomic success rates of 67% to 81% for pneumatic retinopexy.^{14–18}

Recently, postoperative outer retinal folds have received increased attention as an anatomic factor that may affect visual function after RRD repair.¹⁹ First described by Benson et al,²⁰ outer retinal folds after RD repair have since been studied by

several groups in the setting of PPV.^{21–25} A distinct entity from full-thickness retinal folds, outer retinal folds are often not appreciated clinically on examination but are easily identified on optical coherence tomography (OCT) imaging,²⁶ characteristically appearing as small hyperreflective lesions extending vertically or obliquely into the outer nuclear layer.²⁵

Previous small studies and a recent single prospective study reported rates of outer retinal fold formation of 34% to 42% after PPV,^{19,21,22} and this finding has similarly been described after pneumatic retinopexy.¹⁹ Dell'Omo et al²² found an association between the number of detachment quadrants involved and the development of outer retinal folds. No association has been found between outer retinal folds and postoperative positioning, use of perfluoro-N-octane (PFO), and the duration of the detachment.^{21,22} Recent data suggest an increased incidence

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of outer retinal folds after PPV for primary RRD repair compared with pneumatic retinopexy and found that patients with postoperative outer retinal folds had decreased VA and increased metamorphopsia.¹⁹

Given the limited data on outer retinal folds rates, outcomes, and predictive factors, we sought to assess the incidence of outer retinal folds after PPV or PPV with scleral buckling for primary RRD repair. Furthermore, we aimed to evaluate the effect of outer retinal folds on postoperative VA and assess the factors that predict their formation.

Methods

Institutional review board approval was obtained from the University of Michigan for all aspects of this retrospective cohort study, including review of patient data. This research was conducted in compliance with the US Health Insurance Portability and Accountability Act of 1996 and the Declaration of Helsinki. Informed consent was not sought for the study because of its retrospective nature with de-identified data collection.

Patient data were obtained retrospectively from a single academic tertiary referral center between January 1, 2011, and March 3, 2021. Patient cases for review were identified using International Classification of Diseases (ICD) diagnostic codes for RD (ICD-10: H33.00, H33.01, H33.02, H33.001, H33.002, H33.009, H33.011, H33.012, H33.019, H33.021, H33.022, H33.029; ICD-9: 361.00, 361.01, 361.02, 361.05) and Current Procedural Terminology (CPT) billing codes for repair of RD with PPV (67108, 67036, 67039, 67040). This collection of vitrectomy codes was used to be maximally inclusive of all primary RRDs, with all cases subsequently reviewed to confirm the diagnosis and surgical repair technique.

A retrospective chart review was performed by 2 trained study personnel. Image analyses, including the primary and secondary outcomes, were performed independently by 2 masked graders (E.A.E., W.W.P.), 1 vitreoretinal surgery attending, and 1 vitreoretinal surgery fellow. Agreement between the graders was then evaluated with the κ statistic. Preoperative, intraoperative, and postoperative data were collected, including patient demographics, preoperative and postoperative examination findings, operative reports, and ophthalmic imaging, including fundus photography and OCTs. Data were extracted from the Michigan Medicine electronic medical record system (Epic Systems Corp).

Patients who had a macula-involving primary RRD repaired with PPV were identified. Eyes with macular OCT imaging of the surgical eye after RD repair with PPV or PPV with scleral buckling were included for review. Eyes were excluded if they had recurrent RD that required a return to the operating room within the first 12 postoperative weeks. Silicone oil (SO) placement was also excluded given potential differences in reapposition forces between gas and oil. The presence of gas tamponade on near interventional radiology images associated with the macular OCT was not an exclusionary criterion unless there

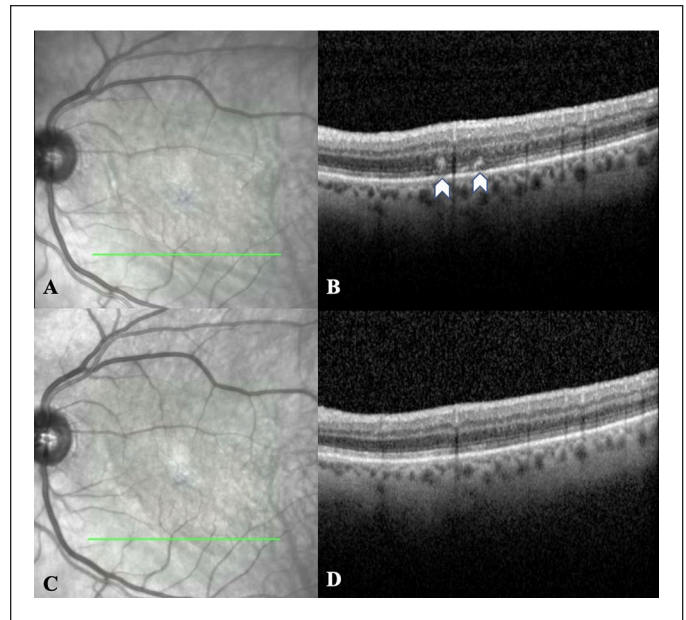


Figure 1. Representative (A) near infrared and (B) macular optical coherence tomography (OCT) images obtained 6 weeks after pars plana vitrectomy with perfluoropropane endotamponade for repair of primary rhegmatogenous retinal detachment show the presence of outer retinal folds (arrowheads), characterized by infoldings of the ellipsoid zone (EZ) and external limiting membrane (ELM). Five months postoperatively, resolution of the outer retinal folds is seen in corresponding (C) near infrared and (D) OCT images.

was significant degradation of the image quality precluding evaluation of the lamellar retinal architecture. PPV was performed with a 23-gauge or 25-gauge system in all cases. Postoperative positioning was dictated by the location of the retinal breaks.

The primary outcome of interest was the incidence of outer retinal folds in eyes of patients with OCT imaging obtained within the first 6 weeks after RD repair. Outer retinal folds were characterized as infoldings of the ellipsoid zone and external limiting membrane creating a vertical hyperreflective foci in the outer retina (Figure 1), as identified on 6 mm \times 6 mm macular cube and 8 mm \times 4 mm horizontal and vertical rasters. Six weeks was chosen as the endpoint based on literature showing that a large portion of outer retinal folds resolved by 3 months postoperatively.^{19,21–23} Patients without imaging during the first 6 postoperative weeks were excluded because the possibility of early fold resolution could not be excluded. Cross-sectional rather than en face OCT images were used for grading given the possibility of false-positive identification of outer retinal folds with the en face modality.¹⁹

Secondary outcomes of the study included the duration of the RD, hemisphere of the RD, and intraoperative subretinal drainage technique with formation of outer retinal folds. Hemispheric predominance was based on whether the majority of the detachment was superior or inferior to the horizontal

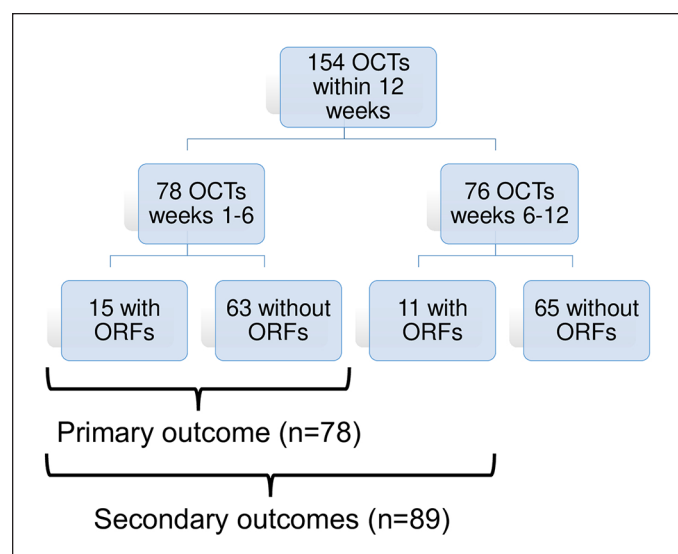


Figure 2. Flowchart shows the inclusion criterion for primary and secondary outcome analysis based on the timing of optical coherence tomography after pars plana vitrectomy with or without scleral buckling and the presence of outer retinal folds. Abbreviations: OCTs, optical coherence tomographies; ORFs, outer retinal folds.

meridian and was classified as equatorial if an equal number of clock hours of detachment were both above and below the horizontal meridian. This information was included in the operative report. The postoperative VA in eyes with and eyes without early outer retinal folds was also evaluated. The distance VA (pinhole or best-corrected with refraction) was recorded based on documentation in the patient chart. The postoperative VA was extracted from the office visit occurring closest to 12 months after PPV. All VA data were initially collected as Snellen VA and then converted to logMAR notation for statistical analysis. Counting fingers, hand motions, and light perception VA were converted to logMAR values as previously established by Reinstein et al.²⁷

For secondary outcomes, patients with initial OCT imaging within 6 weeks of surgery were included for analysis, as were eyes that showed outer retinal folds on OCT between 6 and 12 weeks postoperatively (Figure 2). The presence of outer retinal folds on OCT in the first 6 weeks postoperatively was noted, even if the folds resolved by the time of the subsequent 6-week to 12-week OCT imaging. Eyes without outer retinal folds on OCT obtained between 6 weeks and 12 weeks postoperatively were not included in the secondary outcome analysis because of concerns about misclassification given that early outer retinal folds may have resolved by the 6-week timepoint.

Characteristics of the study population were summarized using the mean \pm SD, mean and range, or frequency and percentage as appropriate. Continuous variables were compared with a 2-sided *t* test. Categorical variables were compared with χ^2 tests. Data analyses were performed using Stata software (version 16.1, StataCorp). Statistical significance was set at $P < .05$.

Results

Overall, 154 eyes had primary macula-involving RRD repaired with PPV or PPV with scleral buckling and gas endotamponade with initial OCT imaging obtained within 12 weeks after surgery. Perfluoropropane (C_3F_8) was the most common tamponade agent, used in 98.1% of patients; sulfur hexafluoride (SF_6) was rarely used (1.3%), and air was used as a tamponade in 1 patient (0.6%).

Seventy-eight eyes had OCT performed within 6 weeks postoperatively and were included in the primary outcome analysis. Postoperative outer retinal folds were identified early in 15 of the 78 eyes, resulting in an incidence of 19.2% after PPV. Although not included in the primary outcome analysis over concern for misclassification of eyes with resolution of outer retinal folds before the 12-week mark, the incidence of outer retinal folds on OCTs obtained between 6 weeks and 12 weeks was 14.4%. Thus, when considering all 154 eyes with OCT imaging within 0 to 12 postoperative weeks, the incidence of outer retinal folds was 16.9% (26/154). The mean time to the initial postoperative OCT was 29.7 ± 4.2 days for those with outer retinal folds and 30.9 ± 4.8 days for those without outer retinal folds in the first 6 weeks ($P = .36$).

Of the 76 eyes that had initial postoperative OCT 6 to 12 weeks after PPV with or without scleral buckling, 11 had outer retinal folds and were added to the cohort for secondary outcome analyses; the remaining 65 eyes were excluded (Figure 2). There was excellent intergrader agreement for the presence or absence of outer retinal folds (Cohen $\kappa = 0.90$; 98.1% agreement).

Table 1 shows the characteristics of the 89 included eyes. The mean age of the entire cohort was 61.8 years (range, 34.5-88.6), with more men (59.6%), left eyes (66.3%), and phakic eyes (58.4%). Of the 21 OCTs, 23.6% had a gas tamponade agent visible on near interventional radiology images; however, none of these eyes was excluded given the preserved cross-sectional OCT scan quality. There was no significant difference between eyes with and eyes without postoperative outer retinal folds except in the preoperative VA, which was statistically significantly worse in the group with outer retinal folds than in the group without folds ($P = .003$).

On average, outer retinal folds resolved by approximately 4 months after PPV (mean, 131.9 days; range, 63-296), and all resolved before the final 12-month postoperative evaluation. No significant difference was observed in the final postoperative VA between eyes with and eyes without outer retinal folds after PPV ($P = .73$), with a similar time to final VA and lens status between the 2 groups (Table 2).

Table 3 shows the features of the RD and repair technique, which were assessed to determine their effect on the formation of outer retinal folds. The mean duration of RD based on patient-reported onset of symptoms before repair was 9.4 days (range, 1.0-90.0) in eyes without postoperative outer retinal folds and 8.0 days (range, 1.0-21.0) in eyes with outer retinal folds ($P = .66$). There was a trend toward significance in the predominant hemisphere of RD and outer retinal fold formation, with inferior detachments more common in eyes that did

Table 1. Baseline Patient and Eye Characteristics Stratified by Those With and Without Early Postoperative Outer Retinal Folds.

Parameter	All Eyes (N=89)	With Outer Retinal Folds (n=26)	Without Outer Retinal Folds (n=63)	P Value ^{a,b}
Age (y)				.64
Mean	61.8	61.0	62.2	
Range	34.5, 88.6	40.5, 80.5	34.5, 88.6	
Male, n (%)	53 (59.6)	17 (65.4)	36 (57.1)	.45
Right eye, n (%)	30 (33.7)	9 (34.6)	21 (33.3)	.91
Phakic, n (%)	52 (58.4)	15 (57.7)	37 (58.7)	.93
PPV and SB, n (%)	4 (4.5)	1 (3.8)	3 (4.8)	.85
25-gauge vitrectomy, no (%) ^c	78 (87.6)	22 (84.6)	56 (88.9)	.58
Tamponade agent visible on OCT	21 (23.6)	5 (19.2)	16 (25.4)	.53
Preoperative VA				.003
Mean logMAR \pm SD	1.25 \pm 0.97	1.74 \pm 0.98	1.06 \pm 0.91	
Snellen equivalent	20/356	20/1099	20/230	

Abbreviations: OCT, optical coherence tomography; PPV, pars plana vitrectomy; SB, scleral buckling; VA, visual acuity.

^aP values represent comparison between eyes with and without outer retinal folds.

^bP < .05 considered statistically significant (t test or χ^2 test).

^cAll other surgeries done with a 23-gauge system.

Table 2. Association of Postoperative VA After PPV With or Without Scleral Buckling for Primary RRD Repair and Presence of Early Outer Retinal Folds.

Parameter	With Outer Retinal Folds (n=26)	Without Outer Retinal Folds (n=63)	P Value ^a
Postoperative VA			.73
Mean logMAR \pm SD	0.39 \pm 0.29	0.36 \pm 0.49	
Snellen equivalent	20/49	20/46	
Days to final VA after PPV			.75
Mean	317.7	306.0	
Range	55, 546	27, 947	
Lens status, n (%)			.75
Phakic	5 (19.2)	14 (22.2)	
Pseudophakic	21 (80.8)	49 (77.7)	

Abbreviations: PPV, pars plana vitrectomy; RRD, rhegmatogenous retinal detachment; SB, scleral buckling; VA, visual acuity.

^aP < .05 considered statistically significant (t test or χ^2 test).

not develop outer retinal folds (25.4% vs 7.7% in eyes with outer retinal folds) and eyes with outer retinal folds more often having superior detachments (72.0% vs 50.8% in eyes without outer retinal folds). However, this did not reach statistical significance ($P=.10$). When analyzing only patients with superior RDs, the rate of outer retinal fold formation was 30.4% compared with 19.2% for all detachments. The method of intraoperative subretinal fluid (SRF) drainage (ie, drainage retinotomy, PFO, or drainage through the primary retinal break) was not significantly different between the groups (Table 3).

Conclusions

In this study, the incidence of outer retinal folds after PPV was 19.2%, with folds typically resolving by 4 months postoperatively. No folds persisted at the final 12-month timepoint. Although there was an initial difference in VA between eyes with and eyes without outer retinal folds, there was no difference in

the 12-month postoperative VA between the 2 groups. This is consistent with a recent meta-analysis showing no influence of outer retinal corrugations (a feature that may lead to the formation of outer retinal folds) on the final postoperative VA.²⁸ Excluded from our calculations were patients whose primary postoperative OCT was obtained more than 6 weeks after surgery and who did not have outer retinal folds, because we could not determine whether they had early outer retinal folds that had already resolved. However, given that the mean time to resolution was 4 months, if we also included all eyes with initial OCT obtained between 6 weeks and 12 weeks postoperatively, our incidence would be 16.9% (26/154), suggesting that the rate of outer retinal folds may in fact be slightly lower than our conservatively reported 19.2%.

The 2 groups were well balanced with regard to preoperative characteristics, with the exception of the preoperative VA, which was worse in the group with outer retinal folds. The etiology of worse vision is unclear because the groups did not

Table 3. Association Between Detachment Characteristics and Intraoperative SRF Drainage Technique With Development of Postoperative Outer Retinal Folds.

Parameter	With Outer Retinal Folds (n=26)	Without Outer Retinal Folds (n=63)	P Value ^a
Duration of detachment (d)			.66
Mean	8.0	9.4	
Range	1.0, 21.0	1.0, 90.0	
Hemispheric predominance of RRD, n (%)			.10
Superior	18 (72.0)	32 (50.8)	
Inferior	2 (7.7)	16 (25.4)	
Equatorial	5 (23.1)	15 (23.8)	
SRF drainage technique n (%)			.27
Retinotomy	17 (65.0)	48 (76.0)	
PFO	3 (11.5)	2 (3.2)	
Primary break	6 (23.1)	13 (20.6)	

Abbreviations: PFO, perfluoro-N-octane; RRD, rhegmatogenous retinal detachment; SRF, subretinal fluid.

^aP < .05, t test or χ^2 test considered statistically significant.

have a significant difference in the duration of the detachment or lens status at the time of presentation. One possibility is a more elevated macular detachment in the group with outer retinal folds, which has been shown to be associated with worse VA²⁹ and conceivably may increase fold formation, although this relationship has not been previously established. Given the retrospective nature of the study, many patients did not have preoperative OCT imaging available for review; therefore, the preoperative macular fluid height could not be comprehensively evaluated.

It has been postulated that differences in surgical technique underlie the development of outer retinal folds. Vitrectomy with drainage of SRF and placement of a gas tamponade and the more rapid reattachment of the retina may lead to persistent outer retinal corrugations being put in apposition to the retinal pigment epithelium (RPE), leading to outer retinal fold formation. In contrast, nondrainage (pneumatic retinopexy) or minimal drainage (PPV with drainage through a peripheral break with significant residual SRF) techniques may allow for slower retinal reattachment with time for outer retinal corrugations to resolve.¹⁹ In the current study, we did not find that surgical technique affected outer retinal fold formation. Specifically, there was no difference in intraoperative SRF drainage technique (PFO, drainage retinotomy, or draining through a primary break) between the groups. This is consistent with previously reported findings from Peiretti et al,²¹ who found the use of PFO had no impact on the rate of postoperative outer retinal fold development.

Another factor to consider is postoperative positioning. The majority of surgeons at our institution use reading or face-down positioning for at least the first 24 hours after surgery in macula-involving RRDs. The emphasis on this positioning, followed by 7 to 10 days of mandated strict positioning as dictated by the location of the retinal breaks, may explain the lower rate of outer retinal folds in our PPV groups compared with what has been previously described.^{19,21,22} However, a study of the incidence of outer retinal folds in patients positioned supine vs prone after PPV found no difference in fold formation.²¹

Although it did not reach statistical significance, we found that eyes with superior RDs developed outer retinal folds more frequently than those with inferior RDs. Dell'Omo et al²² reported an association between outer retinal folds and increasing quadrants of RD but did not assess the location of such quadrants. Outer retinal folds are hypothesized to occur from outer retinal corrugations that fail to resolve before contact with the retina and RPE during the retinal reattachment process.¹⁹ Given the dependent nature of SRF with greater fluid height occurring at the inferior edge of a detachment, superior detachments may tend to have the highest SRF and most prominent outer retinal corrugations in the macula (in contrast to inferior detachments, which may have the more bullous aspect of the detachment sitting more inferiorly). This is one possible explanation for an increased rate of outer retinal folds with superior detachments, a trend that may also explain the higher rate of outer retinal folds after PPV (34.1%) in a recent study that included a group of patients who had pneumatic retinopexy because the technique would be ideal for a population with superior detachments.¹⁹

This study did not examine the presence and visual outcomes of outer retinal folds after redetachment surgery and the use of various endotamponade agents such as SO. Future investigations into whether outer retinal folds form under SO may deepen our understanding of the best procedural techniques for various circumstances.

This study has several strengths, including that to our knowledge it is the largest primary cohort of PPV with or without scleral buckling to date to assess outer retinal folds after primary RRD repair. All OCT images were reviewed by 2 masked graders to confirm the presence of outer retinal folds and avoid false-positive characterizations. Although ICD-9, ICD-10, and CPT codes were used to identify RRDs, all electronic medical records were reviewed individually to confirm the diagnosis and avoid misclassification.

The current study has a number of limitations. Given the retrospective nature of the study, postoperative OCTs were obtained at the surgeons' discretion; thus, only a portion of the total RRD

repairs performed were included for analysis. Similarly, this leads to inconsistencies in the frequency of repeat OCT imaging to pinpoint the exact time of outer retinal fold resolution. Of those individuals who had OCT imaging within 12 weeks, almost all had C₃F₈ endotamponade (1 had tamponade with air and 2 had SF₆). As such, many of the OCTs were performed in the continued presence of a gas bubble. This limited the resolution of the OCT scan and may have led to a missed outer retinal fold, although the layers of the retina in the scan under the gas bubble were still clearly visible and demarcated. In addition, preoperative macular fluid height could not be comprehensively evaluated because we did not require a preoperative OCT.

In addition, although we found no difference in the postoperative VA between the 2 groups, a lack of consistent postoperative Amsler grid evaluation or subjective reporting of metamorphopsia precluded us from commenting on this aspect of postoperative visual function. Qualitative and quantitative metamorphopsia have been previously described in conjunction with the presence of outer retinal folds,^{19,22,24} and this should be explored further in a larger prospective PPV cohort. Indeed, our secondary analysis evaluated subgroups that were at times underpowered, which limits the conclusions that can be made regarding the use of PFO. Yet to our knowledge, this is the largest primary PPV cohort to date to assess outer retinal folds after primary RRD repair and the preoperative characteristics between the 2 groups were similar in this study.

In conclusion, in this largest-to-date cohort of primary macula-involving RRDs repaired with PPV or PPV with scleral buckling, we found the incidence of postoperative outer retinal folds to be 19.2%, which is lower than previously reported. Larger prospective studies are needed to elucidate how surgical technique affects the formation of outer retinal folds; nonacuity-based visual function can also be assessed. When assessing all patients with 6- to 12-week imaging, the incidence of outer retinal folds was 14.4%, which is consistent with previous reports of most outer retinal folds resolving by week 12.^{19,21,22} The presence of early outer retinal folds had no impact on postoperative VA. Given this and the excellent single-surgery anatomic success rate of primary PPV (83% to 95%)^{6–12} and PPV with scleral buckling (84% to 91%),^{7,11,12} vitrectomy remains a good option for repair of RRDs.

Ethical Approval

Ethical approval was obtained from the University of Michigan Institutional Review Board (HUM00145843) for all aspects of this retrospective cohort study.

Statement of Informed Consent

Informed consent was not sought for the study because of its retrospective nature with de-identified data collection.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of the article: Dr. Besirli has royalty interest in ONL Therapeutics and royalty and

equity interest in Ocutheia, Inc. Dr. Zacks has equity, royalty, and board membership in ONL Therapeutics. Dr. Wubben has royalty and equity interests in Ocutheia, Inc. None of the other authors declared potential conflicts of interest with respect to the research, authorship, and/or publication of the article. None of the aforementioned organizations had any role in the design or conduct of this research.

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