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Influence of Vitreous Cortex Remnants on Normal Retinal Anatomy in Eyes with Primary Rhegmatogenous Retinal Detachment

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Purpose: To investigate the influence of vitreous cortex remnants (VCRs) removal on normal retinal anatomy in eyes with rhegmatogenous retinal detachment (RRD).

Design: Prospective cohort study.

Subjects: Patients with primary RRD operated with pars plana vitrectomy (PPV).

Methods: Blue fundus autofluorescence and spectral-domain OCT were obtained preoperatively, and at 1 and 6 months after operation.

Main Outcome Measures: Primary outcomes: rate of retinal displacement and outer retinal folds (ORFs) at 1 month after operation. Secondary outcomes: continuity of the external limiting membrane (ELM) and ellipsoid zone (EZ), and the logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) at 6 months after operation.

Results: One hundred three eyes were included. Intraoperatively, peripheral VCRs (pVCRs) were found in 42 eyes (40.8%) and successfully peeled off from ≥2 quadrants in 37 eyes. Macular VCRs (mVCRs) were detected in 37 (35.9%) and successfully peeled off in 29 eyes. At the end of operation 44.7% and 55.3% of the eyes were tamponaded with 20% sulfur hexafluoride gas and silicone oil 1000 centistokes, respectively. The only variable significantly associated with displacement was the use of gas tamponade versus silicone oil ($P = 0.001$), whereas no significant association was found between retinal displacement and pVCRs ($P = 0.58$) or number of quadrants from which pVCRs were peeled off ($P = 0.39$). At 1 month postoperatively, ORFs were globally detected in 24 eyes (23.3%). Regression analysis showed a direct correlation between ORFs and the intraoperative detection of mVCRs ($P = 0.02$) and an indirect correlation between ORFs and mVCRs peeling ($P = 0.004$). Macular VCRs peeling did not influence the continuity of ELM and EZ at the 6-month follow-up (FU). Intraoperative absence of mVCRs ($P = 0.0016$) and peeling of mVCRs ($P = 0.003$) were associated with logMAR BCVA ≤0.3 at the 6-month FU.

Conclusions: Peeling of pVCRs did not seem to influence the rate of retinal displacement, whereas peeling of mVCRs was associated with a reduced risk of developing ORFs without detrimental effect on the continuity of ELM/EZ at 6-month FU. The patients without mVCRs detected intraoperatively, or who underwent mVCRs peeling during operation, showed a significantly better visual acuity at the 6-month FU.

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The anatomic repair of fovea-off rhegmatogenous retinal detachment (RRD) often does not correlate with restoration of normal anatomy of the reattached retina. In fact, many eyes with fovea-off RRD may exhibit postoperative changes such as outer retinal folds (ORFs), discontinuity in the outer retinal bands (i.e., the external limiting membrane [ELM], the ellipsoid zone [EZ] and the interdigitation zone), and unintentional retinal displacement.[1−5]

All of these alterations, although frequently overlooked by the surgeon, are of paramount significance to patients, as they can lead to reduced visual acuity (VA), metamorphopsia, and aniseikonia.[6,7]

The choice of a surgical technique for repairing RRD carries varying risks in determining these postoperative alterations. For example, scleral buckle is associated with a lower rate of unintentional displacement compared with pars plana vitrectomy (PPV).[8] The pneumatic retinopexy versus Vitrectomy for the Management of Primary RRD Outcomes Randomized Trial (known as "PIVOT") and subsequent studies have shown that pneumatic retinopexy

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is linked to a lower incidence of retinal displacement and ORFs, along with a higher incidence of ELM/EZ continuity compared with PPV.[9,10]

However, due to the high rate of single-operation success in achieving anatomic reattachment and advancements in machinery and microsurgical instrumentation, PPV remains the preferred management option for many surgeons worldwide in the treatment of RRD.

Therefore, there is a strong desire for refinements in the technique of PPV. These refinements aim to maintain a very high anatomic success rate while simultaneously ensuring better anatomic recovery.

One of the most intriguing topics recently discussed in the literature is the debate surrounding the role of vitreoschisis-induced vitreous cortex remnants (VCRs)[11] in eyes with RRDs. These VCRs can be located both over the macula (mVCRs) and on the peripheral retinal surface posterior to the vitreous base (pVCRs),[12,13] and they may exhibit variable histopathological compositions, including different cell types, collagen, and fibrosis.[14] Specifically, the prevalence of myofibroblasts and fibrosis may lead to the formation of fibrocontractile membranes,[15] which could alter the elasticity of the detached retina and potentially be associated with retinal abnormalities after reattachment.

This study aims to investigate whether the presence and removal of VCRs have an impact on the postoperative anatomic recovery of normal retinal anatomy and functional outcomes in eyes undergoing PPV for primary RRD repair.

Methods

This prospective cohort study included patients with primary fovea-off RRD who underwent vitrectomy at the University of Molise in Campobasso from June 2020 to February 2023. All subjects received treatment in accordance with the Declaration of Helsinki.

We obtained approval from the Institutional Review Board of the University of Molise. Patients provided written informed consent after receiving a detailed description of the surgical procedure. We documented various parameters, including a comprehensive medical and ophthalmic history, gender, age, eye laterality, lens status, duration of symptoms suggestive of RRD, location and extent of RRD, number and location of retinal tears, fovea status, and proliferative vitreoretinopathy (PVR) grade.[16]

We obtained axial length (AXL) measurements using optical biometry (Lenstar LS 900, Haag-Streit). These measurements were taken preoperatively and postoperatively in all cases.

We assessed best-corrected VA (BCVA) using the ETDRS chart at a distance of 4 meters both before and after the operation. Visual acuity measurements of counting fingers were converted to 1.4 logarithm of the minimum angle of resolution (logMAR), hand movements to 2.7 logMAR, and light perception to 3.7 logMAR.

Based on OCT images, we excluded patients with fovea-on or fovea-split detachment and patients in whom the visualization of the fovea and the underlying retinal pigment epithelium was hindered by bullous detachment, or patients in whom the height of detachment fell outside the range of acquisition. Also excluded were patients who had undergone previous vitreoretinal surgery or had RRD secondary to diabetes, retinal vascular diseases, uveitis, trauma, or those with RRD associated with a macular hole or giant retinal tear. Additionally, patients who experienced redetachment during the follow-up (FU) period were also excluded.

The primary outcomes of the study were the rate of retinal displacement and ORFs at 1 month after operation. Secondary outcomes were the continuity of the ELM and EZ, and the logMAR BCVA at 6 months after operation.

OCT and Blue Fundus Autofluorescence Evaluation

Spectral-domain OCT scans and blue fundus autofluorescenece (B-FAF) images were acquired both before (baseline) and after the operation during predefined visits (at 1 month and 6 months postoperation) using the Heidelberg Spectralis (version 1.9.13, Heidelberg Engineering). The scanning protocol involved capturing a sequence of horizontal and radial sections (B-scans) with an approximate length of 17.5 mm that respectively covered an area spanning 55 degrees horizontally and 40 degrees vertically (horizontal sections) or 55 degrees (radial sections). These sections were recorded in high-resolution mode, with each section consisting of 1536 A-scans and a spacing of 120 μm (for horizontal sections) or 15 degrees (for radial sections) between individual sections. The "Automatic Real-Time" function, set at 16, was employed during acquisition. Only images with a quality rating of $\geq$70 were deemed suitable for subsequent analysis.

Furthermore, B-FAF images, with an excitation wavelength of 488 nm and a barrier filter set at 500 nm (55 and 35 degrees), were obtained after pupil dilation preoperatively and at each FU examination.

OCT and B-FAF Imaging Analysis

Two experienced graders (F.V. and A.D'A.) independently assessed the preoperative OCT images, whereas 2 other graders (M.A. and G.R.), who were blinded to the preoperative findings and the timing of FU, evaluated the postoperative images. Any disagreements in their assessments were resolved by a fifth senior grader (P.C.), who was also masked to the details.

The presence or absence of outer retinal corrugations (ORCs) and ORFs were determined based on their detection or absence in the macular area on OCT scans before and after the operation, respectively. Specifically, on the basis of OCT features, ORCs are defined as undulations or folds of the detached outer retina involving the outer nuclear layer, the ELM, EZ, and interdigitation zone, forming as a consequence of lateral expansion of the outer retina relative to the inner layers (Fig 1). Outer retinal folds are defined as hyperreflective lesions consisting of folded ELM, EZ, and interdigitation zone visible on reattached retina and often located in correspondence of sites featuring ORCs on detached retina (Fig 2).

The status of the ELM and EZ lines was categorized as either continuous or discontinuous.

The height of detachment was manually measured using the caliper function integrated into the Spectralis software. This involved drawing a line from the outer border of the retina at the fovea perpendicularly to the retinal pigment epithelium (Fig 1).

The evaluation of postoperative retinal displacement was based on the identification of retinal vessel printings (RVPs)[1] in B-FAF images (Fig 2).

The preoperative OCT images were further analyzed to identify biomarkers indicative of mVCRs, such as the presence of a preretinal hyperreflective layer (PHL) and a saw-toothed aspect of the

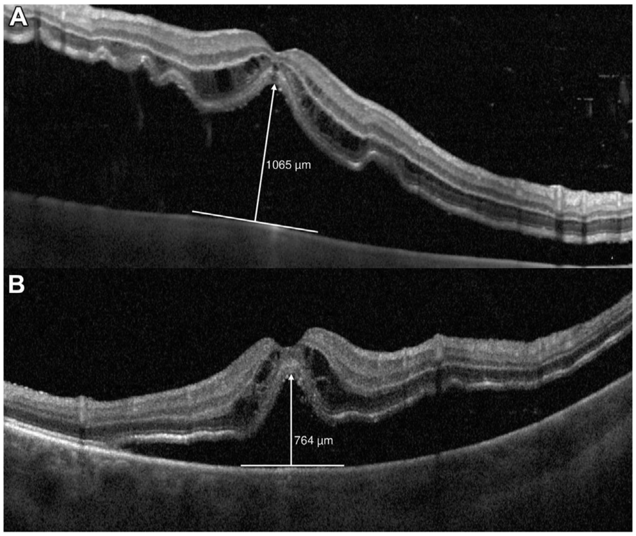

Figure 1. A, B, Representative examples of how the measurement of the height of detachment was calculated on OCT scans: a line was manually drawn from the outer border of the retina at the fovea perpendicularly to the retinal pigment epithelium using the caliper function integrated into the Spectralis software which automatically provided the measured distance in μm. Note the undulations of the outer retina involving the outer nuclear layer, the external limiting membrane, the ellipsoid, and interdigitation zones, defined as outer retinal corrugations.

retinal surface (SRS), as recently described.[13] To briefly explain, PHL is characterized by a fine, discrete line of increased reflectivity that adheres to the inner limiting membrane without any signs of wrinkling of the underlying retina and without the presence of hyporeflective spaces between the PHL and the inner limiting membrane. On the other hand, SRS is defined as a corrugation of the inner retinal surface that is not associated with an overt PHL.

Surgical Technique

All eyes underwent surgical management with either 25G or 23G PPV using the Constellation Vision System (Alcon). A noncontact wide-angle viewing system (Resight Fundus Imaging System, Carl Zeiss Meditec AG) was employed for visualization during the procedures, which were performed by a single surgeon (R.d'O.).

After inducing local anesthesia by peribulbar injection of a mixture of 4% lidocaine and bupivacaine, before vitrectomy, phacoemulsification and intraocular lens implantation were carried out for all phakic eyes using the same surgical platform. After achieving complete vitreous separation and performing core/peripheral vitrectomy, 0.5 mL of triamcinolone acetonide (Triesence 40 mg/mL, Alcon Laboratories, Inc) was injected into the vitreous cavity. The presence of VCRs was determined by gently scraping the retinal surface with a disposable nitinol loop (Alcon Grieshaber 25G Finesse Flex Loop, Alcon). If VCRs were detected, they were meticulously removed from the surface of the detached retina, both at the macula and in the periphery, using the nitinol loop. Because deemed potentially risky, removal of VCRs on attached peripheral retina was neither attempted nor carried out.

Perfluorocarbon liquid was used at the surgeon's discretion after staining and removing the VCRs. In all cases, an air/fluid exchange was performed with drainage of the subretinal fluid (SRF) from the original peripheral retinal break(s). In no cases additional posterior or peripheral retinotomies to drain the residue SRF were performed. Then, either 20% sulfur hexafluoride gas or silicone oil (SO) with a viscosity of 1000 centistokes were used as an internal tamponade. In general, SO was the preferred choice over gas in cases of PVR C and in eyes with multiple breaks in the upper and lower quadrants. After completion of the procedure,

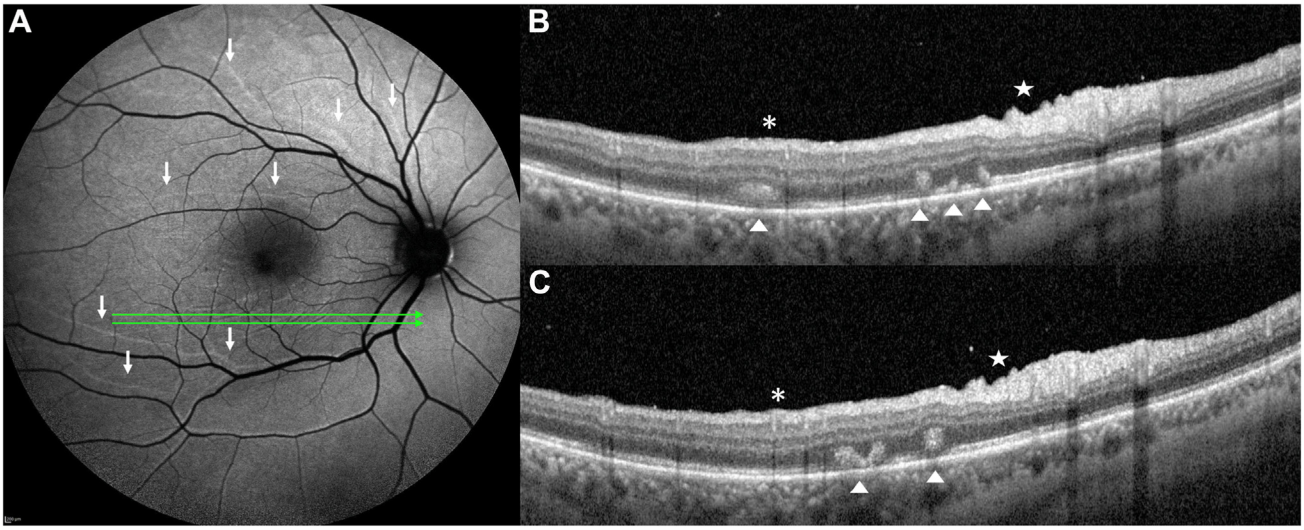

Figure 2. Blue fundus autofluorescence (B-FAF) and OCT scans of a 62-year-old man who underwent pars plana vitrectomy (PPV) and sulfur hexafluoride 20% tamponade for fovea-off rhegmatogenous retinal detachment. One month after PPV, B-FAF image (**A**) showed lines of increased autofluorescence running parallel and superior to corresponding retinal vessels (white arrows), defined as retinal vessel printings, indicating downward displacement of the reattached retina. Inferotemporally to the macula, thick sharply demarcated lines of decreased autofluorescence, showing a caliber and orientation not related with adjacent retinal vessels, are visible. The green arrows on B-FAF image show the location and direction of the OCT scans. OCT scans (**B, C**) showed hyperreflective lesions formed by the folded hyperreflective bands constituted by the external limiting membrane, ellipsoid zone, and interdigitation zone and defined as outer retinal folds (arrowheads) corresponding to the lines of decreased autofluorescence visible on B-FAF image. Note the preretinal hyperreflective layer (asterisk) and the saw-toothed aspect of the retinal surface (star) on the inner retinal surface.

regardless of the tamponade agent and the location of the breaks, all patients were asked to keep a prone posture while moving from the operating trolley to an adjacent wheel chair (with no transition through upright) and instructed to maintain a face-down position strictly for 24 hours after the operation.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation along with a 95% confidence interval, whereas categorical variables were expressed as absolute frequency and percentage. The comparison between the absence and presence of ORFs was assessed using the z-proportion test, whereas the comparison between the absence and presence of ORCs and factors such as age, AXL, and height of detachment was evaluated using the Brunner−Munzel test.

The analysis of repeated measures of BCVA was conducted using the GLIMMIX (Generalized Linear Mixed Model) with a gamma link function, and post hoc analysis was performed using the Tukey method. The normality of the residuals was assessed using the Shapiro−Wilk test and by examining the Q-Q plot, whereas homoscedasticity was verified by inspecting the studentized residuals.

Univariable and multivariable logistic and linear regression analyses, employing a backward selection method, were employed to assess the associations between various variables (including detachment onset, quadrants of detachment, fovea status, PVR grade, preoperative ORCs, intraoperative detection of mVCRs/pVCRs, intraoperative use of perfluorocarbon liquid [PFCL], and type of tamponade) that could potentially influence the rates of RVPs, ORFs, and ELM/EZ discontinuity. The results of logistic regressions were expressed as odds ratios with 95% confidence intervals and *P* values (adjusted using the false discovery rate test by Benjamini−Hochberg for multivariable logistic regression analyses), whereas the results of linear regressions were presented as beta ± standard error with 95% confidence intervals and *P* values. The agreement between graders was assessed using Gwet's AC1 coefficient.

The statistical analysis was conducted using SAS v.9.4 TS level 1M8 (SAS Institute Inc). A P value < 0.05 was considered statistically significant.

Results

All 103 participants enrolled in this study were fovea-off cases, with an estimated mean duration of fovea-off of 12.2 ± 14.9 days on the basis of subjective impression of the patients. Among these participants, 70 of 103 (68%) were male, with a mean age of 63.7 ± 10.5 years. Before the operation, 68% of participants were phakic. The mean AXL was 24.6 ± 1.9 mm, and the mean number of breaks was 2.3 ± 1.7.

Detachment involved only the superior quadrants in 17 (16.5%) eyes, only the inferior quadrants in 14 (13.6%) eyes, and both superior and inferior quadrants in 72 (69.9%) eyes. The mean number of detached quadrants was 2.8 ± 0.9. Proliferative vitreoretinopathy was grade 0 in 8 (7.8%) cases, grade A in 26 (25.2%) cases, grade B in 57 (55.3%) cases, and grade C in 12 (11.7%) cases. The height of detachment at the fovea ranged from 35 to 2210 μm, with a mean of 976.2 ± 708.7 μm.

Outer retinal corrugations were observed in 88 (85.4%) of the eyes. No relationship was found between ORCs and age or AXL ($P = 0.75$, $P = 0.45$, respectively). However, ORCs were significantly related to the height of detachment at the fovea ($P < 0.0001$).

During the intraoperative procedure, pVCRs were discovered in 42 eyes (40.8%). They were successfully peeled off from 1 quadrant in 5 eyes, from 2 quadrants in 19 eyes, from 3 quadrants in 12 eyes, and from all 4 quadrants in 6 eyes. Preoperatively, on the basis of OCT sections of the macula, SRS was found in 58 eyes (56.3%) and PHL in 71 eyes (68.9%), whereas mVCRs were detected intraoperatively in 37 eyes (35.9%). Sensitivity and specificity of macular SRS and PHL for the intraoperative detection of mVCRs were 89.1% and 62.1%, and 94.5% and 45.4%, respectively. Macular VCRs were successfully removed from the macula up to the main arcades in 29 of 37 eyes (78.4%). Peeling of the mVCRs took (mean ± standard deviation) 2.3 ± 1.2 minutes (Video S1, available at www.ophthalmologyretina.org), whereas removal of peripheral pVCRs took (mean ± standard deviation) 31.1 ± 15.4 minutes.

Perfluorocarbon liquid was employed in 54 eyes (52.4%). At the conclusion of the operation, 46 eyes (44.7%) were tamponaded with SF_6 20%, whereas 57 eyes (55.3%) received SO with a viscosity of 1000 centistokes. The SO was removed approximately 64 ± 17 days after the initial operation. None of the patients included in the study had SO tamponade at the 6-month FU visit.

In the first month postoperatively retinal displacement, as indicated by the presence of RVPs on B-FAF (Fig 2), was observed in 25 eyes (24.3%). Among these, 19 were tamponaded with gas, and 6 were tamponaded with SO. The rate of displacement was 41.3% in the eyes tamponaded with gas and 10.5% in the eyes tamponaded with SO. Univariate logistic regression analysis showed no statistically significant association between retinal displacement and the presence of pVCRs ($P = 0.58$) or the number of quadrants from which pVCRs were peeled off ($P = 0.39$). The only variable that exhibited a statistically significant association with retinal displacement on multivariable analysis was the choice of gas tamponade versus SO ($P = 0.001$, Table 1).

A post hoc power analysis, calculated with respect to the relationship between peeling of pVCRs and unintentional displacement, was 20%.

One month postoperatively, ORFs were detected in 24 eyes (23.3%). The intergrader agreement for determining the presence or absence of ORFs between the 2 masked readers was very good, with a Gwet's AC1 coefficient of 0.85 (0.81−0.95).

All 24 eyes that exhibited postoperative evidence of ORFs had shown ORCs on OCTs recorded preoperatively. Overall, ORFs were observed in 27.3% of the eyes that had demonstrated ORCs preoperatively.

Multivariable logistic regression analysis revealed a direct association between the presence of ORFs and the intraoperative detection of mVCRs ($P = 0.02$) and the height of detachment ($P = 0.042$). Additionally, there was an indirect association between the presence of ORFs and the intraoperative use of PFCL ($P = 0.039$) and the peeling of mVCRs ($P = 0.004$, Table 1).

Among the 29 eyes that underwent mVCRs peeling (25 of which had ORCs preoperatively), only 6 (20.7%) developed ORFs postoperatively. On the other hand, 4 of 8 eyes in which ORCs were detected preoperatively, and mVCRs were intraoperatively found but not peeled off, developed ORFs (Figs 3, 4).

The post hoc power analysis, with respect to the relationship between peeling of mVCRs and incidence of ORFs, was 72%.

One month after the operation, continuous ELM and EZ were observed in 46 eyes (44.7%) and 23 eyes (22.3%), respectively. Six months after the operation, continuous ELM and EZ were observed in 63 (61.2%) eyes and 56 (54.4%) eyes, respectively.

Table 1. Univariable and Multivariable Logistic Regression Examining Factors Associated with Unintentional Retinal Displacement and with Outer Retinal Folds at the Macula Observed at 1 Month after Operation

Unintentional Retinal Displacement					**Outer Retinal Folds**				
Variable	*Univariable Analysis Odds Ratio (95% CI)*	P	*Multivariable Analysis Odds Ratio (95% CI)*	P*	*Variable*	*Univariable Analysis Odds Ratio (95% CI)*	P	*Multivariable Analysis Odds Ratio (95% CI)*	P*
PFCL					PFCL				
Yes vs. no	0.33 (0.13–0.85)	**0.02**	0.53 (0.19–1.49)	0.56	*Yes vs. no*	0.36 (0.14–0.94)	**0.036**	0.25 (0.08–0.74)	**0.039**
Tamponade type					Tamponade type				
Gas vs. silicone oil	5.98 (2.14–16.74)	**0.0007**	5.98 (2.14–16.74)	**0.001**	*Gas vs. silicone oil*	2.06 (0.81–5.20)	0.13	–	–
Intraoperative detection of pVCRs					Intraoperative detection of mVCRs				
Yes vs. no	0.77 (0.30–1.95)	0.58	–	–	*Yes vs. no*	8.32 (1.23–48.20)	**0.021**	9.04 (1.54–52.99)	**0.02**
Quadrants of RRD	0.81 (0.49–1.32)	0.39	–	–	Height of detachment at the fovea	1.001 (1.00–1.002)	**0.005**	1.001 (1.001–1.002)	**0.042**
Peeling of pVCRs n° of quadrants	1.12 (0.80–1.55)	0.52	–	–	Preoperative ORCs				
PVR_grade	0.72 (0.41–1.29)	0.27	–	–	*Yes vs. no*	6.32 (0.05–76.89)	0.96	–	–
					Peeling of mVCRs				
					Yes vs. no	0.08 (0.01–0.78)	**0.002**	0.10 (0.01–0.70)	**0.004**

Bold indicates statistical significance.
CI = confidence interval; mVCR = macular vitreous cortex remnant; ORC = outer retinal corrugation; PFCL = perfluorocarbon liquid; pVCR = peripheral vitreous cortex remnant; PVR = proliferative vitreoretinopathy; RRD = rhegmatogenous retinal detachment.
*False discovery rate adjusted.

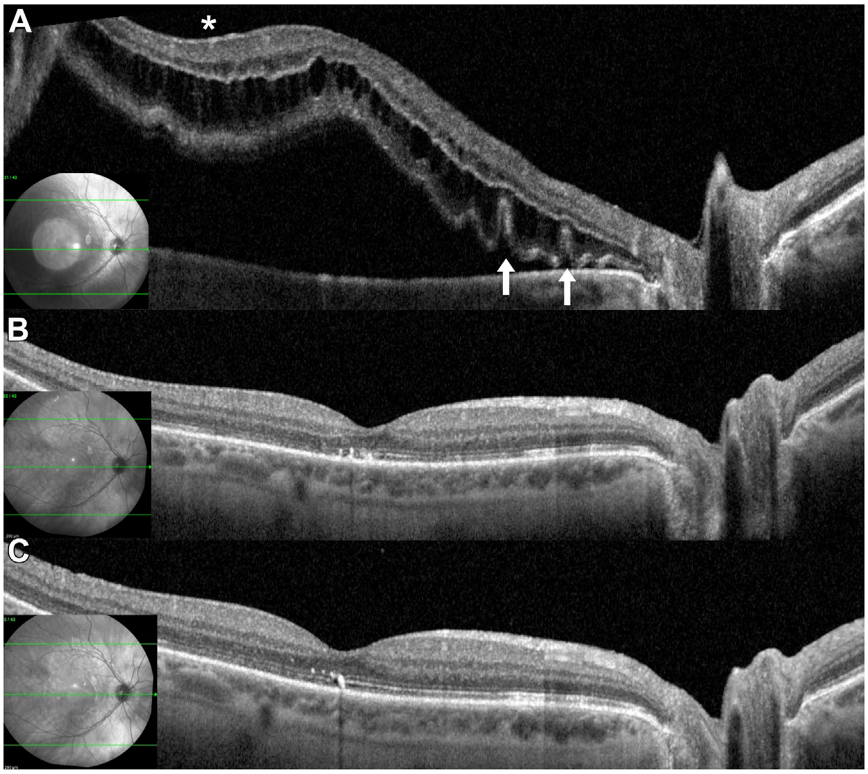

Figure 3. OCT scans of a 58-year-old woman who underwent pars plana vitrectomy (PPV) and sulfur hexafluoride 20% tamponade for fovea-off rhegmatogenous retinal detachment. Intraoperatively, macular vitreous cortex remnants were detected and removed from the macula. **A**, Preoperative OCT scan showed a hypereflective preretinal layer temporally to the fovea (asterisk) and outer retinal corrugations at the nasal aspect of the macula (white arrows). Logarithm of the minimum angle of resolution best-corrected visual acuity (BCVA) was 0.5. **B**, OCT scan at 1 month after PPV and peeling of macular vitreous cortex remnants showed a reattached retina, discontinuous external limiting membrane (ELM) and ellipsoid zone (EZ) at the fovea, and flat ELM and EZ bands at the site where ORCs had been detected. **C**, OCT scan at 6 months after operation showed partial recovery of ELM and EZ continuity at the fovea. The retinal surface appeared smooth without evidence of inner retinal dimplings. Logarithm of the minimum angle of resolution BCVA improved at 0.1. The green arrows on infrared pics show the location and direction of the OCT scans.

At 1 month postoperation, a continuous ELM was directly correlated with the use of gas tamponade ($P = 0.001$) and inversely correlated with the height of detachment ($P = 0.008$; Table S2, available at www.ophthalmologyretina.org). However, at the 6-month FU, no statistical association was found with the same variables.

At 1 month postoperatively, continuous EZ was correlated with the intraoperative presence of mVCRs ($P = 0.03$) and inversely correlated with mVCRs peeling ($P = 0.009$; Table S2, available at www.ophthalmologyretina.org). At 6 months, the continuity of the EZ was inversely associated with the height of detachment ($P = 0.038$).

The interreader agreement for evaluating the continuity/discontinuity of ELM and EZ between the 2 masked readers was very good, with Gwet's AC1 coefficient measuring 0.81 (0.78−0.98).

During the 6-month FU, macular edema was observed in 13 eyes, epiretinal membrane (ERM) in 17 eyes, and both conditions were present in 2 eyes, totaling 32 cases (31%). Specifically, ERM was observed in 6 of 8 eyes with intraoperatively detected mVCRs that were not removed, in 4 of 29 eyes where mVCRs were peeled, and in 9 of 66 eyes with no intraoperative evidence of mVCRs.

In the multivariable regression analysis, the only variable associated with the presence of ERM, macular edema, or both was the intraoperative use of PFCL ($P = 0.045$).

The mean logMAR BCVA was 1.5 ± 1.0 preoperatively, and it improved to 0.5 ± 0.4 at 1 month of FU and further to 0.3 ± 0.3 at 6 months of FU ($P < 0.0001$).

The variables associated with logMAR BCVA ≤0.3 (equivalent to 20/40 or better) were a continuous ELM ($P = 0.007$) and the intraoperative absence of mVCRs ($P = 0.028$) at 1 month and the intraoperative absence of mVCRs ($P = 0.0016$), peeling of mVCRs ($P = 0.003$), a continuous ELM ($P = 0.04$), and the intraoperative use of gas tamponade ($P = 0.01$) at 6 months postoperation (Table 3).

Discussion

In this study, we examined the impact of VCRs, in conjunction with other factors, on the postoperative normal anatomy of the retina in eyes that underwent PPV to repair RRD.

Our findings revealed that peeling pVCRs did not have an impact on the rate of unintentional retinal displacement; this phenomenon was primarily linked to the choice of tamponade used.

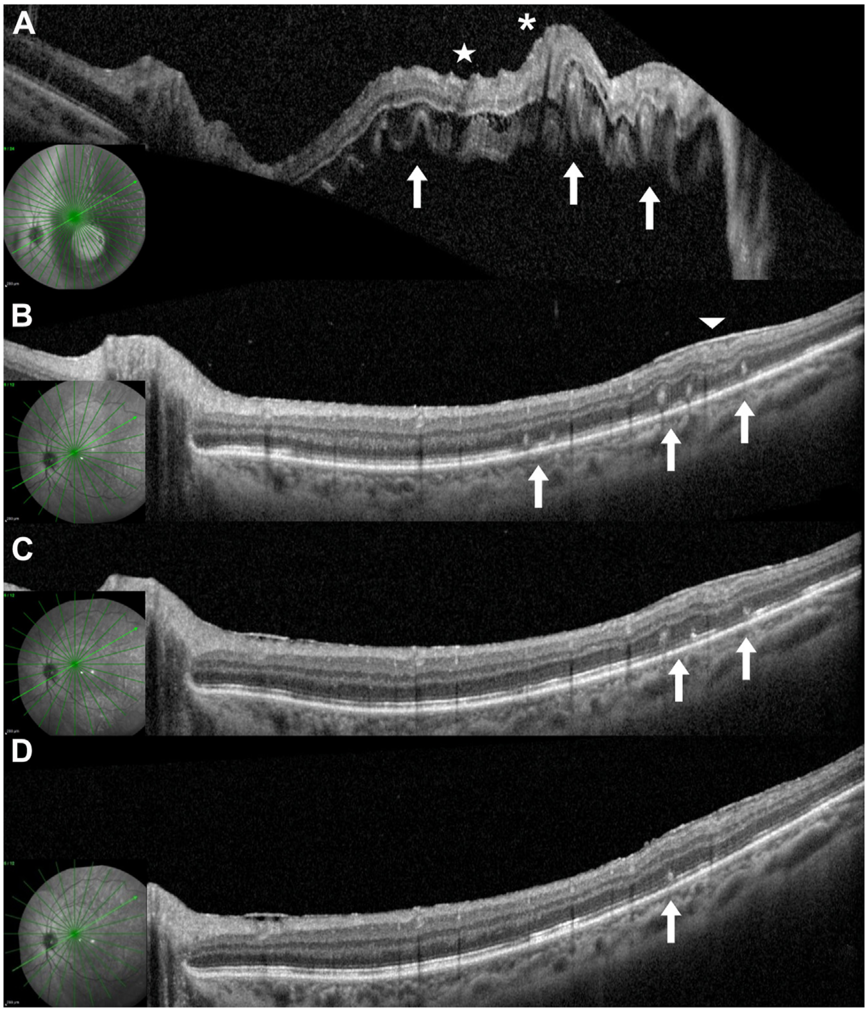

Figure 4. OCT scans of a 67-year-old woman who underwent pars plana vitrectomy (PPV) and sulfur hexafluoride 20% tamponade for fovea-off rhegmatogenous retinal detachment. Intraoperatively, macular vitreous cortex remnants were detected but their removal was deemed risky because of the tenacious adherences with the underlying retina and not carried out. **A**, Preoperative OCT scan showed preretinal hyperreflective layer (asterisk), saw-toothed aspect of the retinal surface (star) and outer retinal corrugations (white arrows). **B**, OCT scan at 1 month after PPV showed multiple outer retinal folds (ORFs, white arrows) which appear concentrated and higher in correspondence of an epiretinal membrane (ERM, white arrowhead). **C**, Three months after operation only the ORFs underneath the ERM are visible (arrows), whereas the others have resolved. **D**, Six months after operation, a subtle ORF (arrow) underneath the ERM is still visible. The green arrows on infrared images show the location and direction of the OCT scans.

On the contrary, peeling mVCRs was associated with a reduced risk of postoperative ORFs development. The peeling of mVCRs did not adversely impact the continuity of the ELM/EZ at the 6-month FU. Patients who did not have mVCRs detected intraoperatively, or who underwent mVCRs peeling during the operation, exhibited a statistically better VA at the 6-month FU.

Vitreous cortex remnants refer to the outermost lamellae of the posterior vitreous cortex that remain attached to the retina due to anomalous vitreous cortex detachment.[11] Currently, it remains uncertain whether the removal of VCRs in eyes with primary RRDs may yield long-term anatomic and functional benefits. Some authors have proposed that peeling VCRs may reduce the rate of ERM development[11] and redetachment caused by PVR,[11,17,18] whereas others have challenged this assumption. They reported that keeping VCRs does not seem to affect the initial success rate of PPV or the growth of PVR or ERM.[19,20]

In addition to addressing single-operation success and the development of macular ERM after surgery, there is a growing interest in the field of RRD repair regarding the restoration of normal retinal anatomy after reattachment through high-resolution multimodal imaging.[21]

In the present study, our objective was to prospectively assess whether the presence and removal of VCRs could impact the postoperative restoration of normal retinal anatomy. We specifically concentrated on the following abnormalities: unintentional displacement, as revealed by RVPs detected on B-FAF, and the presence of ORFs as well as the

Table 3. Univariable and Multivariable Linear Regression Examining Factors Associated with Best-Corrected Visual Acuity at 6 Months after Operation

Variable	Univariable Analysis Beta ± SE; (95% CI)	*P*	Multivariable Analysis Beta ± SE; (95% CI)	*P*
Intraoperative detection of mVCRs				
Yes vs. no	0.35 ± 0.09; (0.17–0.53)	**0.001**	0.32 ± 0.10; (0.13–0.52)	**0.0016**
Peeling of mVCRs				
Yes vs. no	−0.28 ± 0.08; (−0.44 to −0.12)	**0.001**	−0.32 ± 0.10; (−0.52 to −0.11)	**0.003**
Tamponade type				
Gas vs. silicone oil	−0.21 ± 0.07; (−0.34 to −0.08)	**0.002**	−0.16 ± 0.06; (−0.28 to −0.03)	**0.01**
Continuous ELM				
Yes vs. no	−0.22 ± 0.07; (−0.35 to −0.09)	**0.001**	−0.18 ± 0.09; (−0.36 to −0.006)	**0.04**
Continuous EZ				
Yes vs. no	−0.19 ± 0.07; (−0.32 to −0.06)	**0.005**	−0.04 ± 0.09; (−0.22 to 0.14)	0.66
PFCL				
Yes vs. no	0.09 ± 0.07; (−0.04 to 0.23)	0.17	–	–
Height of detachment at the fovea	0.00008 ± 0.00005; (−0.00002 to 0.00002)	0.11	–	–

Bold indicates statistical significance.
CI = confidence interval; ELM = external limiting membrane; EZ = ellipsoid zone; mVCR = macular vitreous cortex remnant; PFCL = perfluorocarbon liquid; SE = standard error.

continuity of ELM/EZ lines, as evaluated through OCT images.

Unintentional retinal displacement refers to the reattached retina being positioned differently from its original location due to retina stretching.[21,22] The degree of retinal stretching is influenced by several factors, including gravity, surgical techniques, postoperative head positioning, the size and physical properties of the tamponade, and the biomechanical properties of the neuroretina that can be viewed as an anisotropic and viscoelastic membrane[23] characterized by a brief elastic phase followed by a considerably extensive plastic phase marked by irreversible deformation.[24]

In eyes with RRD, the retina can undergo irreversible stretching due to the presence of a substantial amount of SRF and as a result of the iatrogenic flow of SRF under the pressure exerted by a tamponade. Factors such as surface tension, buoyant force, and the volume of the tamponade[25,26] play crucial roles in influencing the severity of retinal stretching and, consequently, the degree of displacement.

Retinal displacement in eyes undergoing PPV can be minimized through immediate prone positioning[1,22,27,28] and by the use of SO instead of gas,[22,29,30] because of distinct physical properties of SO (higher specific gravity, lower interfacial tension, and lower buoyancy force) compared with gas.[31,32]

The impact of PFCL on the incidence of retinal displacement after RRD repair remains uncertain. However, the majority of studies have found no significant correlation between retinal displacement and the use of PFCL.[4,22,25,27,28,33]

In this study, intraoperative PFCL was utilized in 52.4% of the operated eyes, 44.7% were tamponaded with SF6 20%, and 55.3% with SO 1000 centistokes. All patients were instructed to assume a prone position immediately after the operation and maintain it for ≥24 hours. Retinal displacement was observed in 41.3% of the eyes tamponaded with gas and 10.5% of the eyes tamponaded with SO. In the multivariable regression analysis, the use of gas versus SO was the sole factor statistically associated with displacement ($P = 0.001$).

Originally, we had hypothesized that the removal of pVCRs might alter the elastic properties of the retina, potentially influencing the rate of displacement. In fact, during the operation, surgeons often perceive that the retina becomes less rigid once freed from pVCRs. However, after stratifying for the number of detached quadrants and the number of quadrants from which pVCRs were peeled off, no association was found between the presence of displacement (as revealed by RVPs) and pVCRs peeling. Therefore, in accordance with previous observations[22,29] and recently developed mathematical models,[30] the only relevant factor for displacement in eyes undergoing PPV for RRD seems to be the use of gas.

There is another form of retinal displacement which occurs in eyes treated for RRD and that is more subtle compared with that revealed by the presence of RVPs. This displacement is secondary to the formation of ORFs.[34] Since ORFs result from the folding of the outer retinal layers, the adjacent parts of the outer retina must undergo compensatory displacement.

As a consequence, the occurrence of ORFs, characterized by photoreceptor apposition from base to base and compensatory displacement of the adjacent photoreceptors, might be responsible for structural abnormalities of the outer retina, persisting even after an apparent restoration of the normal retinal anatomy on OCT images.

These abnormalities may, in turn, account for functional impairments such as postoperative metamorphopsia and reduced VA. For instance, Fukuyama et al[35] demonstrated that the density of ORFs at 6 months after the operation is associated with quantitative metamorphopsia, as determined using M-CHARTS.

More recently, a subgroup analysis of the PIVOT study, which included only patients who underwent PPV, revealed that the mean ETDRS score at 1 year was significantly better in patients without ORFs ($P = 0.04$).[36]

Therefore, decreasing the incidence of postoperative ORFs may lead to improved anatomic and functional outcomes. Outer retinal folds typically develop at the location of ORCs which are thought to occur as a result of cystoid degeneration of the retina, intraretinal proliferation, alterations in the photoreceptor cytoskeleton, variations in the hydration of the interphotoreceptor matrix between the outer and inner retina, and softening of the outer retina compared with the inner retina.[36–40]

Recently, Melo et al[41] proposed a mathematical model suggesting that in eyes with RRD, the reduction in the modulus of elasticity of the outer retina, combined with intrinsic compressive forces likely generated by hydration and lateral expansion, leads to the formation of ORCs. The frequency of ORCs for a given lateral expansion of the outer retina is determined by a competition between the bending energy of the outer retina and the elastic energy of the inner retina.[41]

In this study, we aimed to investigate whether peeling mVCRs could modify the elasticity of the inner retina and, as a result, change the elasticity ratio between the inner and outer retina, potentially reducing the likelihood of developing ORFs. Multivariable regression analyses revealed that 4 variables were statistically associated with ORFs detected at 1 month postoperatively: intraoperative use of PFCL, mVCRs peeling (indirect association for both), presence of mVCRs, and the height of detachment (direct association for both). The variable most strongly associated with ORFs was mVCRs peeling ($P = 0.004$, Table 1). Therefore, we hypothesize that by removing mVCRs, which may reduce the rigidity of the inner retina, there may be a significant contribution to equalizing the elasticity moduli of the inner and outer retina. This could favor the flattening of the ORCs and, consequently, reduce the likelihood of ORFs development.

Although additional surgical maneuvers to peel mVCRs may reduce the rate of postoperative ORFs, they do not seem to have a negative impact on the continuity of the ELM or EZ on the long term. In fact, we did not observe a higher rate of discontinuity of ELM or EZ at the 6-month postoperative visit in the eyes which underwent mVCRs peeling. Moreover, mVCRs peeling was associated with improved VA recovery at 6 months after the operation ($P = 0.003$, Table 3). Peeling of mVCRs can be usually carried out in few minutes, and is a safe and quite easy procedure when using a retractable loop with adjustable bending stiffness and designed for controlled penetration into the inner limiting membrane, like the one we used in this study. However, we acknowledge that sometimes mVCRs may be tightly adherent to the underlying retina and attempts to peel them may cause retinal breaks in such cases. Indeed, peeling was not performed in 8 eyes of this series because strong attachments between mVCRs and retinal surface were found.

Taken together, these results suggest that mVCRs removal may be advisable in eyes with fovea-off RRD, as it contributes to better anatomic recovery of the retina and improved functional outcomes in terms of VA.

We acknowledge the limitations of this study, including the relatively small sample size analyzed, the limited FU period of 6 months, and the absence of randomization for the peeling of VCRs. Another limitation is that we recorded 55-degree images and we did not use an ultrawidefield camera to acquire FAF images, thus, we potentially underestimated the displacements that affected exclusively the peripheral retina. Furthermore, the use of an ultrawidefield camera would have allowed for an accurate assessment of the magnitude and direction of retinal displacement, although we only categorized displacement as present/absent on the basis of RVPs evidence. Similarly, ORFs were simply categorized as present or absent without considering their number, distance from the fovea, and height.

The strengths of this study include its prospective design and the evaluation of the potential impact of VCRs peeling on normal retinal anatomy recovery. To the best of our knowledge, this is the first study exploring the potential importance of mVCRs peeling to reduce the rate of postoperative ORFs formation possibly by modifying the elasticity modulus ratio between the inner retina and outer retina. However, we do acknowledge that our results are preliminary and our hypothesis needs further studies to be proven. With respect to the relationship between peeling of pVCRs and unintentional displacement, the post hoc power analysis calculated was only 20%, thus no definitive conclusions can be drawn on the basis of this work and further studies recruiting a larger number of patients are warranted to establish if peeling of pVCRs influences the unintentional displacement.

In conclusion, this study shows that in eyes with RRD, peeling of pVCRs does not seem to impact the rate of unintentional displacement and peeling of mVCRs is associated with a reduced risk of postoperative ORFs formation and does not adversely affect the continuity of ELM and EZ lines at the 6-month FU. The absence of mVCRs and the peeling of mVCRs are both associated with significantly better VA at 6 months after the operation.

Future prospective and larger clinical trials should be conducted to further elucidate the long-term anatomic and functional differences between PPV for RRD repair with or without VCRs peeling.

Footnotes and Disclosures

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HUMAN SUBJECTS: Human subjects were included in this study. All subjects received treatment in accordance with the Declaration of Helsinki. We obtained approval from the Institutional Review Board of the University of Molise. Patients provided written informed consent after receiving a detailed description of the surgical procedure.

No animal subjects were used in this study.

Author Contributions:

Conception and design: dell'Omo

Data collection: dell'Omo, Cucciniello, Affatato, Rapino, D'Albenzio, Venturi

Analysis and interpretation: dell'Omo, Cucciniello, Affatato, D'Albenzio, Venturi, Campagna

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Overall responsibility: dell'Omo, Rapino, Campagna

Abbreviations and Acronyms:

AXL = axial length; **BCVA** = best-corrected visual acuity; **B-FAF** = blue fundus autofluorescence; **ELM** = external limiting membrane; **ERM** = epiretinal membrane; **EZ** = ellipsoid zone; **FU** = follow-up; **logMAR** = logarithm of the minimum angle of resolution; **mVCR** = macular vitreous cortex remnant; **ORC** = outer retinal corrugation; **ORF** = outer retinal fold; **PFCL** = perfluorocarbon liquid; **PHL** = preretinal hyperreflective layer; **PPV** = pars plana vitrectomy; **pVCR** = peripheral vitreous cortex remnant; **PVR** = proliferative vitreoretinopathy; **RRD** = rhegmatogenous retinal detachment; **RVP** = retinal vessel printing; **SO** = silicone oil; **SRF** = subretinal fluid; **SRS** = saw-toothed aspect of the retinal surface; **VA** = visual acuity; **VCR** = vitreous cortex remnant.

Keywords:

Rhegmatogenous retinal detachment, Vitreous cortex remnants, Pars plana vitrectomy, Retinal anatomical integrity, OCT.

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