

Optical coherence tomography evaluation of patients with macula-off retinal detachment after different postoperative posturing: a randomized pilot study

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ABSTRACT.

Purpose: To assess the presence of outer and inner retinal folds (RFs) and drop-out of the ellipsoid zone (EZ) occurring after surgical repair of macula-off rhegmatogenous retinal detachment (RRD) with different postoperative posture and preoperative use of adjuvant perfluorocarbon liquid (PFCO).

Methods: In this prospective study, 56 eyes of 56 consecutive patients affected by RRD were subjected to 23- or 25-gauge pars plana vitrectomy (PPV). The patients were randomized in four groups (14 prone 5 hr without PFCO, 14 supine 5 hr without PFCO, 14 prone 5 hr with PFCO and 14 supine 5 hr with PFCO) and followed up with spectral domain optical coherence tomography (SD-OCT).

Results: Spectral domain optical coherence tomography (SD-OCT) was recorded before surgery, at days 30 and 90 to detect the presence of outer RFs, inner RFs and drop-out of EZ and to follow their variation over time. No statistical significance was found in our groups for outer RFs, inner RFs, drop-out of EZ formation and evolution. The postoperative best-corrected visual acuity (BCVA) improved in all groups (mean preoperative BCVA 1.47 logMar \pm 0.19, mean postoperative BCVA 0.27 logMar \pm 0.11, $p < 0.01$), without statistical variations between the four groups in BCVA after surgery.

Conclusion: The use of adjuvant and variation in postoperative position did not change the risk of presenting outer RFs, inner RFs and drop-out of EZ after RRD.

Key words: optical coherence tomography – pars plana vitrectomy – postoperative posturing – retinal detachment – retinal folds

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Introduction

Rhegmatogenous retinal detachment (RRD) is defined as a separation of the neurosensory retina from the retinal pigment epithelium (RPE), which is

caused by at least one retinal break with subsequent shift of intraocular fluid into the subretinal space. When the macula is involved (macula-off),

patients usually complain of a significant visual loss (Eijk et al. 2016). Surgical techniques to treat this condition can be different, but nowadays the first choice is often represented by pars plana vitrectomy (PPV), especially in pseudophakic patients and if multiple breaks or significant vitreous traction is present (Heimann et al. 2007; Miller et al. 2008; Kobashi et al. 2014; Hajari 2016; Poulsen et al. 2016). Even after successful surgery, patients with macula-off RRD often report visual complaints such as distortion and scotomas in the central visual field, with great variability. Many different morphological macular changes have been found using optical coherence tomography (OCT) imaging, such as drop-out of the ellipsoid zone (EZ) in the macular area or the presence of outer and inner retinal folds (RFs; Hagimura et al. 2000; Lecleire-Collet et al. 2006; Nakanishi et al. 2009; Lai et al. 2010; Sheth et al. 2010; Dell’Omo et al. 2012a; Delolme et al. 2012; Gharbiya et al. 2012; Matlach et al. 2015). Several hypotheses have tried to explain why visual recovery is not complete, but the reason is still unclear.

To investigate whether differences in the detachments characteristics or in the surgical procedures play a role in visual alterations after macula-off RRD, we studied a prospective series of 56 patients who underwent a PPV with

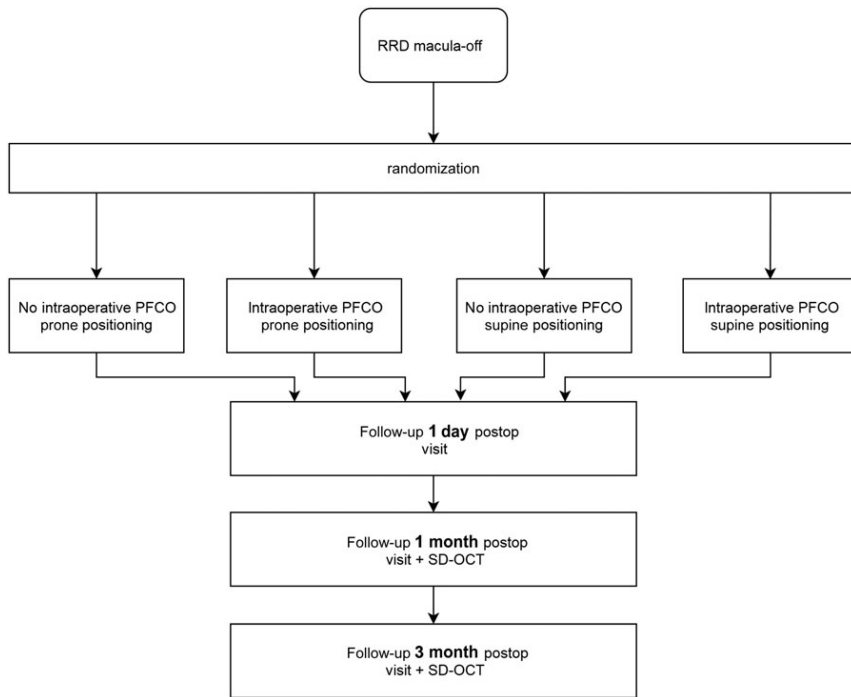


Fig. 1. Flowchart of study participants. PFCO = perfluorocarbon liquid; RRD = rhegmatogenous retinal detachment; SD-OCT = spectral domain optical coherence tomography.

either 23- or 25-gauge technique. Patients were randomized with the use of heavy liquid adjuvant (PFCO) and different postoperative posturing to understand whether there is a correlation with post-surgical retinal folds

formation. Spectral domain optical coherence tomography (SD-OCT) scans were collected at baseline and during the follow-up (1 and 3 months) and related to the final visual changes as well as to the quality of vision after surgery.

Materials and Methods

In this randomized four-arm single-blind pilot study, 56 patients (56 eyes) with primary macula-off RRD involving one or more quadrants were recruited prospectively. They all underwent a successful 23- or 25-gauge PPV performed by four experienced surgeons at the Academic Medical Center (AMC), Amsterdam, the Netherlands. The study protocol was approved by the local institutional review board, and all patients signed an institutional review board-approved informed consent form before any image registration and data analysis. The study adhered to the tenets of the Declaration of Helsinki. Only patients in whom it was possible to obtain a good quality preoperative spectral domain optical coherence tomography (SD-OCT) scan of the macula were enrolled in this study. Patients with any preexisting ocular disease affecting the central vision function and any previous history of retinal surgery or laser therapy were excluded.

Hypothesis of the study was that use of PFCO during the operation and/or immediate postoperative posturing could reduce inner RFs and/or outer RFs formations after macula-off RRD surgical repair.

Table 1. Characteristics of patients included in this analysis. Perfluoron group indicates perfluoron use during surgery; nonperfluoron group indicates no use of perfluoron during surgery. Prone and supine are the positions of patients after the surgery. ± indicates standard deviation.

	Group 1 (prone without perfluoron)	Group 2 (prone with perfluoron)	Group 3 (supine without perfluoron)	Group 4 (supine With perfluoron)
Number of patients, N (%)	14 (25)	14 (25)	14 (25)	14 (25)
Gender, N				
Male	10	10	8	10
Female	4	4	6	4
Age (years)	63 ± 10.634	65 ± 10.505	63 ± 10.954	61 ± 10.842
Days complaints (days)	6.89 ± 6.047	9.31 ± 6.76	6.86 ± 6.032	9.36 ± 6.40
Instrumentation during surgery				
23G	2	2	2	2
25G	12	12	12	12
Quadrants involved				
2	12	4	12	4
3	0	4	2	6
4	2	6	0	4
Lens status				
Pseudophakic	2	8	2	6
Phakic	12	6	12	8
Height of detachment (µm)	782	>1000	938	987
Presence of retina undulations (Yes/no) %	YES (100%)	YES (100%)	YES (100%)	YES (100%)
Thickness of the fovea (µm)				
No 36 patients (others not measurable)	210	276	243	241
Thickening of the photoreceptors (µm)				
No 34 patients (others not measurable)	149	171	139	138

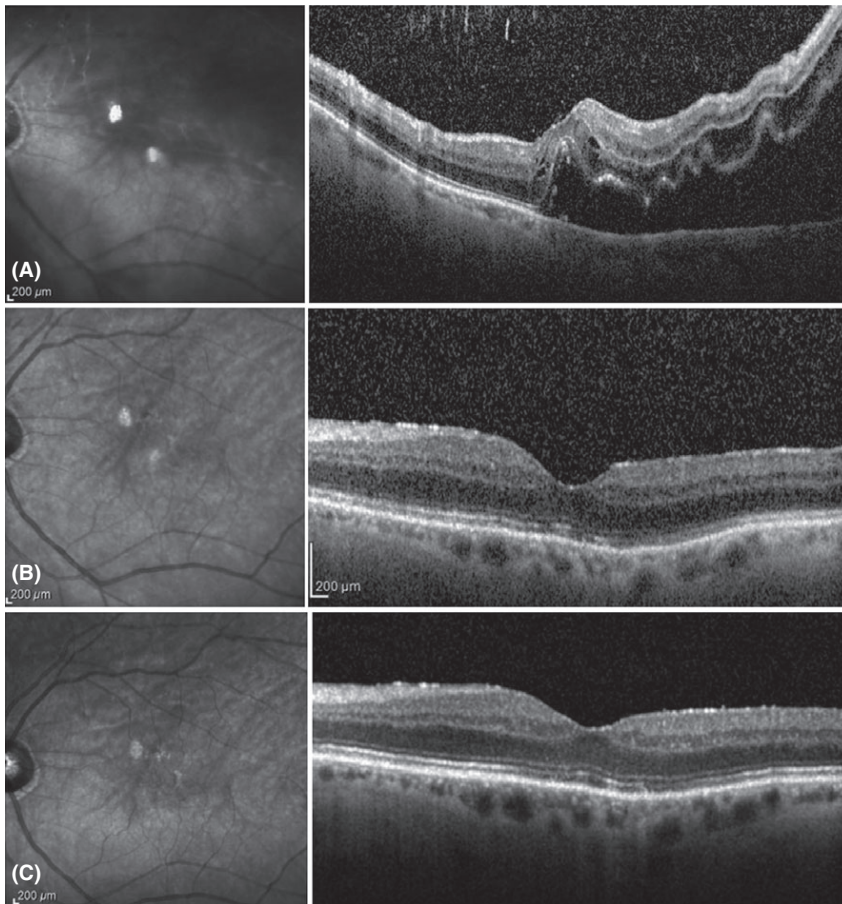


Fig. 2. Patient from group 3 (supine without PFCO). In the upper part of the picture, infrared (IR) shows the area of the superior detachment with macula involvement (A); OCT detected the presence of sub-/intraretinal fluid as well as intraretinal separation and outer retina undulation before surgery. At 1-month follow-up, there is still some micro-intraretinal cyst (B) and at 3-month follow-up, foveal scan appears completely normal (C). Patient recovery 1.0 best-corrected visual acuity.

A complete vitrectomy with relief of all vitreous traction on retinal tears was performed using the Alcon Constellation (Alcon Labs, Fort Worth, TX, USA). After performing complete vitreous removal, particular care was paid to maximal drainage of the subretinal fluid during air–fluid exchange through a preexisting retinal break or through a drainage retinotomy if necessary; then, cryopexy or laser was applied to the single or multiple breaks found in the retina. The use of PFCO was randomized. Twenty per cent of sulphur hexafluoride gas (SF_6) was used as internal tamponade in all cases. Patients were positioned in prone or supine position for 5 hr after surgery depending on the randomization of our series. This position was kept by the patient only 5 hr immediately after surgery to see whether the mechanic pressure of the gas could affect the possible formation of any fold at the posterior pole. The

duration (5 hr) of the positioning was chosen based on results of Quintyn and Brasseur's studies who calculated the rate of egress of subretinal fluid in the human eye through the retinal pigment epithelium as 3.5 ml/day, which is more than 50% of the total volume of vitreous, and on the results of others experimental works who showed that small amount of saline solution injected into the subretinal space of rabbit eye was absorbed within 2–6 hr (Frambach & Marmor 1982; Marmor 1990; Quintyn & Brasseur 2004).

After the 5-hr posturing implied by the randomization, the patient was then requested to keep a further position on the basis of the break position: patients with superior break were kept in sitting position and sleeping at 45 degrees for the following 5 days, patients with temporal or nasal breaks were kept in supine position in the opposite side of the

break at day and night for the following 5 days, and the patients with inferior break were kept in supine position laying in the left or right side at the patients discretion for the next 5 days.

Patients examination was performed at baseline, 24 hr after the operation, at 1 month and finally after 3 months and consisted of best-corrected visual acuity (BCVA) evaluation (logMAR), measurement of the intraocular pressure (Goldmann applanation tonometer) and fundus ophthalmoscopy examination using an indirect +20-dioptre lens and at the slit lamp with a + 90-dioptre lens. At baseline, patients were randomized in four groups (1:1:1:1) depending on the use or not of intraoperative PFCO and on the prone or supine postoperative positioning: Group 1 (14 patients): no intraoperative use of PFCO and prone positioning during the first 5 hr after surgery. Group 2 (14 patients): intraoperative use of PFCO and prone positioning during the first 5 hr after surgery. Group 3 (14 patients): no intraoperative use of PFCO and supine positioning during the first 5 hr after surgery. Group 4 (14 patients): intraoperative use of PFCO and supine positioning during the first 5 hr after surgery. Optical coherence tomography (OCT) images were acquired with the Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany), which combines a confocal scanning laser ophthalmoscope with SD-OCT. The OCT recording protocol consisted of a sequence of 97 horizontal high-resolution sections (1024 A-scans/30°), covering an area of 20° (horizontal) \times 20° (vertical) with a distance of approximately 60 μm between individual sections. Patients were scanned at baseline and at 1- and 3-month follow-up. Infrared pictures (50 degrees) were also obtained at each examination (Fig. 1).

The presence of inner RFs and/or outer RFs such as EZ drop-out in OCT images in the four groups, and the eventual statistically significant difference among the groups, was considered the outcomes of the study.

During the follow-up, metamorphopsia was also evaluated using Amsler grid test as was performed in a previous study (Dell'Omo et al. 2012a).

Statistical analysis was performed using SPSS software (SPSS Inc, Chicago, IL, USA) and MEDCALC version 1.5.1

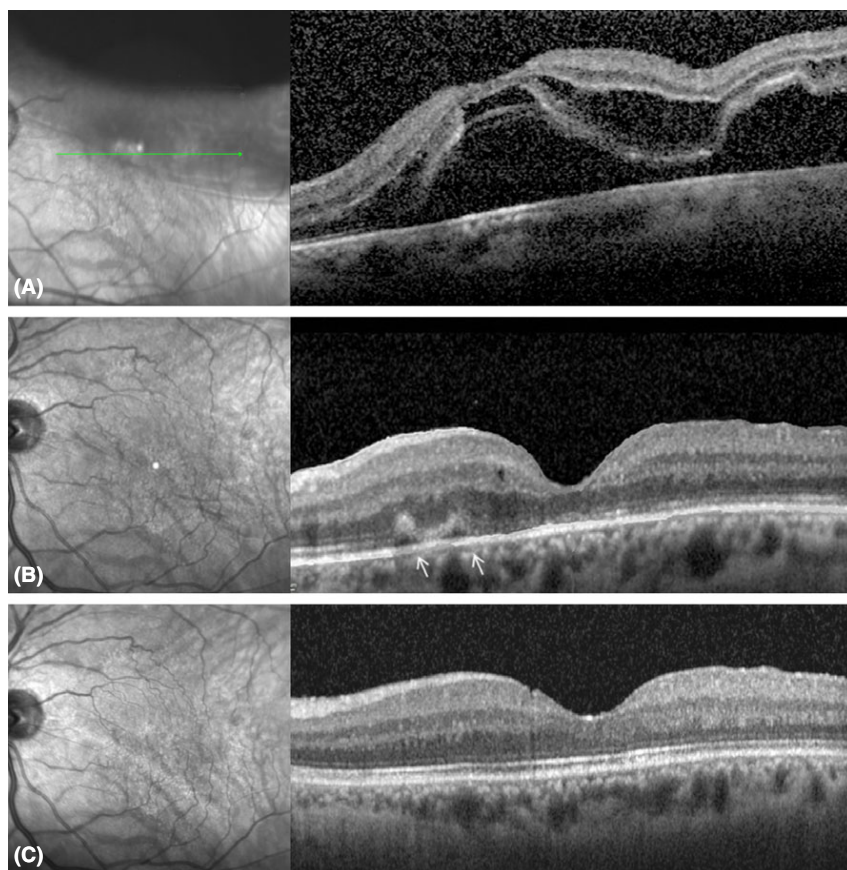


Fig. 3. Patient from group 2 (prone with PFCO). Infrared picture allows to see the detachment with foveal involvement, while OCT defines the presence of sub-/intraretinal fluid as well as intraretinal separation and outer retina undulation (A). Same patient after 1 month revealed on IR the presence of some hyperreflective line, and the OCT better recorded the presence of outer retinal folds (see white arrows in B). After 3 months from operation, the hyperreflective lines are not visible anymore on IR and OCT scan confirmed the disappearance of the retina folds (C).

Table 2. Group 1 prone without PFCO, Group 2 prone with PFCO, Group 3 supine without PFCO, Group 4 supine with PFCO. IRF is inner retinal folds, ORF is outer retinal folds, DO is drop-out of foveal junction. Images for inner and outer retinal folds were obtained by SD-OCT HRA Spectralis.

	Group 1 (mean of 14 patients)	Group 2 (mean of 14 patients)	Group 3 (mean of 14 patients)	Group 4 (mean of 14 patients)
IRF 1 month (No. and % of patients)	2 (14%)	2 (14%)	2 (14%)	0 (0%)
IRF 3 months (No. and % of patients)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ORF 1 month (No. and % of patients)	6 (42%)	4 (28%)	4 (28%)	6 (42%)
ORF 3 months (No. and % of patients)	2 (14%)	2 (14%)	2 (14%)	2 (14%)
DO 1 month (No. and % of patients)	4 (28%)	4 (28%)	4 (28%)	4 (28%)
DO 3 months (No. and % of patients)	0 (0%)	0 (0%)	0 (0%)	2 (14%)

(MedCalc software, Mariakerke, Belgium). Paired *t* tests were used to measure BCVA before and after surgery. One-way ANOVA was used to compare the baseline characteristics, BCVA evaluation and OCT (inner RFs, outer RFs and EZ drop-out presence) data between these groups.

Results

This study included 56 patients (56 eyes), 38 men and 18 women with a mean average \pm standard deviation [\pm SD] age of 63 ± 10.73 . Hundred per cent of patients were examined at baseline, at 1-month and at 3-month

follow-up. Demographic characteristics of the patients including anatomical evaluation of the detachment, mean BCVA, OCT findings and instrumentation for surgery are given in Table 1.

The preoperative characteristics of the RRD and its extension were evaluated for each group (see Table 1). The mean duration [\pm SD] of symptoms and the extension of the RDD were not statistically significantly different between the four groups of patients (8.1 ± 6.3 days, range 1–21 days). Before the surgical procedure, the average of BCVA (\pm SD) was similar in the four groups of patients.

No intraoperative complications were observed. During the 3-month follow-up, no patient experienced redetachments. At baseline, SD-OCT images identified the presence of retina undulations, intraretinal fluid and splitting of the photoreceptors in all 56 (100%) patients (Figs 2A and 3A). The average [\pm SD] height of the retinal detachments (measured manually with the Heidelberg software from the superior edge of the RPE to the inner portion of EZ) at the central fovea was $927 \pm 100 \mu\text{m}$ (ranged from 462 to $>1000 \mu\text{m}$). The thickening of the fovea was measured in 36 patients preoperatively and at 1 month; the average [\pm SD] thickness was $229 \pm 80 \mu\text{m}$ (ranged from 96 to $400 \mu\text{m}$). The thickening of photoreceptors was recorded in 36 (64.28%) patients; the average [\pm SD] thickness was $145 \pm 71 \mu\text{m}$ (ranged from 71 to $370 \mu\text{m}$). In the remaining 20 (35.72%) patients, the thickening of the fovea was not considered for statistical analysis because of the difficulty in clearly identifying the foveal limits as well as the correct detection of the subfoveal EZ.

At 1- and 3-month follow-up, SD-OCT examination was performed for each patient to find out any presence of drop-out of the EZ, inner RFs and outer RFs (Table 2).

The presence of drop-out of the EZ was recorded in 16 (28.57%) patients after the first postoperative month, but only 2 (3.57%) maintained this condition after 3 months.

The presence of inner RFs was documented in 6 (10.71%) of the patients after 1 month, but they disappeared at the end of the third month of follow-up.

After the first month of follow-up, 20 (35.71%) of the patients showed outer RFs (Fig. 3B, C); at 3-month follow-up,

Table 3. Best-corrected visual acuity at baseline and after surgery for each group of patients. Group 1 prone without PFCO, Group 2 prone with PFCO, Group 3 supine without PFCO, Group 4 supine with PFCO.

BCVA (logMar ± SD)	Group 1 (mean of 14 patients)	Group 2 (mean of 14 patients)	Group 3 (mean of 14 patients)	Group 4 (mean of 14 patients)
Baseline	1.39 ± 0.18	1.56 ± 0.23	1.38 ± 0.18	1.54 ± 0.17
After surgery	0.22 ± 0.11	0.29 ± 0.09	0.28 ± 0.12	0.3 ± 0.12

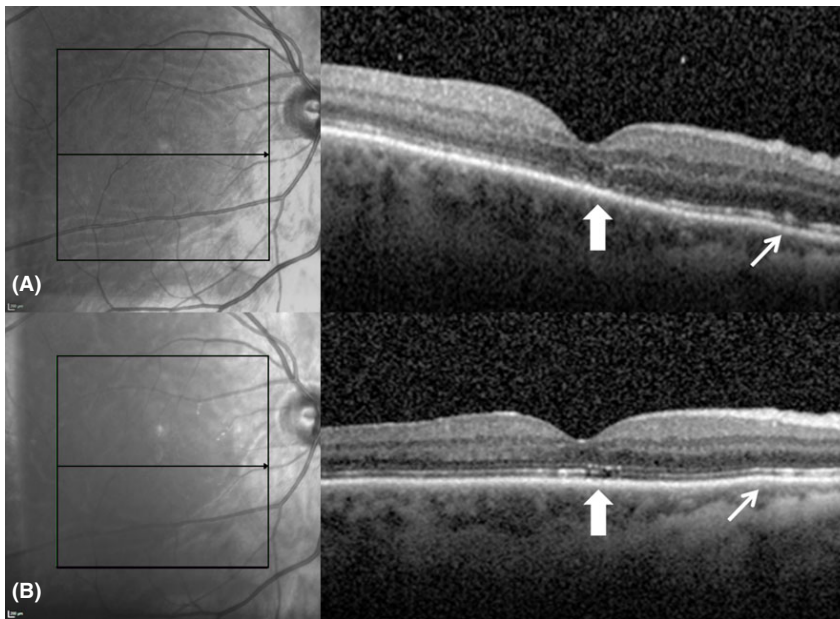


Fig. 4. Patient from group 4 (supine with PFCO). IR image of a patient who had pars plana vitrectomy for RRD 3 months before. There is a drop-out of the ellipsoid zone (see big arrow) in the foveal area, and the small arrow highlights the presence of a tiny outer retina fold (A). After 6 months from the surgery, big arrow in the bottom OCT scan indicates some repopulation of the ellipsoid zone, while the small arrow points out that the outer retina fold disappeared (B).

8 (14.28%) of the patients still presented outer RFs, but no statistical differences between the four groups were observed. The patients with outer RFs maintained metamorphopsia, revealed by Amsler test, for a period longer than the patients who did not show outer RFs.

The preoperative extension of the RRD did not affect the final visual acuity (VA) results or the presence of any retinal folds.

The height of the detachment and the thickening of the fovea or of the photoreceptors were not correlated with any OCT findings or negatively correlated with BCVA at the end of the follow-up in the four different groups.

The postoperative BCVA improved in all groups (Table 3), and the difference is statistically significant between the BCVA before and after surgery ($p < 0.01$). There were no statistically significant differences between the four groups in BCVA after surgery.

Discussion

The causes of the variability of visual outcomes in patients treated for macula-off RRD are still debated. Several studies analysed OCT and fundus autofluorescence (FAF) postoperative macular images to understand which signs can affect the prognosis of those patients.

Some authors correlate the poor final VA with the height of the neurosensory detachment and the duration of the foveal detachment (Ross et al. 2005; Leclaire-Collet et al. 2006). Kim et al. (2013) further remarked that the timing of surgical intervention can be critical for a better visual outcome. In this series of patients, the height of the detachment was not correlated with any important visual loss. Moreover, the duration (\pm SD) of symptoms was not statistically correlated with VA variation or with the presence of retinal folds in the four different groups.

The drop-out of the foveal EZ was described by Nakanishi et al., and it was defined as a focal lack of OCT signal corresponding to a defect of backreflection in contact with an augmented reflectivity of the external limiting membrane (ELM) line in the site of photoreceptor cell loss. They found this defect in eyes with macula-off RRD but not in eyes affected by acute central serous chorioretinopathy, and it was related to a worse postoperative visual outcome (Nakanishi et al. 2009). In our study, 16 (28.57%) patients demonstrated drop-out of EZ after the first postoperative month, but only 2 (3.57%) maintained this condition after 3 months (Fig. 4A,B). No statistically significant difference was found among the four groups at any time of the follow-up.

Dell’Omo et al. (2012a) described the outer RFs and inner RFs as one of the most important alterations that can affect the quality of vision in people who are recovering from macula-off RRD. Outer RFs are seen in OCT as hyperreflective bands constituted by folded EZ and ELM which do not follow the vascular pattern and could be variable in shape and height. Prominent outer RFs distort the outer nuclear layer and could be associated with inner RFs, which are sharp and localized invagination of the inner retinal profile, clearly seen in infrared and red-free images. Even if the majority of the postoperative OCT alteration usually solve within 6 months (Wolfensberger & Gonvers 2002), the presence of outer RFs seems to be associated with persistent metamorphopsia. In our patients, we also found that there are no relations between visual recovery after macula-off RRD and the presence of retinal folds, but visual symptoms like metamorphopsia are strictly correlated with them.

In this study, a supine or prone postoperative positioning has been evaluated, with or without the use of PFCO, to detect whether these differences in the surgical procedure can cause any difference in the occurrence of retinal folds. The results showed that the presence of retinal folds was similar in all groups, so neither the possible use of PFCO nor the different postoperative positioning seems to play a role (Dell’Omo et al. 2013). The immediate pressure on the retina caused by the PFCO use does not seem to affect the occurrence of the retinal folds, also

because the PFCO usually is removed within minutes during surgery. A possible explanation of these results can be that the physiologic reabsorption of the fluid in the retinal layers and the natural release of the retina undulation can be independent from the possible use of PFCO during the operation and the positioning of the patient could not affect the presence of the micro-retinal folds because the folds were already present since the air–fluid exchange, and, as seen in other OCT studies, micro-retinal folds need between 1 and 6 months to disappear (Dell’Omo et al. 2012b).

The pathogenesis of outer RFs is probably multifactorial with several variables concurring with their formation, such as sequestration of subretinal fluid and concomitant use of intravitreal gas, retinal translocation, transient intraoperative hypotony and others (Dell’Omo et al. 2012b). In all patients of our series, OCT scans showed intraretinal fluid and this seems to affect the anatomical changes in the retinal layers. The intraretinal fluid and swelling may be involved in the occurrence of retina folds.

A possible explanation for inner RFs and outer RFs formation could be the different undulations between the inner retina layers and the outer retina layers. The outer retina shows significant oedema, possibly due to ischaemia after being distanced from its nutritional source, the choriocapillaris. The inner retina is less ischaemic and oedematous as well as being ‘tethered’ by the inner limiting membrane. The mismatch in oedema could be one of the main causes in the pathophysiologic process of the inner RFs and outer RFs formation.

This is a pilot study with a limited number of patients; the results should be further investigated and validated with a larger number of patients.

In conclusion, retinal folds can occur in patients with macula-off RRD. The presence of outer RFs or inner RFs does not seem to be affected by the use of PFCO or by the postoperative positioning.

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