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Correlation between microstructural changes evident on optical coherence tomography and use of perfluorocarbon liquids for repair of primary rhegmatogenous retinal detachment

Mohamed Amr Azab[1], **Mostafa Hamed Nabih**[2], **Ayman Mohamed Khattab**[2], **Islam Abdallah Mohalhal**[1]✉

[1]Research Institute of Ophthalmology, Ministry of High Education, Giza, Egypt
[2]Department of Ophthalmology, Faculty of Medicine, Cairo University, Cairo, Egypt

Contact Information

Mohamed Amr Azab	mohamedamrazab@gmail.com
Mostafa Hamed Nabih	mosnabih@hotmail.com
Ayman Mohamed Khattab	aymkhattab@yahoo.com
Islam Abdallah Mohalhal	dr.islamabdallah@hotmail.com

✉**Corresponding author**
Research Institute of Ophthalmology, Ministry of High Education, Giza, Egypt
Email: dr.islamabdallah@hotmail.com

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ABSTRACT

Purpose: To describe optical coherence tomography (OCT) features of the macula after pars plana vitrectomy for treatment of primary rhegmatogenous retinal detachment with and without using perfluorocarbon liquids (PFCLs). *Patients and methods*: This study is a prospective randomized study. Thirty eyes of 30 patients with repaired primary rhegmatogenous retinal detachment by pars plana vitrectomy and gas injection, 15 eyes without adjuvant use of perfluorocarbon liquids (PFCLs) and 15 eyes with use of PFCLs, were investigated with OCT imaging using Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany) and Amsler grid within a few weeks after the operation after absorption of intraocular gas. *Results*: Microstructural changes detected on OCT imaging of the macula were diffuse retinal thickening (DRT), epiretinal membrane (ERM), cystoid macular oedema (CME), outer retinal corrugations (ORC), subretinal fluid (SRF) and macular hole (MH). These changes were observed in 16 of 30 eyes (53.3%), 10 eyes (66.7%) in the group (without PFCL), and 6 eyes (40.0%) in the group (with PFCL), (p value = 0.143). PFCL use has no statistical significance in the incidence of OCT changes. There was no statistically significant difference in the final mean best corrected visual acuity between the two groups. Metamorphopsia was detected in 12 of 16 (75%) of eyes showing OCT changes. *Conclusion*: OCT changes occur commonly after vitrectomy for repair of primary rhegmatogenous retinal detachment and the use of PFCLs does not seem to affect the incidence of these changes.

Keywords: Rhegmatogenous retinal detachment, Optical coherence tomography, Pars plana vitrectomy, Perfluorocarbon liquids, Macula

1. INTRODUCTION

The goal of pars plana vitrectomy (PPV) for repair of rhegmatogenous retinal detachment (RRD) is to eliminate vitreoretinal traction, reattach the retina and close retinal breaks by laser photocoagulation. In order to close the retinal breaks by laser coagulation, the retina around them must be reattached. This may be achieved in surgery by drainage of subretinal fluid, which includes direct aspiration of the subretinal fluid through the retinal breaks or a retinotomy, or with the use of perfluorocarbon liquids (PFCLs). PFCLs have high specific gravity, moderate surface tension and low viscosity, which make them a useful surgical adjuvant to attain retinal reattachment (Sargent & Seffl, 1970; Yu et al., 2014). Although PFCLs facilitate surgery, and are helpful especially in complicated cases such as traumatic retinal detachment and RRD with giant tears or proliferative vitreoretinopathy (PVR), their use is not needed in every case. Additionally, PFCL use may result in complications, as their intraocular retention can induce inflammation and subretinal retention can cause retinal toxicity (Lesnoni et al., 2004; Elsing et al., 2001; Lai et al., 2003; Tewari et al., 2009; Singh et al., 2001).

Optical coherence tomography (OCT) was first introduced for cross sectional retinal imaging in 1991 by a team headed by Fujimoto in Massachusetts Institute of Technology (MIT) (Huang et al., 1991). Since then, it has become an indispensable tool in evaluating the macula. OCT is unique in its cross-sectional scanning of the tissue, which provides anatomic tomographic representation of the retinal layers and their pathologies (Drexler et al., 2001). Retinal OCT imaging provides high-resolution imaging of subsurface retinal features that were previously inaccessible with fundus fluorescein angiography and ophthalmic ultrasound. The contrasting structures and reflectivity in the retinal layers allows the differentiation of the retinal nerve fiber layer (RNFL), nuclear layer, plexiform layers, external limiting membrane, retinal pigment epithelium, photoreceptor layers, and choriocapillaris. In OCT images of the retina, the horizontal cell orientation is correlated with high reflectivity, while the nuclei and vertical structures have low reflectivity (Zysk et al., 2007).

Patients with RRD often experience poor visual acuity or metamorphopsia or both in the early postoperative period despite successful retinal attachment (Nork et al., 1995).Visual disturbances are mainly related to macular abnormalities, most of them may be overlooked during standard clinical examination with slit-lamp biomicroscopy (Sabates et al., 1989; Michels et al., 1990). Time-domain (OCT) has shown that epiretinal membranes and persisting shallow subretinal fluid (SF) or macular edema can be associated with poor visual outcomes after repair of RRD (Wolfensberger & Gonvers, 2002; Hagimura et al., 2002; Yetik et al., 2004; Benson et al., 2006). Spectral-domain OCT has allowed detailed study of such abnormalities and also has provided important insights about morphologic and structural changes occurring at the level of the external limiting membrane and photoreceptor inner segment/outer segment (IS/OS) junction, which may relate to the integrity of the photoreceptor layer (Schocket et al., 2006; Wakabayashi et al., 2009; Smeth et al., 2010; Pierro et al., 2011).

To date, there have been many studies about OCT changes after vitrectomy for repair of RRD (Wolfensberger & Gonvers, 2002; Benson et al., 2006; Dell'Omo et al., 2012). However, the aim of our study was to provide a detailed description of some peculiar features easily detectable on OCT recorded a few weeks after PPV for repair of primary rhegmatogenous retinal detachment with and without using PFCLs, then to correlate them with the final best corrected visual acuity (BCVA) and postoperative visual disturbances if present.

2. MATERIAL AND METHODS

This study is a prospective randomized study. It included 30 eyes of 30 patients underwent PPV for repair of primary RRD. The primary outcome of the study was to evaluate the microstructural changes evident on OCT. Secondary outcomes were postoperative visual acuity and symptoms of distortion especially metamorphopsia, if present. Patients were recruited from the outpatient clinic of the Research Institute of Ophthalmology in Giza from the period of June 2017 till April 2018. It was approved by the Institutional Review Board and was conducted in compliance with principles of Helsinki declaration.

We included patients with primary RRD (with (PVR) grade A or B) assigned for primary vitrectomy. Cases were divided randomly into two groups A and B; each included 15 eyes: Group A: underwent pars plana vitrectomy without the use of PFCLs. Group B: underwent pars plana vitrectomy with the use of PFCLs. Randomisation was done by putting the intervention in closed envelops that were opened during the operation. The intervention was double blinded that the doctor and the participant did not know the type of intervention until opening the envelop during the operation.

We excluded cases with PVR more than grade B, cases that had performed previous retinal detachment surgeries; pneumatic retinopexy, scleral buckle or PPV, cases with old standing retinal detachment, exudative or tractional retinal detachment, giant retinal tears, macular holes and pediatric cases.

Baseline evaluation

Complete ocular examination was done including BCVA (with Snellen chart, which was converted to logMAR for statistical analysis), intraocular pressure (IOP) using Goldmann applanation tonometry and anterior segment biomicroscopy. The retinal detachment in all cases was evaluated using slit lamp biomicroscopy using (Super Field lens; VOLK, Mentor, Ohio, USA) and indirect ophthalmoscopy determining extent and configuration of the retinal detachment, macular status, number and position of the breaks and grade of PVR.

Surgical procedure

In Group A cases: Local anesthesia was induced by peribulbar block. PPV was done using 23-gauge system (Constellation system. Alcon, Fort Worth, TX). Posterior vitreous detachment induced via suction with the vitrectomy probe around the optic nerve head, followed by core vitrectomy and assisted by using triamcinolone acetonide to stain the vitreous in order to achieve near complete vitreous removal, followed by shaving of the vitreous base assisted by scleral indentation. Shift to fluid air exchange, followed by drainage of subretinal fluid through retinal breaks. Finally, laser was applied around all marked breaks and augmented by 360 degrees barrage if the retinal condition required this. This was followed by closure of the sclerotomies, then by the use of two syringes one filled with gas and the other acting as a chimney replacing the air with the non expansile concentration (20%) of the sulfur hexafluoride (SF_6) gas. Periocular antibiotic steroid combination was given and the (IOP) was adjusted.

In Group B cases: The same steps applied except that after completion of the core vitrectomy step, PFCL was infused over the optic disc to displace the subretinal fluid to the periphery followed by complete shaving of the vitreous base. This was followed by more injection of PFCL and then either applies the laser under PFCL or replaces the PFCL by air and apply laser under air. After complete removal of PFCL, all cases were tamponaded with gas intra-operatively. Patients were advised to take the face down position immediately following the operation. All patients were prescribed topical antibiotics and steroids after the operation.

Post-operative follow up

Patients were followed up on the 1st day post-operatively then after 1 week, 2 weeks, 1 month and 3 months respectively, examination included: BCVA by refraction; slit lamp examination, anterior segment biomicroscopy, IOP measurement using Goldmann applanation tonometry, dilated fundus examination with binocular slit-lamp biomicroscopy (using 90 diopters lens) and indirect ophthalmoscopy (using 20 D lens) In addition, each patient was questioned about the presence of visual disturbances. Amsler grid testing for metamorphopsia was shown in all cases, and the patients were specifically asked to show to the examiner the location of the distorted lines on the grid, if present. No quantitative assessment of the metamorphopsia was performed. Imaging (OCT) was typically performed following absorption of intraocular gas tamponade using Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany), which combines confocal scanning laser ophthalmoscope with spectral domain OCT.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 20. The quantitative data were presented as mean, standard deviations when their distribution found parametric while qualitative data were presented as number. The comparison between two independent groups with qualitative data was done by the use of Chi-square test. The comparison between two independent groups with quantitative data and parametric distribution was done by the use of Independent t-test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the P-value was considered significant as the following: $P > 0.05$: Non-significant, $P < 0.05$: Significant, $P < 0.01$: Highly significant.

3. RESULTS

This study included 30 eyes of 30 patients divided into 2 groups 15 eyes each; Group A: underwent PPV without the use of PFCLs, Group B: underwent PPV with the use of PFCLs. With a mean age of 56.27 ± 11.82 for Group (A) patients and 49.13± 13.09 for Group (B) patients. In Group (A) 9 eyes belonged to 9 females and the other 6 eyes belonged to 6 males, while in Group (B) 5 eyes belonged to 5 females and the other 10 eyes belonged to 10 males. The baseline characteristics of the studied groups are summarized in Table 1. Baseline characteristics of the two groups were homogeneous with no significant statistical difference between both groups in terms of age and gender.

Table 1 Age and Gender distribution of the studied groups

		Group A (Without PFCL) No.= 15	Group B (With PFCL) No.= 15	P-value	Sig.
Age	Mean±SD	56.27 ± 11.82	49.13 ± 13.09	0.128	NS
	Range	30 – 72	25 – 73		
Sex	Females	9 (60.0%)	5 (33.3%)	0.143	NS
	Males	6 (40.0%)	10 (66.7%)		
Eye	Right	9 (60.0%)	5 (33.3%)	0.143	NS
	Left	6 (40.0%)	10 (66.7%)		

SD = Standard Deviation of age mean; NS = Not Significant; P = Probability level; PFCL = Perfluorocarbon Liquids.

Primary anatomical success (defined as successful retinal reattachment after the first surgery) has been achieved in all 15 eyes of Group A patients (100%) and in 14 of the 15 eyes of Group B patients (93.3%), which wasn't statistically significant (p value = 0.309).On the other hand, the Final anatomical success (defined as successful retinal reattachment regardless the number of procedures) was achieved in all 30 eyes of the studied groups.

OCT images were reviewed for disrupted retinal structure postoperatively. Of the 30 eyes treated with vitrectomy and gas for rhegmatogenous retinal detachment, 53.3% (16/30) had an OCT abnormalities on the first follow up visit following absorption of intraocular gas tamponade. Of these OCT abnormalities 10/15 were recorded in the Group (A) eyes (66.7%) and 6/15 in Group (B) eyes (40%), with no statistically significant difference between both groups (p value = 0.143). Of the Group (A) eyes the abnormalities detected were diffuse retinal thickening (DRT) (n=2), epiretinal membrane (ERM) (n=4), (with ERM+DRT (n=1)), cystoid macular oedema (CME) (n=4), outer retinal corrugations (ORC) (n=1) and subretinal fluid (SRF) (n=1).

On the other hand, 6 eyes from Group (B) showed OCT abnormalities such observed abnormalities were DRT (n=2), ERM (n=2), (with ERM+DRT (n=1)), CME (n=1), iatrogenic macular hole (MH) (n=1) and SRF (n=1) (Table 2).

Table 2 OCT changes in the studied groups

OCT findings		Group A (Without PFCL)		Group B (With PFCL)		P-value	Sig.
		No.	%	No.	%		
CME	No	11	73.3%	14	93.3%	0.142	NS
	Yes	4	26.7%	1	6.7%		
DRT	No	13	86.7%	13	86.7%	1.000	NS
	Yes	2	13.3%	2	13.3%		
ERM	No	11	73.3%	13	86.7%	0.361	NS
	Yes	4	26.7%	2	13.3%		
ORC	No	14	93.3%	15	100%	0.309	NS
	Yes	1	6.7%	0	0.0%		
SRF	No	14	93.3%	14	93.3%	1.000	NS
	Yes	1	6.7%	1	6.7%		
MH	No	15	100.0%	14	93.3%	0.309	NS
	Yes	0	0.0%	1	6.7%		
Total OCT positivity	Negative	5	33.3%	9	60%	0.143	NS
	Positive	10	66.7%	6	40%		

NS = Not Significant; P = Probability level; PFCL = Perfluorocarbon Liquids; CME= Cystoid macular edema; ERM= Epiretinal membrane; DRT= Diffuse retinal thickening; ORC = Outer retinal corrugations; SRF = Subretinal fluid; MH = Macular Hole.

The mean post-operative BCVA was 0.70 ± 0.42 for Group (A) patients and 0.85 ± 0.42 for Group (B) patients during the first follow up visit following the absorption of intra-ocular gas tamponade. BCVA was measured using the Snellen's chart and converted to LogMAR for statistical analysis. There was no statistically significant difference between both groups (P value = 0.327).All patients underwent screening for symptoms of distortion using Amsler grid test, 9 patients from Group (A) reported to have symptoms of distortion post-operatively in comparison to the 10 patients from Group (B) who also reported to have post-operative symptoms of distortion (Table 3).

Table 3 Statistical values of the subjective post-operative data collected (best corrected visual acuity and visual disturbances) of the studied groups

		Group A (Without PFCL)	Group B (With PFCL)	P-value	Sig.
Postoperative BCVA (logMAR)	Mean ± SD	0.70 ± 0.42	0.85 ± 0.42	0.327	NS
	Range	0.1 – 1.5	0 – 1.5		
Visual Disturbances	No	6 (40.0%)	5 (33.3%)	0.713	NS
	Metamorphopsia	6 (40.0%)	7 (46.7%)		
	Metamorphopsia+Micropsia	3 (20.0%)	2 (13.3%)		
	Micropsia	0 (0.0%)	1 (6.7%)		

SD = Standard Deviation of BCVA mean; P = Probability level; NS = Not Significant; PFCL = Perfluorocarbon Liquid.

Ten patients in Group A had a disrupted retinal structure post-operatively on OCT, 8 of whom (80%) reported to have symptoms of distortion. On the other hand, of the five patients with an apparently normal OCT post-operatively, only one patient complained of metamorphopsia (Table 4, Figure 1).

Table 4 Correlation between OCT changes and the postoperative symptoms of distortion in Group (A) patients

		Negative OCT No.= 5	Positive OCT No.= 10	P-value	Sig.
Visual Disturbances	No	4 (80.0%)	2 (20.0%)	0.072	NS
	Metamorphopsia	1 (20.0%)	5 (50.0%)		
	Metamorphopsia+Micropsia	0 (0.0%)	3 (30.0%)		
	Micropsia	0 (0.0%)	0 (0.0%)		

NS = Not Significant; P = Probability level; OCT = Optical Coherence Tomography.

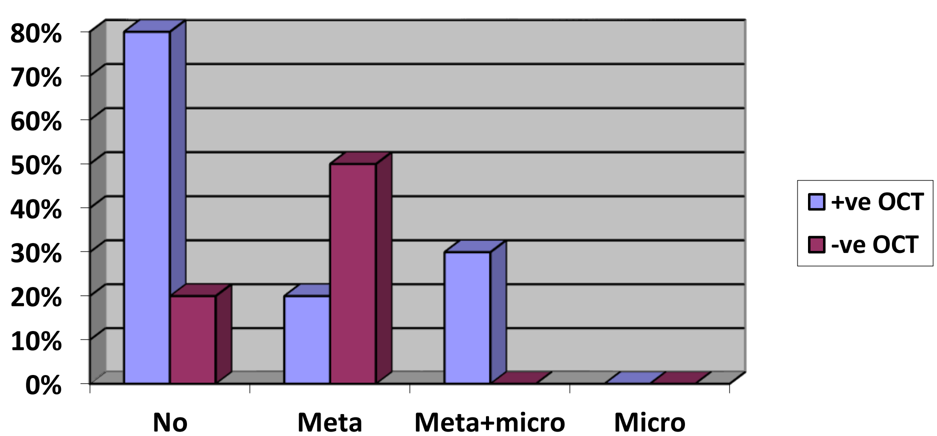

Figure 1 Correlation between OCT changes and the postoperative symptoms of distortion in Group (A) patients

Six patients in Group B had microstructural changes post-operatively on OCT, 4 of whom (66.6%) reported to have symptoms of distortion. However, of the remaining nine patients with an apparently normal OCT post-operatively, six patients (66.6%) still reported to have post-operative distortive symptoms (Table 5, Figure 2).

Table 5 Correlation between OCT changes and the postoperative symptoms of distortion in Group (B) patients

		Negative OCT	Positive OCT	P-value	Sig.
		No.= 9	No.= 6		
Visual Disturbances	No	3 (33.3%)	2 (33.3%)	0.580	NS
	Metamorphopsia	5 (55.6%)	2 (33.3%)		
	Metamorphopsia+Micropsia	1 (11.1%)	1 (16.7%)		
	Micropsia	0 (0.0%)	1 (16.7%)		

NS = Not Significant; P = Probability level; OCT = Optical Coherence Tomography.

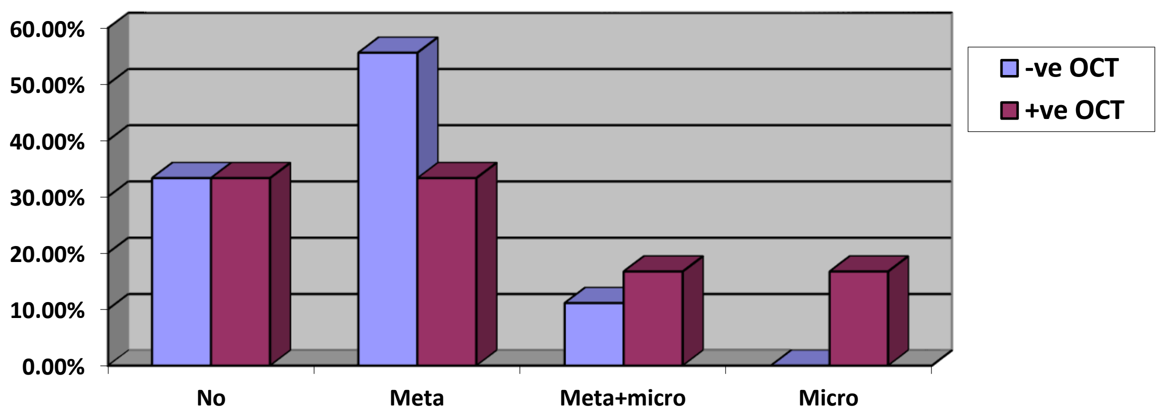

Figure 2 Correlation between OCT changes and the postoperative symptoms of distortion in Group (B) patients

4. DISCUSSION

Rhegmatogenous retinal detachment has a great impact on retinal function. The histopathologic substrate of functional impairment following RRD repair has been related to the presence of cystoid macular edema, epiretinal membranes, and significant atrophy of the outer retinal layers with disorganization of the lamellar architecture of the retina (Wilson & Green, 1987; Barr, 1990). Spectral-domain OCT has confirmed these findings and in addition has provided evidence of further intervening subtle abnormalities like distortion and disruption of the photoreceptor IS/OS junction and discontinuity of the external limiting membrane which may account for poor postoperative visual acuity and metamorphopsia (Schocket et al., 2006; Wakabayashi et a., 2009; Smeth et al., 2010; Pierro et al., 2011).

PFCLs have become popular in retinal detachment surgery because of their physical properties (optical transparency, low viscosity, immiscibility with water) (Garcia-Valenzuela et al., 2004). They allow the retina to reattach without the need for retinotomies and intraoperative stabilization of the retina in more complex situations, such as trauma with presence of PVR (Garcia-Valenzuela et al., 2004; Scott et al., 2003). The main side effects of PFCL arise from their abnormal intraocular fate, in the vitreous cavity, subretinally or in the anterior chamber (Kinori et al., 2011). Benefits of the presented PFCL-free technique include, in addition to avoiding possible side effects of the lagging PFCL, better visualisation of the anterior retina in the air-filled eye, which may additionally facilitate retinal reattachment (Bartz-Schmidt et al., 2008).

In our study the primary anatomical success was achieved in all 15 eyes (100%) of Group (A) patients where PFCL wasn't used, and in 14 of the 15 eyes of Group (B) patients (93. 3%) where PFCL was used, with both groups (100%) successfully achieving the final anatomical success. Comparable results between both approaches have been documented in literature as regards the anatomical outcomes of PPV in cases having primary RRD with primary anatomical success rates ranging from 90.0% to 98.0% in cases with routine PFCL use (Martínez-Castillo et al., 2005; Brazitikos et al., 2005; Martinez-Castillo et al., 2009). It was 95.7% in the study published by Schneider et al., (2012) in which PFCL wasn't used. With all of these mentioned studies achieving a near 100% final anatomical success.

OCT images were reviewed in our study for disrupted retinal structure postoperatively. Of the 30 eyes treated with vitrectomy and gas for RRD, 53.3% (16/30) had an OCT abnormalities at the time of imaging (first follow up visit following absorption of intraocular gas tamponade). Of these OCT abnormalities 10 (8 of which were fovea-involving) were recorded in the Group (A) eyes

(33.3% of total cases) and 6 (5 of which were fovea-involving) in Group (B) eyes (20% of total cases). In studies using PFCL the rates of epiretinal membranes were 2.7-10% (Kinori et al., 2011; Bartz-Schmidt et al., 1996; Albrieux et al., 2011). Although not all the studies distinguish between membranes that are worthy of surgery and asymptomatic membranes. In our study epiretinal membranes have been observed in 26.6% (4/15) in Group (A) cases and in 13.3% (2/15) of cases in Group (B) where PFCL was used. Macular holes are generally described as a rare complication of retinal detachment surgery, occurring in less than 1% of cases (Shibata et al., 2012). Weichel et al., (2006) and Albrieux et al., (2011) in their studies using PFCL, reported rates of 3.3-4.4%. Although a lot of the other studies using PFCL did not report the presence of macular holes (Kinori et al., 2011; Brazitikos et al., 2005; Martinez-Castillo et al., 2009; Bartz-Schmidt et al., 1996).

In our study postoperative macular hole was observed in only 1 case of the 30 eyes included in this study and was among the Group (B) cases where PFCL was used, which wasn't statistically significant (p value = 0.309). Subretinal fluid was found post-operatively in the OCT of 6.6% (1/15) eyes of Group (A) as well as (1/15) eyes of Group (B), furthermore Outer retinal corrugations and folds were found only in one eye (6.6%) of Group (A) patients. Similar results have been documented in the study by Dell'Omo et al., 2012 which included 33 eyes tamponaded intra-operatively with gas where subretinal and intra-retinal fluid was evident post-operatively on OCT in 2/15 (13.3%) eyes where PFCL was used and in 2/18 (11.1%) eyes where PFCL wasn't used. However, they reported a much higher incidence of Outer retinal corrugations and folds in 9/15 eyes (60%) with PFCL use and 5/18 eyes (27.7%) without PFCL use. The contrast in this finding is most probably due to the meticulous approaches we applied during the surgery through repetitive fluid air exchange to achieve complete drainage of any subretinal fluid.

None of the cases enrolled in our study exhibited subretinal PFCL on OCT which can be explained by the rather small number of cases experiencing such a complication reported in literature in a frequency of 0.9-11.1% of the cases in which PFCL was used (Shulman et al., 2013; Suk & Flynn, 2011). Furthermore, metamorphopsia was detected in 8/10 patients (80%) with positive OCT findings in Group (A) (p value = 0.072), and in 4/6 patients (66.6%) with positive OCT findings in Group (B) (p value = 0.580), hence not denoting a statistically significant correlation between metamorphopsia and the disrupted retinal structure post-operatively. Furthur studies with larger sample size are needed to statistically correlate between metamorphopsia and OCT changes and to prove whether the metamorphopsia is directly related to the microstructural changes evident on OCT or other causes like retinal displacement or both.

Our study was limited by the small sample size, although it does hold the advantage over other studies being prospective and randomized in terms of PFCLs use. Also, the group tamponaded with gas without adjuvant PFCLs use and the group tamponaded with gas together with adjuvant PFCL use differed with respect to some baseline features like number of detached quadrants, foveal involvement and concomitant involvement of the upper and lower quadrants. Further researches including larger sample size are needed to evaluate the microstructural changes evident on OCT after PPV for repair of primary RRD and its implications.

5. CONCLUSION

In conclusion, we described the microstructural abnormalities evident on OCT after repair of primary RRD and their correlation with the mean post-operative best corrected visual acuity and metamorphopsia. The use of PFCLs does not seem to affect the incidence of these abnormalities.

Abbreviations

BCVA	Best Corrected Visual Acuity
CME	Cystoid Macular Edema
DRT	Diffuse Retinal Thickening
ERM	Epi-retinal membrane
IOP	Intra-ocular Pressure
IS/OS	Inner Segment /Outer Segment
LogMAR	Logarithm of Minimal Angle of Resolution
M.H	Macular hole
OCT	Optical Coherence Tomography
ORC	Outer Retinal Corrugations
PFCL	Perfluorocarbon Liquids
PPV	Pars Plana Vitrectomy
PVR	Proliferative Vitreo-retinopathy
RNFL	Retinal Nerve Fiber Layer

RRD	Rhegmatogenous Retinal Detachment
SF	Subretinal Fluid
SRF	Sub- Retinal Fluid

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Conflict of interest
The authors declare that they have no conflict of interest.

Informed consent
Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval
The study was approved by the Institutional Review Board of the Research Institute of Ophthalmology and was conducted in compliance with principles of Helsinki declaration.

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Data and materials Availability

All data associated with this study are present in the paper.

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