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Treatment of Myopic Foveoschisis with Air Versus Perfluoropropane: A Retrospective Study

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Background: The aim of this study was to compare the efficacy of air and perfluoropropane (C3F8) combined with vitrectomy to treat myopic foveoschisis (MF).

Material/Methods: A retrospective comparison of a consecutive series of surgical patients was performed. Ninety-seven eyes of 91 patients with MF were assigned to undergo 23G vitrectomy. After internal limiting membrane (ILM) peeling, the vitreous cavity was filled with air in 48 eyes of 45 patients (Air Group). Fluid-air exchange was performed in 49 eyes of 46 patients (C3F8 Group) followed by an injection of 14% C3F8. Patients were evaluated using best-corrected visual acuity (BCVA) and optical coherence tomography.

Results: Preoperatively, there was no significant difference in clinical features between the groups. After surgery, BCVA was markedly improved and the foveoschisis height was reduced in both groups compared with baseline ($P < 0.01$), but the difference between the groups was not significant ($P > 0.05$). No significant differences were noted in BCVA improvement and retinal restoration ($P = 0.33$ and 0.39 , respectively) in the mild and moderate subgroups (foveoschisis height $\leq 400 \mu\text{m}$) between the tamponades. However, in the severe group (foveoschisis height $> 400 \mu\text{m}$), C3F8 had a more favorable cure rate and foveoschisis height reduction improvement compared with air ($P = 0.04$ and 0.04 , respectively) at the last visit.

Conclusions: Vitrectomy combined with ILM peeling is effective in the treatment of myopic foveoschisis, and the choice of tamponade depends on the severity of foveoschisis. Air can be used for patients with a foveoschisis height $\leq 400 \mu\text{m}$, but C3F8 is more effective for patients with a foveoschisis height $> 400 \mu\text{m}$.

MeSH Keywords: **Fovea Centralis • Myopia • Vitrectomy**

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Background

Myopic foveoschisis (MF), which is a complication of pathological myopia, refers to cleavage of the retinal neuroepithelial layer (which is typically split into a thicker inner layer and a thinner outer layer in the macular region) [1]. In 1958, Phillips defined MF as un-rhegmatogenous posterior retinal detachment for the first time [2]. MF occurs in 8–34% of eyes with high myopia. Since Takano and Kishi described the characteristics of MF by optical coherence tomography (OCT) in 1999, OCT has become the criterion standard for the diagnosis of MF [3].

MF may remain stable for several years without any visual acuity decrease [4]. Once progressive MF presents with visual loss or abnormal structure, such as epiretinal membrane, surgical intervention is necessary [5]. Previous studies have demonstrated that vitrectomy combined with internal limiting membrane (ILM) peeling was an effective treatment for symptomatic MF, with a reported cure rate of 66–89% [6–8]. Although gas tamponades were useful for flattening a split retina, some questions remain about the necessity of using gas tamponade in MF patients. When and how to use an intraocular tamponade in MF are mainly based on the surgeon's experience. Therefore, information about gas tamponade selection in treating MF is important for improving clinical management. In this study, we researched a series of 97 eyes using OCT or other methods and evaluated the anatomical and visual outcomes to investigate the safety of vitrectomy and ILM peeling. By comparing the results of 2 gas tamponades (air and C3F8) in the treatment of MF, we sought to determine which gas is safer and more effective for the postoperative anatomical and visual improvement of patients with MF.

Material and Methods

Patients

This was a retrospective study of 97 myopic eyes of 91 patients with MF treated at Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, China, from March 2011 to March 2013. The study was approved by the Ethics Committee of the hospital and adhered to the principles of the 1983 Declaration of Helsinki. The eligibility criteria of patients were defined as follows: a definite diagnosis of MF, a spherical equivalent of -6.0 D or greater; an axial length of ≥ 26.5 mm; at least 12 months of follow-up; and obvious clinical symptoms, such as progressive visual loss, metamorphopsia, and obscured view. The exclusion criteria included non-progressive MF, MF associated with macular hole or retinal detachment since foveal anatomical status was related to surgical results in MF [9] and other ocular diseases that would compromise vision or visual field, such as dense cataract and

multifocal choroiditis. All patients were informed of the risks of treatment and provided signed informed consent before surgery. The patients were divided into 2 groups according to the postoperative tamponade (Air or C3F8 Group). Then, patients were divided into 3 subgroups according to severity of MF (measured 3 times, integers obtained): mild (foveoschisis height < 200 μm); moderate (foveoschisis height ≥ 200 μm , ≤ 400 μm); and severe (foveoschisis height > 400 μm).

Preoperative ophthalmic examination

All patients underwent comprehensive preoperative ophthalmic examinations performed by 2 masked examiners (Dr. Jing Jiang and Dr. Xiaofang Xu). Best-corrected visual acuity (BCVA) and refractive error were determined by use of a standard visual acuity chart (subjective refraction). BCVA was converted to the logarithm of the minimal angle of resolution (logMAR) units for statistical analysis. Axial length was determined by A-scan (ProBeam; Quantel Medical, Aviso, France) and IOL-master (Carl Zeiss Meditec AG, Jena, Germany). Slit-lamp biomicroscopy (SL-3G; Topcon, Tokyo, Japan) combined with indirect ophthalmoscopy (90D digital wide field lens; Volk, OH, USA) were performed preoperatively and postoperatively by the same examiners. The presence/absence of subretinal or intraretinal fluid and obvious retinal detachment (RD) was evaluated by horizontal B-scan (B1-10 MHz; Quantel Medical, Aviso, France). OCT (Cirrus™ HD-OCT 4000; Carl Zeiss Meditec, Jena, Germany) was used to diagnose, follow up, and assess the surgical and anatomical outcomes.

Surgical methods

Surgical indications were foveoschisis without foveal detachment confirmed by OCT and symptomatic visual loss or metamorphopsia attributable to MF. All surgeries were performed by the same experienced ophthalmologist (Dr. Zhiliang Wang). All patients underwent 3-port, transconjunctival pars plana vitrectomy using a 23G system (1. AccuRus400VS; Alcon Laboratories, Inc., TX, USA; 2. Constellation Table-Top Vision System; Alcon). Phacoemulsification and foldable intraocular lens (Tecnis; Advanced Medical Optics, Inc., IL, USA) implantation were performed simultaneously in all phakic eyes. Triamcinolone acetonide (TA, 4%; Shanghai General Pharmaceutical Co. Ltd., Shanghai, China) was injected into the vitreous cavity for visualization of the vitreous cortex. Then, the epimacular membrane was peeled, and the vitreous cortex was cut as far peripherally as possible during vitrectomy. The retinal surface was stained with indocyanine green (ICG; Shanghai General Pharmaceutical Co. Ltd., Shanghai, China) in all eyes (0.1 ml, 0.025%, < 15 s) to visualize the ILM, which was peeled around the entire posterior retinal surface, ranging from up to down vascular arcades. Finally, the vitreous cavity was filled with air in 48 eyes of 45 patients (Air Group). Fluid–air exchange was performed

Table 1. baseline characteristics of the patients in two groups.

	Air group (48 eyes of 45 patients)	C3F8 group (49 eyes of 46 patients)	P value
Age (years)	67.42±8.98	64.49±8.58	0.104 (t)
Sex (male/female)	12/33	14/32	0.691 (χ^2)
Axial length (mm)	29.56±2.15	30.16±1.76	0.131 (t)
BCVA (logMAR)	1.61±0.44	1.57±0.40	0.660 (t)
FH (μ m)	311.38±163.81	318.59±165.21	0.829 (t)

BCVA – best corrected visual acuity; logMAR – logarithm of the minimum angle of resolution; FH – foveoschisis height by OCT; t – T-test; χ^2 – Chi-square test.

in the other 49 eyes of 46 patients (C3F8 Group), followed by injection of 14% C3F8 (Tianjin Jingming New Technological Development Co. Ltd., Tianjin, China). Patients were randomly assigned to the Air Group or C3F8 Group. Patients were instructed to maintain a prone position postoperatively for 1 week in the Air Group and 2 weeks in the C3F8 Group.

Follow-up

Follow-up examinations were performed at 1, 3, 6, and 12 months after surgery. Slit-lamp biomicroscopy examination combined with indirect ophthalmoscopy, BCVA measurement, and OCT were performed in all patients. If persistent foveoschisis or other complications such as MH or RD were identified, operative interventions were performed immediately. We used a 5-raster scan to score posterior retina and defined the foveoschisis height as the maximum vertical distance from the outer face of the inner layer to the inner face of the outer layer within 1 mm, centered at the fovea. Treatment was assessed by OCT as follows: cure, foveoschisis disappeared; remission, foveoschisis height reduced >50%; invalid, foveoschisis height remained; and recurrence, foveoschisis reappeared after 3 months.

Statistical analysis

SPSS for Windows version 22.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. Independent-samples *t*-test and chi-square test were used for the analyses. $P < 0.05$ was considered statistically significant.

Results

Patients' characteristics

There were 48 eyes of 45 patients in the Air Group and 49 eyes of 46 patients in the C3F8 Group. The mean age was 65.94±8.56

years (range, 51–87 years). The mean refractive error was -14.71 ± 4.83 D (range, -7.17 to -30.15 D), and the mean axial length was 29.86 ± 1.98 mm (range, 26.50–36.06 mm). The mean BCVA was 1.59 ± 0.42 (with logMAR charts). The mean foveoschisis height was 315.02 ± 163.70 μ m (range, 66–737 μ m), as measured by OCT. All patients were phakic.

Table 1 summarizes the baseline characteristics of the patients in both groups. There were no significant differences in age, sex, axial length, visual acuity, or foveoschisis height between the groups.

Visual outcomes

The mean preoperative BCVA was 1.61 ± 0.44 logMAR (Air Group) and 1.57 ± 0.40 logMAR (C3F8 Group). The mean postoperative BCVA was 0.91 ± 0.47 logMAR (Air Group) and 0.72 ± 0.42 logMAR (C3F8 Group) at the final visit, and it exhibited significant improvement ($P < 0.01$) in both groups.

Anatomical outcomes

OCT was performed at 3, 6, and 12 months after initial vitrectomy. OCT revealed that the cure rate of MF was 66.7% in the Air Group and 81.6% in the C3F8 Group at 12 months after the operation. The difference between the groups was not significant ($P > 0.05$).

In the Air Group, the mean preoperative and postoperative foveoschisis heights were 311.38 ± 163.81 μ m and 61.90 ± 113.51 μ m, respectively. The difference was significant ($P < 0.01$). In the C3F8 Group, the mean preoperative and postoperative foveoschisis heights were 318.59 ± 165.21 μ m and 30.76 ± 71.81 μ m, respectively. The difference was also significant ($P < 0.01$). However, there was no difference in the mean postoperative MF height between the groups ($P = 0.08$). The visual and anatomical outcomes are presented in Table 2.

Table 2. Visual and anatomical outcomes after operative of two groups.

	Air group	C3F8 group
BCVA (LogMAR)		
Pre-	1.61±0.44	1.57±0.40
Post- (12 months)	0.91±0.47	0.72±0.42
P value	<0.01 (t)	<0.01 (t)
FH (um)		
Pre-	311.38±163.81	318.59±165.21
Post- (12 months)	61.90±113.51	28.39±65.42
P value	<0.01 (t)	<0.01 (t)
Cure rate		
12 months (cure/total)	66.7% (32/48)	81.6% (40/49)

BCVA – best corrected visual acuity; LogMAR – logarithm of the minimal angle of resolution; Pre- – pre-operative; Post- – post-operative; FH – foveoschisis height by OCT; t – T-test.

In all 3 subgroups, regarding the severity, both tamponades had similar efficacy in BCVA improvement (Table 2). In the mild and moderate subgroups, the cure rate and mean postoperative foveoschisis height of the 2 tamponades did not differ significantly (Table 3; Figure 1A–1D; Figure 2A–2D). In the severe subgroup, there were significant differences in the cure rate and mean postoperative foveoschisis height of the 2 tamponades (Table 3; Figure 3A–3D). C3F8 exhibited significantly increased efficacy in improving the cure rate and reducing postoperative foveoschisis height compared with air (Table 3).

Table 3. The BCVA and OCT results of different degree MF in the air and C3F8 groups.

		Mild subgroup (<200 um)			Moderate subgroup (200–400 um)			Severe subgroup (>400 um)		
		Air group (16 eyes)	C3F8 group (17 eyes)	P value	Air group (16 eyes)	C3F8 group (14 eyes)	P value	Air group (16 eyes)	C3F8 group (18 eyes)	P value
BCVA (LogMAR)	Pre-	1.49±0.43	1.58±0.40	0.55	1.62±0.42	1.54±0.42	0.61	1.71±0.46	1.58±0.40	0.40 (t)
	Post-	0.71±0.38	0.61±0.29	0.38	0.90±0.43	0.70±0.35	0.17	1.10±0.53	0.84±0.55	0.17 (t)
FH (um)	Pre-	148.75±35.02	151.35±31.06	0.82	278.38±56.23	286.36±57.64	0.70	507.00±97.48	501.61±96.58	0.87 (t)
	Post-	0.00±0.00	0.00±0.00	–	48.88±62.33	41.07±75.09	0.76	136.81±161.97	45.33±80.81	0.04 (t)
Cure rate (12 months) (cure/total)		100% (16/16)	100% (17/17)	0.33	56% (9/16)	71% (10/14)	0.39	31.2% (5/16)	66.7% (12/18)	0.04 (χ ²)

BCVA – best corrected visual acuity; Pre- – pre-operative; Post- – post-operative; LogMAR – logarithm of the minimal angle of resolution; FH – foveoschisis height by OCT; t – T-test; χ² – Chi-square test.

Complications

During follow-up, full-thickness MHRD was observed in 2 eyes of 2 patients in the severe group; one in the Air Group and another in the C3F8 Group. The BCVA of these 2 patients after initial surgery was <20/200 (20/1000 with air, 20/500 with C3F8). The patient with air tamponade was cured by reoperation with C3F8 tamponade (Figure 4A–4C), and the patient with C3F8 tamponade was cured by reoperation with oil tamponade, which was removed after 3 months (Figure 5A–5C). The retina, including the fovea, was anatomically reattached, although the macular hole was not completely closed in both patients, and the BCVA improved to 20/167 and 20/133, respectively. No other ocular or systemic complications, such as fundus hemorrhage, secondary glaucoma, endophthalmitis, or choroidal detachment, related to this procedure were observed during follow-up. There was no recurrence during follow-up in any patients.

Discussion

In this study, we performed vitrectomy combined with 2 different gases in 97 eyes of 91 patients with MF and finally obtained anatomical restoration in 72 eyes (66.7% in the Air Group and 81.6% in the C3F8 Group). BCVA markedly improved in most eyes.

Vitrectomy is currently widely used to treat rapidly progressive MF. Vitrectomy can remove the epiretinal membrane, vitreous cortex, and rigid ILM, which have been postulated to be the main relevant factors in the progression of MF [10–12].

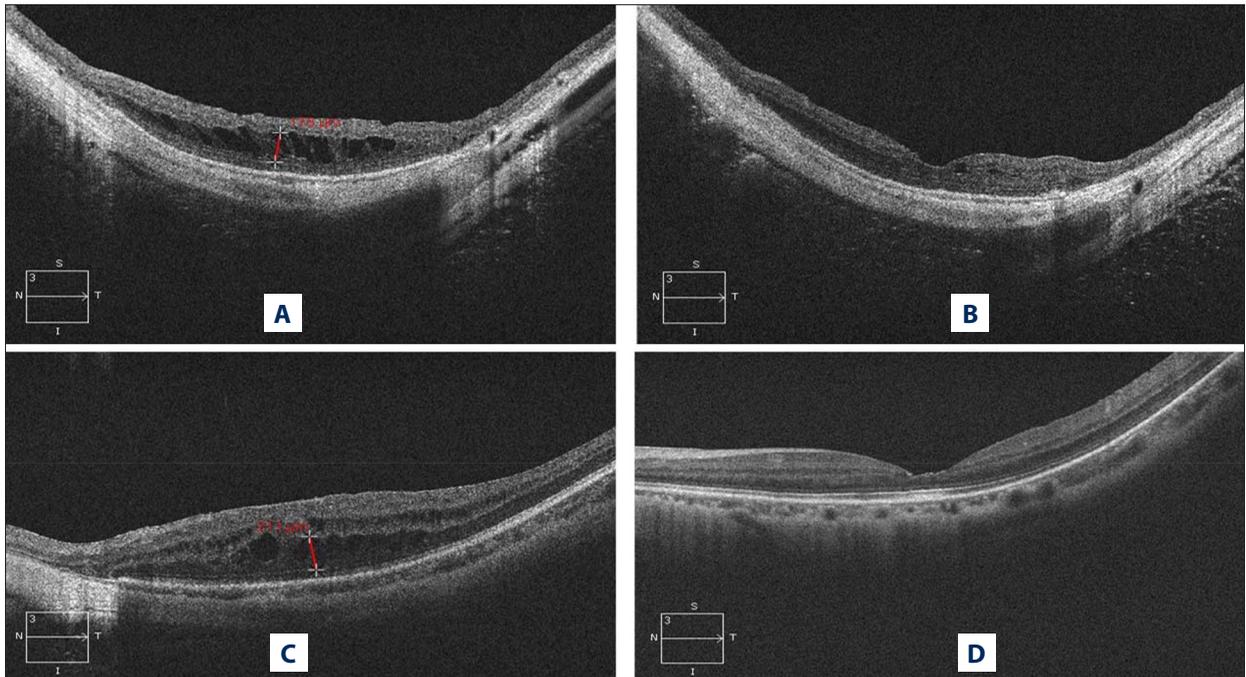


Figure 1. OCT images of the mild MF group with different tamponades. Air tamponade: (A) Preoperation, (B) Postoperation, C3F8 tamponade: (C) Preoperation, (D) Postoperation. These images showed foveoschisis disappeared, retina reduced anatomically after surgery in both air and C3F8 tamponades.

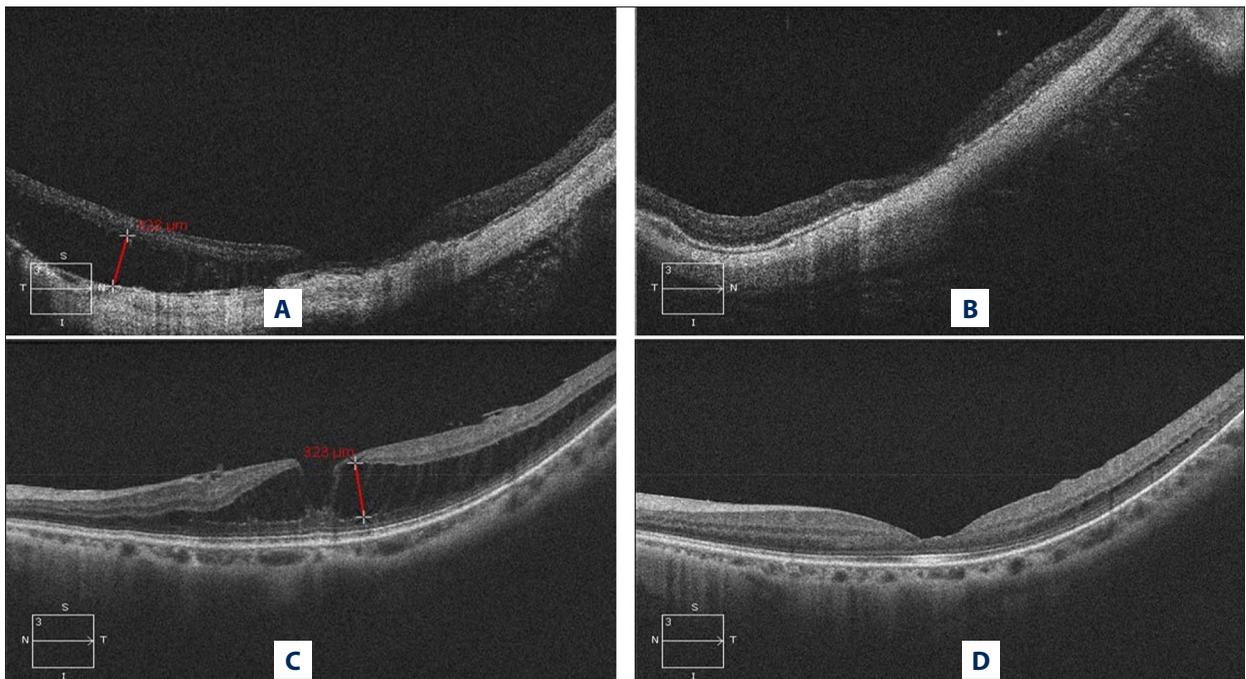


Figure 2. OCT images of the moderate group with different tamponades. Air tamponade: (A) Preoperation, (B) Postoperation, C3F8 tamponade: (C) Preoperation, (D) Postoperation. These images also showed foveoschisis disappeared, retina reduced anatomically after surgery in both air and C3F8 tamponades.

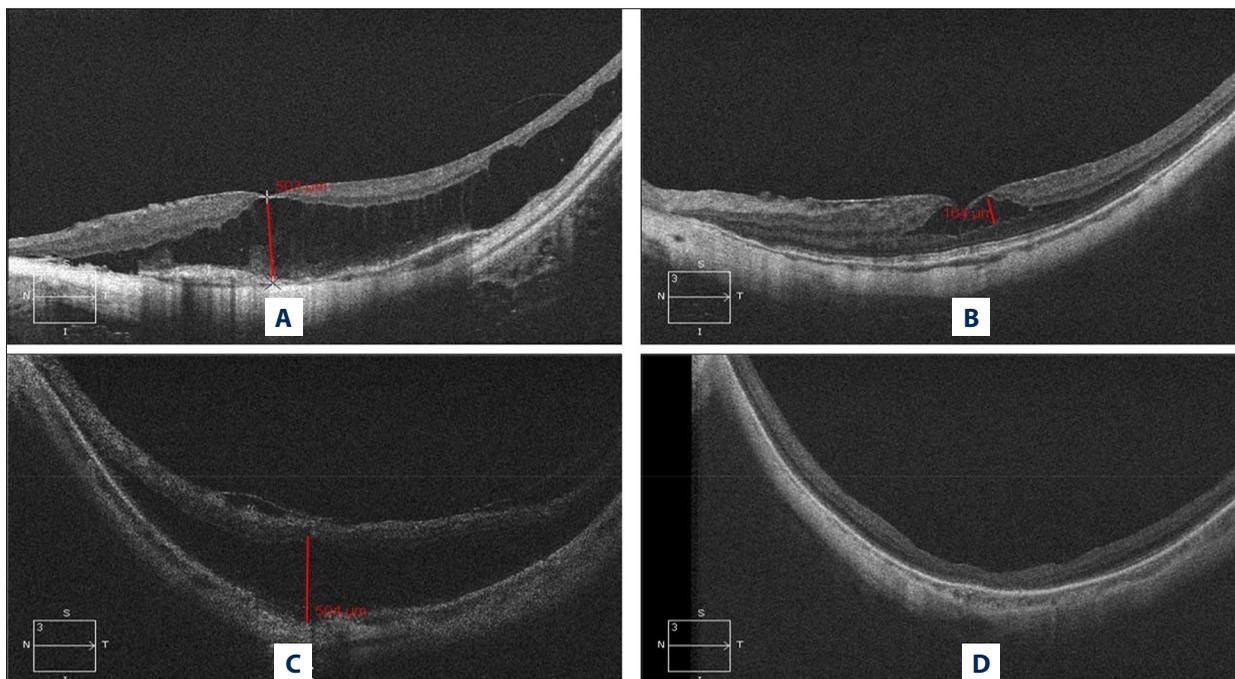


Figure 3. OCT images of the severe group with different tamponades. Air tamponade: (A) Preoperation, (B) Postoperation, C3F8 tamponade: (C) Preoperation, (D) Postoperation. These images showed in air tamponade group, the foveoschisis height decreased and retina had not fully reduced (A, B), and in C3F8 tamponade group, the foveoschisis disappeared, retina reduced anatomically after surgery (C, D).

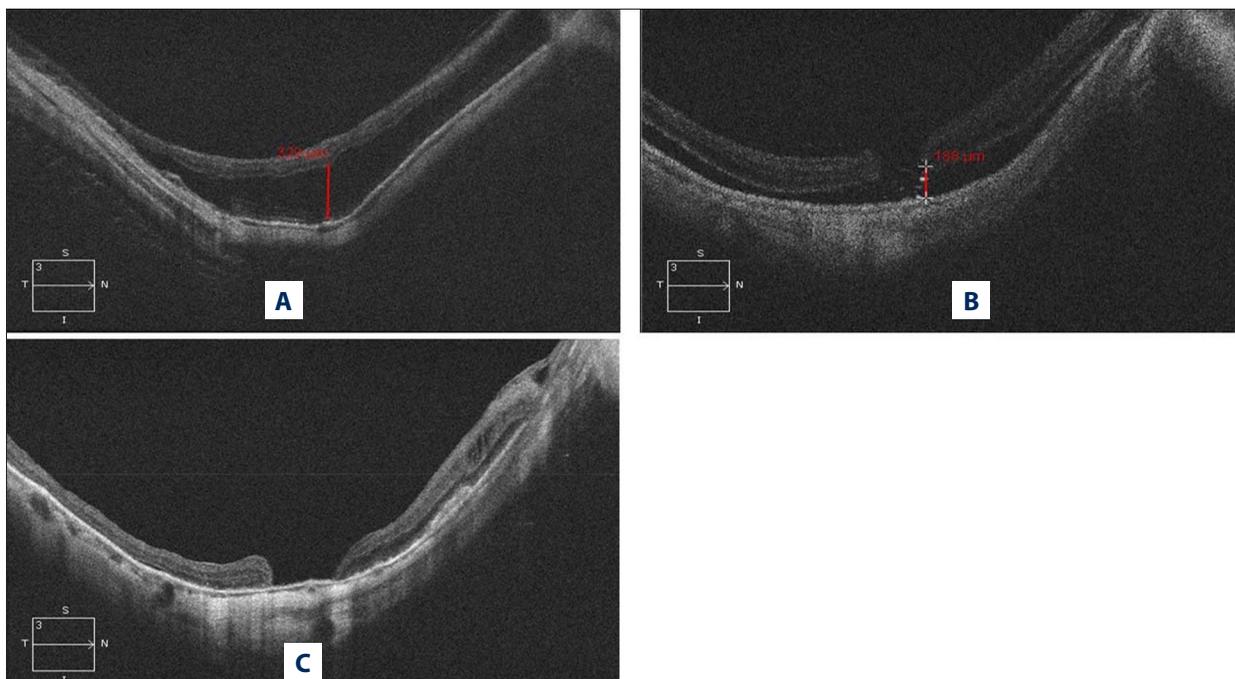


Figure 4. Case 1, (A) preoperative OCT, (B) with air tamponade, postoperative OCT at 3 months showed MHRD formed. (C) Undergoing reoperation (vitrectomy with C3F8 tamponade), postoperative OCT at 3 months showed RD disappeared, retina reattached but MH formed.

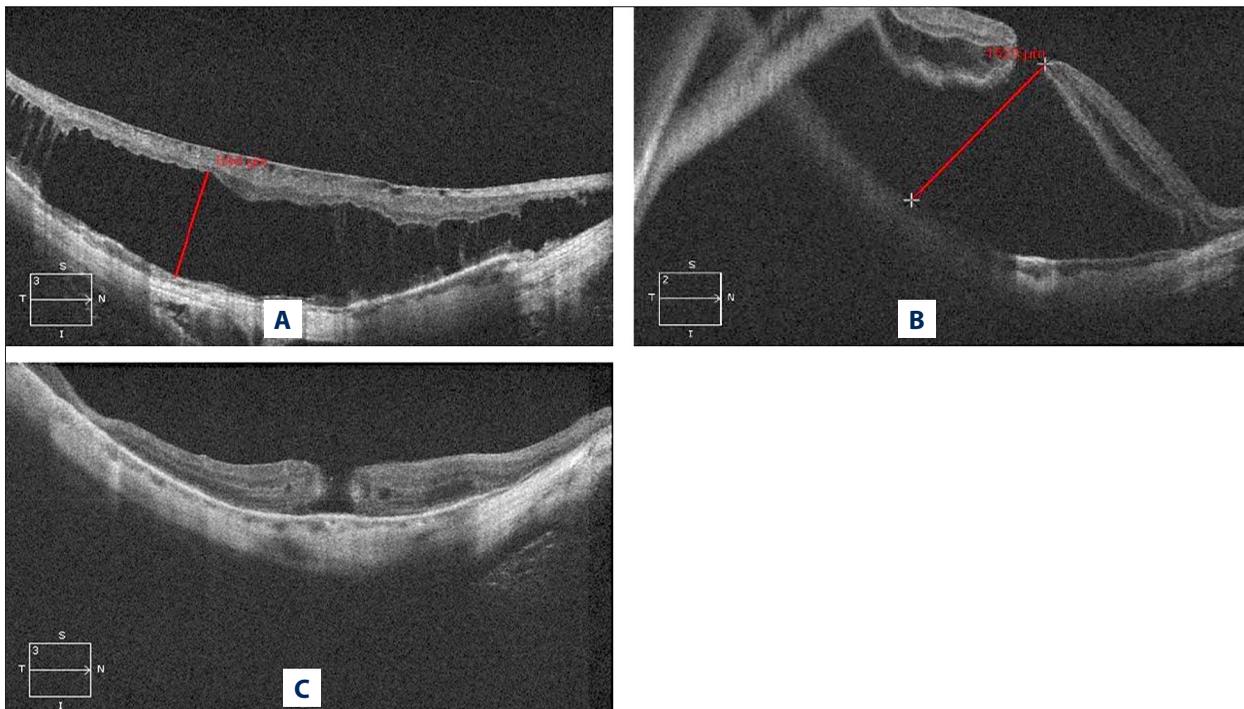


Figure 5. Case 2, (A) preoperative OCT, (B) with C3F8 tamponade, postoperative OCT at 3 months showed MHRD formed. (C) Undergoing operation (vitrectomy with silicone tamponade), postoperative OCT at 3 months showed RD disappeared, retina reattached but MH formed.

Previous studies have demonstrated that vitrectomy results in rapid anatomical restoration and improvement in BCVA in MF patients, regardless of the use of different surgical procedures and tamponades [6,8,13]. The necessity of ILM peeling for MF remains controversial. Some researchers have argued that ILM peeling can release the retina from the traction and contractile tissue under pathological conditions and reduce both the occurrence of epimacular membrane and the long-term recurrence of MF after vitrectomy [14,15].

Other studies found that ILM peeling may be a risk factor for postoperative MH in highly myopic eyes, given the thin retina [8]. Dyes such as ICG, which is used to improve the visualization of the ILM, have potentially toxic effects on the retina, especially the photoreceptor cells [16,17].

In the present study, all patients underwent vitrectomy combined with ILM peeling. At the final follow-up, resolution of MF was observed in 72 of 97 eyes (74.2%), and most patients exhibited significant visual improvement. The results were consistent with or better than those of previous studies. We also made small changes to improve surgical safety. The concentration of ICG used in the present study was 0.025%, which was lower than the typical 0.5%, and it was injected only once, with a short duration (15 s).

Vitreous tamponades played a key role during surgery for MF. Gas can induce pneumatic displacement of outer layer detachments and quicker repositioning. Eyes treated with gas tamponade showed more rapid resolution of myopic foveoschisis; air and C3F8 are the most widely used tamponades [8]. Air generally lasts 1 week, with a short-term effect, whereas C3F8 remains for 40 days, thus providing lasting tension along with long-term blurred vision, prone position, and relatively more complications, such as high intraocular pressure and a macular hole [8]. There are no uniform standards for the necessity of gas tamponades in MF. In this study, we compared the treatment effect of air and C3F8 tamponades in MF. The results demonstrated that air and C3F8 had the same efficacy in BCVA improvement and foveoschisis height reduction in mild and moderate MF. However, C3F8 displayed superior results in severe MF. Retinal recovery was a slow process (mean, 4.4 months; range, 1–12 months), so it is necessary to provide a sufficiently long tamponade effect in severe MF patients for retinal resolution [18,19].

The incidence rate of MH after surgery is 12.5 to 27.3% [20]. Full-thickness MHRD occurred in 2 eyes (2.2%, 2/91) in the severe MF subgroup in our study. These patients underwent a second vitrectomy combined with C3F8 (Air Group) or silicone oil (C3F8 Group) and eventually achieved retinal reattachment and visual improvement. Maalej et al. [21] showed that MHRD had little effect on BCVA. We also found that patients

showed BCVA improvement after a second operation, despite the formation of MH.

The limitations in this study included a relatively small sample size, a short follow-up period of 1 year, and limited evaluation criteria (only BCVA and OCT). Future studies should introduce additional ophthalmological examinations, such as microperimetry and multifocal visual electrophysiology, to assess macular function and therapeutic effects more accurately and objectively.

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Conclusions

In conclusion, our study proved that vitrectomy combined with ILM peeling was effective in the treatment of MF. For patients with a foveoschisis height $\leq 400 \mu\text{m}$, air can be a good choice to reduce the time during which the patient must be in the prone position, as well as reducing blurred vision and decreasing complications such as secondary glaucoma. For patients with a foveoschisis height $>400 \mu\text{m}$, C3F8 should be chosen to reduce the risks of recurrence and lack of healing.

Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.