· Clinical Research ·

Internal limiting membrane peeling combined with silicone oil or air tamponade for highly myopic foveoschisis

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Abstract

● **AIM:** To compare the efficacy of pars plana vitrectomy (PPV) combined with internal limiting membrane (ILM) and silicone oil or sterile air tamponade for the treatment of myopic foveoschisis (MF) in highly myopic eyes.

● **METHODS:** This retrospective study included 48 myopic eyes of 40 patients with MF and axial lengths (ALs) ranging from 26-32 mm treated between January 2020 and January 2022. All patients were underwent PPV combined with ILM peeling followed by sterile air or silicone oil tamponade and followed up at least 12mo. Based on the features on spectral-domain optical coherence tomography (SD-OCT), the eyes were divided into the MF-only group (Group A, n=15 eyes), MF with central foveal detachment group (Group B, n=20 eyes), and MF with lamellar macular hole group (Group C, n=13 eyes). According to AL, eyes were further divided into three groups: Group D (26.01-28.00 mm, n=12 eyes), Group E (28.01-30.00 mm, n=26 eyes), and Group F (30.01-32.00 mm, n=10 eyes). The best-corrected visual acuity (BCVA), central foveal thickness (CFT), and complications were recorded.

● **RESULTS:** The patients included 16 males and 24 females with the mean age of 56±9.82y. The BCVA and CFT improved in all groups after surgery (P<0.01), while there was no significant difference of the CFT in Group A, B, and C postoperatively (P>0.05). The intergroup differences of BCVA and CFT postoperatively were statistically significant in Group D, E, and F. Twenty eyes were injected with sterile air, and 28 eyes were injected with silicone oil for tamponade based on the AL. However, there was no statistically significant difference among Groups D, E, and F in terms of the results of sterile air or silicone oil tamponade. The mean recovery time was 5.9mo for MF patients subjected to silicone oil tamponade and 7.7mo for patients subjected to sterile air tamponade, and the difference was not statistically significant.

● **CONCLUSION:** PPV and ILM peeling combined with silicone oil or sterile air tamponade can achieve good results for MF in highly myopic eyes with ALs≤32 mm.

● **KEYWORDS:** axial length; myopic foveoschisis; highly myopic; internal limiting membrane; pars plana vitrectomy

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INTRODUCTION

Myopic foveoschisis (MF) in highly myopic eyes is the occurrence of a split in the layers of the neuroretina of the macula, which can manifest as splitting at various levels and extents. MF is one of the most common mechanisms behind impaired visual function in patients with high myopia, occurring in 34% of highly myopic eyes[1]. While the pathogenesis of MF is closely related to traction exerted on the posterior pole of the retina, it is also associated with abnormal posterior vitreous detachment, vitreous cortical remnants, increased internal limiting membrane (ILM) stiffness, posterior scleral staphyloma, and retinal vascular sclerosis[2-4], the exact pathogenesis of which requires further exploration[5-7]. According to its morphology, its occurrence can be divided into inner, outer, or inner and outer retinoschisis. Complications can be further divided into simple retinoschisis, retinal detachment (RD), and macular hole (MH)[8]. When MF in highly myopic eyes develops into MH and central foveal RD, it can cause severe impairment of visual function or even blindness[9]. Timely and appropriate surgical treatment is currently advocated for eyes with MF that have significant loss of central vision and/or complications such as central foveal RD and MH[10]. Pars plana vitrectomy (PPV) is the main treatment for MF, but there is still much controversy over whether to combine ILM peeling, the extent of ILM peeling, and the choice of vitreous substitute[11]. Studies have shown that PPV can relieve centripetal traction on the posterior vitreous cortex, while ILM peeling can relieve the tangential traction of the macula; thus, PPV combined with ILM peeling can ameliorate foveoschisis and therefore stabilize and improve visual acuity[12]. The effectiveness and overall safety of PPV combined with ILM peeling and gas tamponade for the treatment of MF have been documented both domestically and internationally, but data concerning its exact long-term efficacy are scarce. Additionally, there is still much controversy regarding the differences in the prognosis of different MF types and the occurrence of MH postoperatively[11]. The success rate for treating MF with PPV combined with gas or balanced saline solution tamponade is approximately 75%-100%, while the use of gas tamponade has shown relatively better results in terms of best-corrected visual acuity (BCVA) improvement and anatomical resolution[13]. Hattori *et al*[14] concluded that fundus surgeons prefer to use durable material as a tamponade for more severe MF patients with myopic tractional maculopathy. Yao *et al*[15] reported that vitrectomy with silicone tamponade and without ILM peeling, as an optional surgical protocol for treating MF, is effective and safe. Therefore, scholars have investigated the efficacy of silicone oil tamponade for treating MF in terms of its long-term effect on the retina. Thus, we treated MF eyes with PPV combined with ILM peeling and with either silicone oil or sterile air tamponade and then evaluated the long-term outcomes. We compared the differences in BCVA and macular anatomic recovery between eyes with different MF types, different axial lengths (ALs), and different types of vitreous substitutes. We have also summarized the factors influencing the MF recovery process.

SUBJECTS AND METHODS

Ethical Approval The study protocol was implemented in accordance with the Declaration of Helsinki and was approved by Xi'an People's Hospital (Xi'an Fourth Hospital, No.KJLL-Z-H-2023001). Patients provided written informed consent for participation before study enrolment.

Study Design and Patients This was a retrospective study of 48 myopic eyes of 40 patients with MF treated at Xi'an People's Hospital (Xi'an Fourth Hospital) from January 2020 to January 2022. The inclusion criteria were as follows: $32.00>AL\geq 26.00$ mm and spectral-domain optical coherence tomography (SD-OCT) clearly showing foveoschisis in the macula that seriously affects visual acuity. The exclusion criteria were as follows: other kinds of highly myopic retinopathy, such as full-thickness MH and choroidal neovascularization; previous ocular surgery, except for cataract surgery; and concurrent ocular diseases, such as ocular trauma, glaucoma, uveitis, or other systemic diseases.

This retrospective study included 48 myopic eyes of 40 patients with MF and axial lengths (ALs) ranging from 26-32 mm treated between January 2020 and January 2022. All patients were underwent PPV combined with ILM peeling followed by sterile air or silicone oil tamponade and followed up at least 12mo. Based on the features on spectral-domain optical coherence tomography (SD-OCT), the eyes were divided into the MF-only group (Group A, *n*=15 eyes), MF with central foveal detachment group (Group B, *n*=20 eyes), and MF with lamellar macular hole group (Group C, *n*=13 eyes). According to AL, eyes were further divided into three groups: Group D (26.01-28.00 mm, *n*=12 eyes), Group E (28.01-30.00 mm, *n*=26 eyes), and Group F (30.01-32.00 mm, *n*=10 eyes). The best-corrected visual acuity (BCVA), central foveal thickness (CFT), and complications were recorded (Table 1).

Preparation and Procedure Each surgery was performed by the same experienced surgeon. All patients underwent standard 25G PPV (Alcon Constellation Vision System) under retinoscopy. Many patients who undergo vitrectomy develop cataracts, which tend to progress rapidly and therefore increase the risk of secondary surgery; therefore, we combined cataract surgery with vitrectomy to avoid the need for secondary surgery for patients and thereby significantly reduce the economic burden. More importantly, the image of the fundus obtained in combined cataract surgery is clearer. A total of 30 eyes underwent simultaneous phacoemulsification and intraocular lens (IOL) implantation. After adequate posterior vitreous detachment, vitrectomy was performed. The posterior vitreous cortex was removed, and diluted 0.025 mg/mL indocyanine green was injected for no more than 15s. Multiple staining procedures could be performed if staining was difficult. Some studies[16-18] have shown that vitrectomy with complete ILM peeling results in comparable outcomes to those achieved with preservation of the epifoveal membrane in treating patients with MF. There was no statistically significant difference in the final visual acuity between the two groups. Therefore, for the patients who underwent vitrectomy with complete macular ILM peeling, the ILM was entirely peeled between the upper and lower vascular arcades[19], and after air-liquid exchange, silicone oil (Silicon 5000, Fluoron GmbH) was injected into 28 eyes, and sterile air was injected into 20 eyes as tamponade. All patients subjected to sterile air tamponade were kept in the face-down position for at least 1wk after surgery, and patients subjected to silicone oil tamponade were kept in the face-down position for at least

Table 1 The clinical characteristics, and the differences in BCVA, AL, and CFT among the group A, B, and C

Groups	Eyes	Age (y)	M:F	BCVA (logMAR)	CFT (μm)	AL (mm)
Group A	15	40.65±10.45	5:10	0.88±0.24	407.87±121.93	27.18±0.56
Group B	20	55.65±10.90	6:14	1.10±0.22	495.40±105.80	29.25±0.45
Group C	13	62.30±8.90	4:9	1.37±0.43	481.07±114.33	30.46±1.35
F	-	0.124	0.487	9.446	2.748	102.007
P	-	0.894	0.369	<0.05	0.07	<0.05

AL: Axial length; CFT: Central foveal thickness; logMAR: The logarithm of the minimum angle of resolution; BCVA: Best-corrected visual acuity.

3mo after surgery. All patients were instructed to maintain their prone position postoperatively, silicone oil for 3mo, and sterile air for 5-7d.

Recovery, improvement and no change following treatment for MF was defined with reference to previous research[20] as follows: 1) the disappearance of the cystic cavity and columnar or filamentary connections in the neuroretina paramacula on the SD-OCT image; 2) the reduction of the cystic cavity of the neuroretina around the MH and the thickness of the neuroretina, as well as the shortening of the columnar or filamentary connections; 3) the continued presence of MF, no decrease or even worsening in height, or no change in the cystic cavity and filamentary junctions, respectively.

Statistical Analysis SPSS 23.0 statistical software was used for statistical analysis. The measurement data are expressed as the mean±standard deviation. The BCVA and CFT of all the eyes before and after surgery, as well as in each group, were compared using a *t*-test. Analysis of variance was used to compare the BCVA and CFT of the three groups of affected eyes. A Chi-square test was used to compare the effectiveness of the different tamponades and the proportion of eyes with an intact ellipsoid band. Finally, a *t*-test was used to compare the postoperative recovery time with different tamponades for eyes with different ALs. A *P* value <0.05 indicated statistically significant difference.

RESULTS

At the final follow-up visit, the mean logMAR and CFT were 0.59±0.28 and 157.94±9.34 μm, respectively, for all 48 eyes. These values were significantly different from the preoperative logMAR and CFT values (*t*=14.796 and 17.623, *P*<0.001). Visual acuity improved in 47 eyes, and all eyes with MF recovered, except for one eye with a full-thickness macular hole in Group B. The ellipsoidal band of the macula was intact in 33 eyes, and the integrity of the macula was missing in 15 eyes.

Visual acuity: The difference in preoperative visual acuity among Groups A, B, and C was found to be statistically significant (*F*=9.446, *P*<0.05). The logMAR values in Groups A, B, and C at the last follow-up visit were 0.39±0.24, 0.59±0.19, and 0.84±0.25, respectively (Table 2). Notably, the logMAR improved in all three groups after surgery (*P*<0.01), and the postoperative intergroup difference was also statistically significant (*F*=14.373, *P*<0.01). The difference in preoperative visual acuity among Groups D, E, and F was also statistically significant (*F*=10.263, *P*<0.05), and the logMAR values of the three groups at the final follow-up visit were 0.38±0.27, 0.67±0.25, and 0.55±0.22, respectively (Table 3). Furthermore, the postoperative logMAR values of the three groups improved significantly (*P*<0.01), and the intergroup difference in postoperative visual acuity was statistically significant (*F*=5.330, *P*<0.05).

Table 2 BCVA in patients after surgery according to feature on SD-OCT

Parameters	Group A	Group B	Group C	All
Preop.	0.88±0.24	1.10±0.22	1.37±0.43	1.10±0.35
Postop.	0.39±0.24	0.59±0.19	0.84±0.25	0.59±0.28
t	10.911	9.083	6.477	14.796
P	<0.001	<0.001	<0.001	<0.001

BCVA: Best-corrected visual acuity; SD-OCT: Spectral-domain optical coherence tomography; Preop.: Preoperative; Postop.: Postoperative.

Table 3 BCVA in patients after surgery according to AL

Parameters	Group D	Group E	Group F	All
Preop.	0.82±0.26	1.23±0.29	0.99±0.24	1.08±0.32
Postop.	0.38±0.27	0.67±0.25	0.55±0.22	0.57±0.27
t	5.117	14.546	7.117	15.281
P	<0.001	<0.001	<0.001	<0.001

BCVA: Best-corrected visual acuity; AL: Axial length; Preop.: Preoperative; Postop.: Postoperative.

Macular Thickness and Anatomic Recovery There was no significant difference among the eyes in Groups A, B, and C preoperatively (*F*=2.748, *P*=0.075), and the mean CFTs for each group postoperatively were 170.00±10.92 μm, 167.30±8.25 μm, and 166.36±8.97 μm, respectively. All three groups showed significant improvement in the CFT (*P*<0.001), while there was no significant difference in the CFT among these groups during the postoperative period (*F*=0.548, *P*=0.582; Table 4). There was a significant difference during the preoperative period (*F*=6.820, *P*<0.01) among the eyes in Groups D, E and F. All the postoperative CFTs improved significantly (*P*<0.001), with the mean CFTs decreasing to 170.50±12.16 μm, 166.88±7.84 μm, and 167.00±9.92 μm in Groups D, E and F, respectively. However, there was no

Table 4 CFT in patients after surgery according to feature on SD-OCT mean±SD, μm

Parameters	Group A	Group B	Group C	All
Preop.	407.87±121.93	495.40±105.80	481.07±114.33	464.88±118.63
Postop.	170.00±10.92	167.30±8.25	166.36± 8.97	167.94±9.34
t	7.836	14.290	10.170	17.623
P	<0.001	<0.001	<0.001	<0.001

CFT: Central foveal thickness; SD-OCT: Spectral-domain optical coherence tomography; Preop.: Preoperative; Postop.: Postoperative.

Table 5 CFT in patients after surgery according to AL mean±SD, μm

Parameters	Group D	Group E	Group F	All
Preop.	381.25±52.47	475.23±121.42	527.50±41.52	462.63±107.22
Postop.	170.50±12.16	166.88±7.84	167.00±9.92	167.81±9.41
t	13.63	13.261	27.419	19.374
P	<0.001	<0.001	<0.001	<0.001

CFT: Central foveal thickness; AL: Axial length; Preop.: Preoperative; Postop.: Postoperative.

statistically significant difference among these groups after surgery (F=0.643, P>0.05; Table 5). Postoperatively, MF was cured in all eyes of the three groups. There were 13, 12, and 8 eyes with intact ellipsoidal bands in Groups A, B, and C, respectively, but the intergroup difference was not statistically significant (χ^2=3.269, P>0.05).

Results of Different Tamponades Twenty eyes were injected with sterile air, and 28 eyes were injected with silicone oil for tamponade based on the AL. The difference between the two groups was not statistically significant (χ^2=3.269, P>0.05) according to the corrected Chi-square test, as shown in Table 6. For the overall recovery time, the mean recovery time for MF patients subjected to silicone oil tamponade was 5.9mo, while the mean recovery time for MF patients subjected to sterile air for tamponade was 7.3mo, with no statistically significant difference (F=0.003, P>0.05).

Table 6 Results of different tamponade according to AL

AL (mm)	Silicone oil	Sterile air	All
26.01-28.00	4	8	12
28.01-30.00	18	8	26
30.01-32.00	6	4	10
F			4.367
P			0.113

AL: Axial length.

Complications No serious complications occurred during surgery, although one eye in Group B developed a full-thickness MH during the postoperative follow-up period. In addition, among the 18 eyes that underwent cataract surgery, 8 were pseudophakic, and the other 10 were phakic. Among them, 2 eyes required surgery for ongoing vision loss due to cataracts at 1y postoperatively, and 2 eyes required cataract surgery when the silicone oil was removed.

DISCUSSION

Treatment for MF is considered primarily for patients who experience significant progression, a notable loss of central vision, and/or complicated MH and retinal pigment epithelial detachments. The main treatments include PPV, posterior scleral reinforcement surgery, and PPV combined with posterior scleral reinforcement[21-23]. Among them, PPV is considered the mainstream treatment for MF[24], although there are still debates about whether to perform ILM peeling, the extent to which it should be peeled, the best choice of intraocular tamponade, and so on. MF is caused by the splitting of the posterior vitreous cortex, which remains on the ILM, generating traction and pulling the retinal tissue. Moreover, the ILM thickens and induces traction on the macular tissues. All of these tractions lead to the occurrence and aggravation of MF. Therefore, PPV combined with ILM peeling can completely release traction on macular tissue from the vitreous and from the ILM, thus promoting the recovery from MF. ILM peeling not only reduces the tangential traction on the macula but also better accommodates the relative extension of the retina caused by posterior staphyloma. Most studies have reported that fovea-sparing ILM peeling inhibits intraoperative or postoperative full-thickness MH formation but increases the incidence of postoperative contractions of the remaining ILM (0-60%)[25-27]. Several studies have concluded that the full-thickness MH formation rate of traditional ILM peeling is comparable to that of fovea-sparing ILM peeling[17]. After treatment with PPV combined with ILM peeling, all eyes in this study recovered from MF. Apart from one patient with reduced vision due to a postoperative MH, all eyes had improved visual acuity to varying degrees. The proportion of visual acuity improvement was consistent with that of MF recovery. Thus, the anatomic recovery following surgery for MF is the basis for improved or stable visual acuity. In addition, there may be a relationship between the prognosis of visual acuity and cataract removal in the 30 patients in this study who were treated with simultaneous phacoemulsification and IOL implantation.

MF is a pathological process that progresses from simple MF to central macular foveal RD and eventually to a full-thickness MH. The efficacy of surgery varies depending on the stage of MF. Previous studies have shown[28] that MF develops with the splitting of the inner retina to form a lamellar MH, gradually progressing to the outer layer and thus a full-thickness MH. Another study[29] concluded that the anatomic recovery after PPV was significantly better in MF patients with foveal RD than in those without foveal RD. Thus, treating MF patients with central foveal RD with PPV surgery is considered more clinically valuable. In this study, we performed PPV combined with ILM peeling and sterile air or silicone oil tamponade and observed the recovery of BCVA and foveal anatomy pre- and postoperatively in three groups of patients with different MF morphologies. The results showed that the patients in Group C had the longest AL and the worst preoperative BCVA among Groups A, B and C. AL and BCVA were significantly different among the three groups, suggesting that AL plays an important role in BCVA and that the longer the AL is, the worse the BCVA may be. The results of this study showed that the postoperative BCVA increased significantly in all three groups of patients with different MF types. The BCVA before and after surgery was better in patients in Group A than in those in Groups B and C, while the patients in Group C had relatively worse visual acuity. It can be inferred that although the postoperative BCVA and macular anatomy in patients in Group C improved significantly compared to those in the preoperative period, the overall postoperative BCVA was still significantly worse than that in the other two groups due to the poor integrity of the ellipsoidal band and the longer ALs. In contrast, the patients in Group A showed anatomic repositioning of the outer retinal layer and retained an intact ellipsoidal band; thus, their postoperative BCVA was significantly better than that of patients in the other two groups. There was no significant difference in the preoperative CFT among Groups A, B, or C, but preoperative visual acuity was statistically significant because the visual acuity of the eye with MF depended on the integrity of the outer layer, and even if there was no difference in CFT among the three groups, there was still a difference in visual acuity. After surgery, the CFT improved well, so the difference in CFT among the three groups after surgery was not statistically significant, and the difference in visual acuity was still statistically significant. This suggests that in clinical practice, surgical intervention should be selected according to the actual situation of the patient's fundus to avoid causing damage to the outer layer of the macular area and a significant reduction in vision. PPV combined with ILM peeling can be rational if vision loss and disease progress, regardless of the type of MF.

There are still debates over the choice of intravitreal tamponade for MF patients undergoing PPV, mainly concerning whether to use tamponade, the choice of tamponade materials, and whether tamponade accelerates postoperative anatomic recovery[14]. A study[13] reported the outcomes of PPV and ILM peeling combined with sterile air tamponade or balanced salt solution tamponade in patients with MF for up to 5y. Both sterile air tamponade and balanced salt solution tamponade achieved positive results, while sterile air tamponade relatively accelerated recovery from MF. Previous studies[13,29-30] have shown faster anatomic recovery and greater improvement in visual acuity after PPV combined with gas tamponade than after balanced salt solution tamponade for MF without a full-thickness MH, with variable yet high success rates (75%-100%). Patients with gas tamponade exhibited good outcomes in terms of BCVA improvement and anatomical recovery, but the sample size was relatively small, and the follow-up time was short. In our study, patients were followed up for longer than 1y after surgery. Both eyes subjected to sterile air tamponade and those subjected to silicone oil tamponade recovered from MF, and patients showed significant improvements in BCVA and CFT. Notably, all 28 eyes subjected to silicone oil tamponade recovered from MF within 6mo, 19 of the 20 eyes subjected to sterile air tamponade recovered, and 1 eye developed a full-thickness MH. Overall, the results showed that patients in the silicone tamponade group may have a significantly shorter duration of disease than those in the air tamponade group.

The development of MH after PPV is a serious complication that can lead to poor prognosis in eyes with MF[2], with an incidence rate of approximately 12.5% to 27.3%. Risk factors include ILM peeling, sterile air tamponade, foveal neuroretina detachment, and disruption of the integrity of the ellipsoid band and outer-layer macular hole before surgery[2,31]. Recently, fovea-sparing ILM peeling has been proposed to reduce the postoperative incidence of MH formation and any secondary injury from ILM peeling in MF patients. A fovea-sparing ILM peeling approach for MF may achieve better outcomes and prevent the postoperative occurrence of MH. However, issues regarding the surgical technique, extent of peeling, and postoperative ILM proliferation and traction require further exploration[32]. Other studies have shown that central foveal tissue with outer-layer MHs is very fragile and susceptible to damage regardless of whether fovea-sparing or complete ILM peeling is performed because the thin central foveal retina of the outer MH can be stretched over a larger arc during reattachment, which can ultimately lead to the postoperative development of full-thickness MHs[2]. In this study, the ILM peeling in all 48 eyes transcended the macular vascular arch and thus provided maximum relief from the traction caused by the ILM. In the group of MF patients with concurrent foveal RD, one patient subjected to sterile air tamponade whose AL exceeded 30 mm developed a full-thickness MH postoperatively. This may be related to the longer AL, absence of the inner retina, thin outer layer structures, damage to the Müller cells and outer layer structures caused by the peeling of the ILM during surgery, or surface tension from the intraocular bubble. Therefore, PPV surgery alone should be performed with caution in patients with ALs greater than 30 mm, the absence of the inner retina, and thin outer layer structures to avoid the occurrence of iatrogenic full-thickness MH.

There are several limitations to this study. First, although the sample size in this study was based on the sample sizes included in previous studies[3-4], the sample size was relatively small. Our surgical technique was standardized, the decision to use either sterile air or silicone oil intraocular tamponade depended on the surgical period (through January 2022) and the surgeon's experience rather than being driven by particular guidelines. Second, this study was a retrospective case series, and there was no random sampling. The follow-up period for this very complex surgery for a very difficult disease was insufficient. Third, this study lacked objective evaluations of macular function, such as micro visual field examination or multifocal electroretinography, and objective studies need to be conducted in the future to further compare and observe postoperative visual effects. Retrospective studies are prone to some bias due to the selection of patients for the three groups, and the results are subject to confirmation in prospective, larger, and long-term studies. Based on our preliminary findings, silicone oil and air tamponade are both safe and effective options for treating highly myopic MF patients with an AL of 28-30 mm or less. Although there was no statistically significant difference in the course of the disease, silicone oil tamponade and sterile air tamponade were good surgical options for the treatment of MF. However, a larger cohort study with a long-term follow-up is needed to confirm the efficacy and safety of this surgical option.

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