

Macular epiretinal membrane in high myopia: timing and prognosis of pars plana vitrectomy surgery

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Abstract

• **AIM:** To investigate the outcomes and prognosis of macular epiretinal membrane (ERM) after pars plana vitrectomy (PPV) in patients with high myopia (HM), focusing on the optimal timing of surgery and its impact on prognosis.

• **METHODS:** The clinical data of 50 eyes from 49 patients diagnosed with ERM, who were highly myopic and underwent PPV were retrospectively analyzed. The patients with ERM were classified into five groups based on the characteristics associated with different levels of myopic traction maculopathy. Group 1: Simple ERM without complex vertical and tangential direction traction on retina on optical coherence tomography (OCT) image; Group 2: ERM with obvious macular foveal schisis, without macular hole (MH); Group 3: ERM with inner lamellar MH, with or without macular foveal schisis; Group 4: ERM with outer lamellar MH, with or without foveal retinal detachment (RD); Group 5: ERM with full-thickness MH. Baseline characteristics, changes in best corrected visual acuity (BCVA) before and after surgery, and anatomical characteristics through spectral domain OCT were compared.

• **RESULTS:** The 50 eyes were followed for 6mo, with an average age of 58.66y and an average axial length (AL) of 28.69 mm. Among the five groups, postoperative logMAR BCVA improved ($P < 0.05$). Group 1 had better mean BCVA at baseline (0.59 ± 0.36) and at 6mo postoperatively (0.16 ± 0.22) compared to the other groups, while Group 5 had worse mean BCVA at baseline (1.68 ± 0.45) and at 6mo postoperatively (1.27 ± 0.64). There were no statistically significant differences in sex, age or AL between the groups

($P > 0.05$). OCT showed that Groups 4 and 5 exhibited poorer macular anatomy compared to the other three groups, as evidenced by lower rates of central retinal reattachment (64.3% in Group 4, 86.7% in Group 5) and integrity of the inner segment/outer segment of photoreceptor junction (28.6% in Group 4, 26.7% in Group 5).

• **CONCLUSION:** PPV is an effective treatment for ERM in patients with HM. All groups showed postoperative improvement in BCVA compared to preoperative levels, demonstrating the necessity of surgical intervention. Early intervention, particularly before the fourth stage of the disease, may lead to better visual outcomes.

• **KEYWORDS:** epiretinal membrane; myopic traction maculopathy; pars plana vitrectomy; high myopia; visual acuity

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INTRODUCTION

Epiretinal membrane (ERM) is characterized by the pre-retinal proliferation of myofibroblastic cells along with the extracellular matrix^[1]. Various causes and pathways contribute to this retinal disease, which can be either idiopathic or secondary^[2-3]. In the past, ERM was diagnosed and classified solely based on clinical examination results. However, advanced imaging techniques are excellent at determining and grading the severity of ERM, and several idiopathic ERM classification schemes have been established based on optical coherence tomography (OCT)^[4-5]. For instance, Govetto *et al*^[6] classify idiopathic ERM into four types based on the shape of the fovea and ectopic fovea. Despite some progress, it is still not possible to distinguish histopathological variations, indicating that ERM is a heterogeneous group of diseases. The standard surgical approach for treating ERM involves pars plana vitrectomy (PPV), removal of the ERM, and optionally, internal limiting membrane (ILM) peeling^[7-8].

In patients with high myopia (HM), myopic traction maculopathy (MTM) is one of the complications of pathological myopia, characterized by lamellar macular hole (MH), full-thickness MH, and foveal retinal detachment (RD)^[9-11]. ERM is invariably associated with MTM, a significant cause of severe visual impairment^[12]. The clinical progression of ERM combined with MTM is more complex and distinctive^[13-14]. MTM associated with ERM demonstrates accelerated progression, greater complexity of changes, and advancement to more severe forms^[15-16]. Consequently, the development of ERM in eyes with HM may differ from that in non-HM eyes. However, there has been a notable lack of focused studies on the progression of ERM in highly myopic patients, warranting further investigation.

Based on the above considerations, this observation aimed to retrospectively analyze the clinical data of five groups of highly myopic patients, each characterized by ERM associated with different levels of MTM, who underwent PPV surgery. By comparing several clinical indicators within and across groups, we gained a better understanding of the progression of ERM with different levels of MTM, providing enhanced guidance for clinical diagnosis.

PARTICIPANTS AND METHODS

Ethical Approval This observation adhered to the principles set forth in the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (No.2024-0691). The informed consent was waived due to the retrospective design.

Participants Patients diagnosed with ERM and HM from January 2022 to December 2023 were retrospectively included. All enrolled patients underwent PPV surgery in the Department of Ophthalmology of the First Affiliated Hospital, College of Medicine, Zhejiang University and were followed up for more than 6mo, with complete clinical data. The patients' age, gender, axial length (AL), and ophthalmologic diagnosis were also collected. At each follow-up visit, best corrected visual acuity (BCVA), integrity of inner-segment/outer-segment (IS/OS), and central retinal reattachment rate were observed. The following inclusion criteria were used: 1) subjective visual symptoms; spherical equivalent refraction over -6.0 diopters at the first visit, with $AL \geq 26.00$ mm; 2) ERM confirmed by OCT and fundus examination; 3) comprehensive ophthalmic examination, including slit lamp biomicroscopy, BCVA measurements, optometry, AL measurements and OCT; 4) observational follow-up over a period of at least 6mo. The exclusion criteria were as follows: 1) intraocular pressure >21 mm Hg; 2) history of ophthalmic surgery (except cataract surgery); 3) coexisting or history of ocular or serious systemic disease (including glaucoma, diabetic retinopathy, diabetic macular edema, and autoimmune disorders); 4) evidence of

other retinopathy unrelated to myopia; 5) poor quality of OCT images.

Assessments Basic patient information, including age and gender, was obtained by reviewing electronic medical records. BCVA was recorded preoperatively and at the 6-month postoperative follow-up visit. BCVA was measured using the E-VA scale, and the results were converted to logMAR units. OCT images containing the central concavity were evaluated at baseline and 6mo after treatment for qualitative morphological features, including IS/OS integrity, and central retinal reattachment. The study eye of each participating subjects was imaged using OCT (Heidelberg Engineering, Heidelberg, Germany). OCT is utilized worldwide to diagnose and monitor macular and optic disc diseases. Images were acquired using the automated eye alignment TruTrack eye tracking technology (Heidelberg Engineering) to obtain perifoveal volumetric retinal scans comprising 61 single lines of 15 frames ($30^\circ \times 25^\circ$ volume scan centered at the fovea). Correction for fovea-disc orientation was provided automatically by the software with the fovea-disc alignment system. Signal quality for all images captured was ≥ 25 dB. The integrity of the IS/OS was assessed. Eyes were classified as intact if they displayed regular and continuous hyperreflective lines corresponding to the IS/OS, whereas they were classified as disrupted if they exhibited hyperreflective breaks. Central retinal reattachment was observed using OCT to qualitatively assess the restoration of normal retinal anatomical structure, particularly focusing on the tight connection between the retinal pigment epithelium layer and the neural retina. Two raters independently assessed each set of OCT images while maintaining the confidentiality of the patients' clinical information.

Groupings Patients with ERM were classified based on characteristics associated with different levels of MTM^[17]. In clinical practice, OCT has proven to be more sensitive than clinical examination for the diagnosis of ERMs^[18-20]. The diagnosis of ERM depends on the recognition of the highly reflective membrane structure at the vitreous macular interface through clinical examination or OCT imaging^[21-22]. In this study, we divided the patients into five groups through their characteristics on OCT images and contemporary understanding of the pathogenesis of ERMs. Group 1: Simple ERM without complex vertical and tangential direction traction on retina on OCT image (Figure 1); Group 2: ERM with obvious macular foveal schisis, without MH (Figure 2A-2B); Group 3: ERM with inner lamellar MH, with or without macular foveal schisis (Figure 2C-2D); Group 4: ERM with outer lamellar MH, with or without foveal RD (Figure 3); Group 5: ERM with full-thickness MH (Figure 4). The classification was performed by two masked, experienced retina specialists.

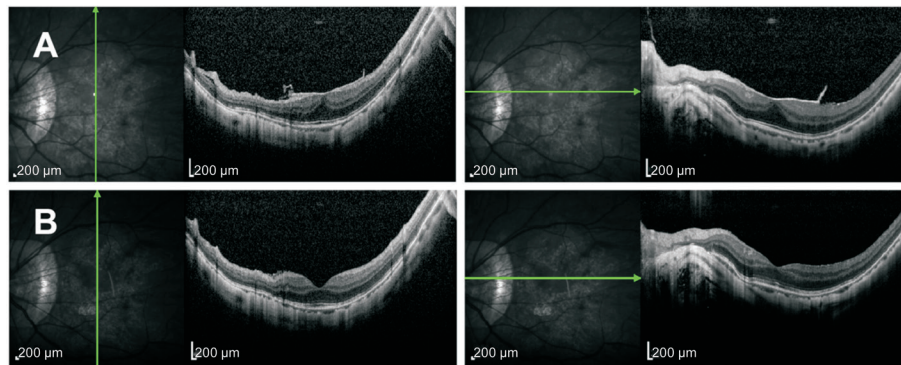


Figure 1 OCT images of an ERM patient A: Pre-operative; B: 6mo after vitrectomy. Surgical procedures: PPV with ERM, standard ILM peeling. PPV: Pars plana vitrectomy; ERM: Epiretinal membrane; ILM: Internal limiting membrane; OCT: Optical coherence tomography.

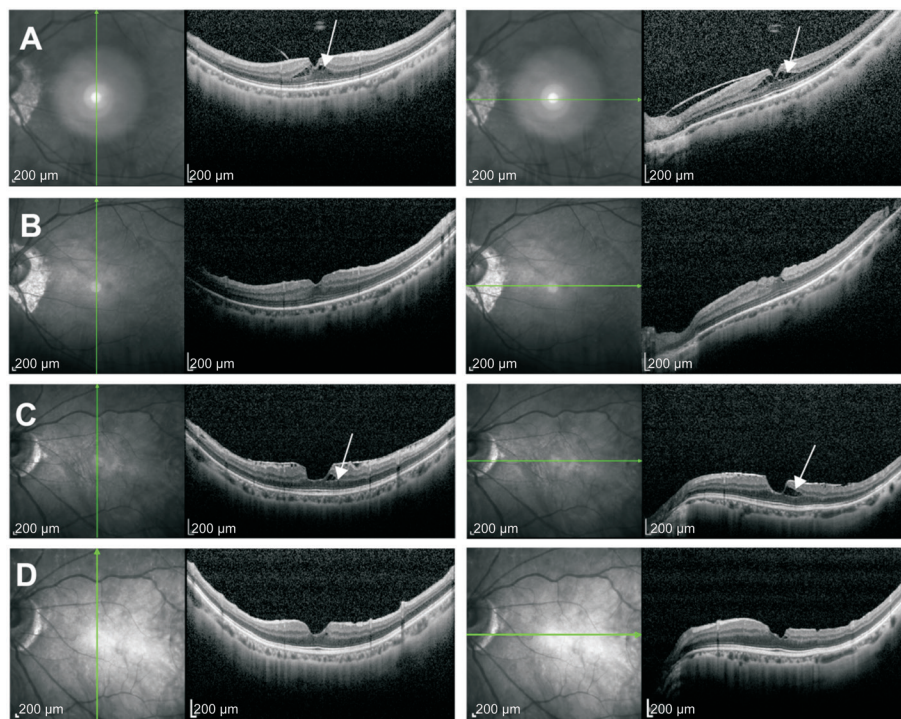


Figure 2 OCT images of representative cases A, C: Pre-operation; B, D: 6mo after vitrectomy. Surgical procedures: PPV with ERM, standard ILM peeling and air tamponade. MH: Macular hole; PPV: Pars plana vitrectomy; ERM: Epiretinal membrane; ILM: Internal limiting membrane; OCT: Optical coherence tomography.

Surgical Criteria and Technique Vitrectomy was scheduled after explaining the pros and cons of the procedure to the patient, who then agreed to undergo the procedure. The vitreous body was removed under retrobulbar anesthesia through a standard three-channel 23G or 25G high-speed vitreous cutting head and optical fiber *via* pars plana of the ciliary body. Triamcinolone acetonide was injected into the vitreous cavity, the remaining posterior vitreous cortex was stained and removed. Using 23G or 25G intraocular forceps, the edge of ERM was clamped, and centripetal peeling was performed along the retina surface to minimize the risk of surgically induced MH. The macular membrane was completely separated from the adherent part of the retina, from the posterior pole to the periphery, and then excised with the vitreous cutting head. The subsequent surgical approach and technique were tailored to the individual conditions, including

personalized ILM peeling. The ILM was peeled carefully using forceps, with *in vivo* staining using indocyanine green, without causing retinal damage to the macula. The choice of endotamponade (gas or oil) was made based on the individual case, considering the severity of traction or other intraoperative complications, and simultaneous cataract surgery was performed when necessary. Postoperative positioning regimens were also adjusted according to the patient's condition.

Statistical Analysis Continuous variables are expressed as mean±standard deviation (SD), and qualitative variables are expressed as numbers (*n*) and percentages (%). Categorical variables were compared across groups using Fisher's exact test. The paired *t*-test or the Wilcoxon signed-rank test was used for related samples in each group. Between-group comparisons were conducted using the Kruskal-Wallis test for non-normally distributed data or one-way ANOVA for

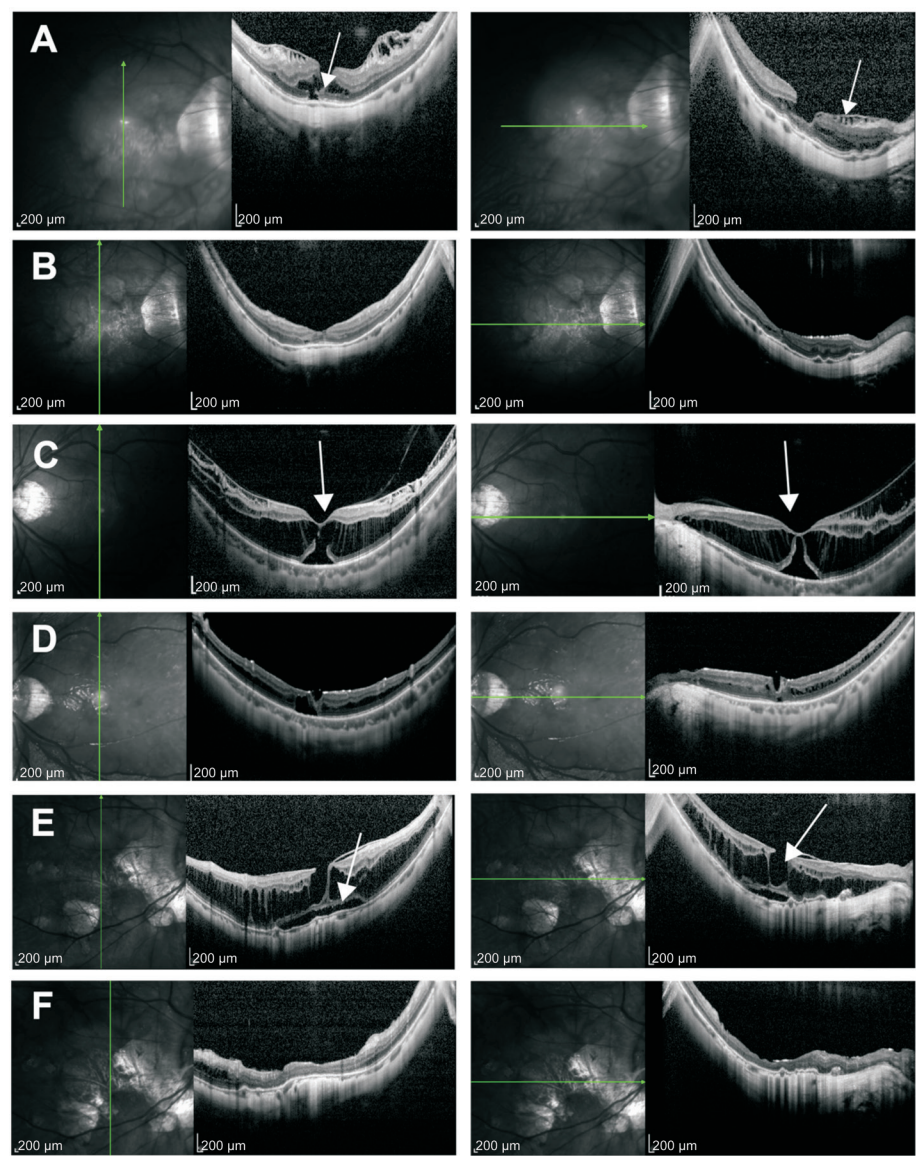


Figure 3 OCT images of representative cases A: Preoperative OCT images; B: 6mo after vitrectomy. Surgical procedures: PPV with ERM, standard ILM peeling and C₃F₈ tamponade. C, E: Preoperative OCT images. D, F: 6mo after vitrectomy. Surgical procedures: PPV with ERM peeling, fovea-sparing ILM peeling and oil tamponade. PPV: Pars plana vitrectomy; ERM: Epiretinal membrane; ILM: Internal limiting membrane; OCT: Optical coherence tomography.

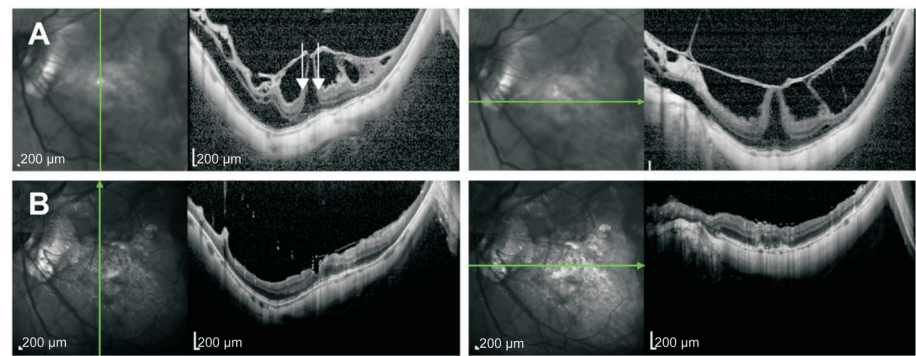


Figure 4 OCT images of an ERM with full-thickness MH patient A: Pre-operative; B: 6mo after vitrectomy. Surgical procedures: PPV with ERM, standard ILM peeling and oil tamponade. MH: Macular hole; PPV: Pars plana vitrectomy; ERM: Epiretinal membrane; ILM: Internal limiting membrane; OCT: Optical coherence tomography.

normally distributed data, with Bonferroni correction applied for multiple comparisons. All data were analyzed with SPSS

version 22.0 software (IBM, NY). *P*-values of less than 0.05 were considered statistically significant.

Table 1 Demographic and clinical characteristics of 50 eyes from 49 patients at baseline n (%), mean±SD

Parameters	Total	Group 1	Group 2	Group 3	Group 4	Group 5	P
No. of eyes	50	8	7	6	14	15	-
Age (y)	58.66±8.36	57.63±9.75	57.86±6.91	56.17±10.61	57.86±8.17	61.33±7.92	0.792 ^a
Right eye	27 (54)	5 (62.5)	3 (42.9)	4 (66.7)	7 (50)	8 (53.3)	0.928 ^b
Male	17 (34.7)	5 (62.5)	4 (57.1)	2 (33.3)	5 (35.7)	2 (13.3)	0.116 ^b
AL (mm)	28.69±1.70	28.38±2.01	28.22±1.14	28.48±1.24	28.96±1.87	28.91±1.84	0.839 ^c
BCVA 20/50 or better	11 (22)	4 (50)	3 (42.9)	2 (33.3)	2 (14.3)	0	0.012 ^b

^aKruskal-Wallis test; ^bFisher's exact test; ^cOne way-ANOVA. BCVA: Best-corrected visual acuity; SD: Standard deviation; AL: Axial length.

Table 2 Comparison of BCVA before and after surgery

Group	BCVA-preoperative, logMAR (Snellen equivalent)		BCVA-postoperative, logMAR (Snellen equivalent)		P
	Mean±SD	Range	Mean±SD	Range	
Group 1	0.59±0.36 (20/70)	0.1-1.3	0.16±0.22 (20/28)	0-0.6	0.016 ^b
Group 2	0.50±0.34 (20/63)	0.1-0.9	0.22±0.19 (20/34)	0-0.52	0.029 ^a
Group 3	0.84±0.66 (20/140)	0.22-2	0.29±0.31 (20/40)	0-0.82	0.024 ^a
Group 4	0.93±0.44 (20/170)	0.22-2	0.65±0.27 (20/89)	0.22-1.22	0.011 ^a
Group 5	1.68±0.45 (20/940)	0.7-2	1.27±0.64 (20/375)	0.4-2	0.025 ^b

P<0.05 was considered statistically significant. ^aThe paired t-test; ^bThe Wilcoxon signed-rank test. BCVA: Best-corrected visual acuity; SD: Standard deviation.

RESULTS

Demographics and Characteristics of Subjects A total of 50 eyes from 49 patients were included in the analysis. The average age was 58.66±8.36y, with 17 males (34.7%) and 32 females (65.3%). Of these, the right eye accounted for 54% of the total number of eyes. The mean AL was 28.69±1.70 mm, reflecting the HM status of the study cohort.

The number of eyes in each group was as follows: Group 1, ERM without MTM (8 eyes, 16%); Group 2, ERM with macular foveal schisis (7 eyes, 14%); Group 3, ERM with inner lamellar MH/foveal schisis (6 eyes, 12%); Group 4, ERM with outer lamellar MH/foveal RD (14 eyes, 28%); Group 5, ERM with full-thickness MH (15 eyes, 30%). The demographic and baseline characteristics of these five groups of patients were detailed in Table 1. There were no statistically significant differences across the five groups in terms of age ($P=0.792$), eye ($P=0.928$), sex ($P=0.116$), and AL ($P=0.839$), BCVA worsened as the disease progressed, with the proportion of BCVA 20/50 or better varying significantly among the groups. This shows a clear trend of poorer visual outcomes in more advanced stages of ERM with MTM features (Table 1). The OCT was used to assess the macular structure in all five groups, providing detailed imaging of the retinal changes associated with ERM at each stage of MTM. The representative OCT findings of five groups of patients are shown in Figures 1-4. These OCT images revealed the extent of macular deformation and provided visual evidence of the progressive structural changes as the disease advanced from ERM without MTM to full-thickness MH.

Visual Outcomes After Surgery The comparisons of pre-

and post-surgery within each group are shown in Table 2. As shown in Table 2, mean baseline BCVA in Groups 1-5 are 0.59 logMAR (Snellen equivalent 20/70), 0.50 logMAR (Snellen equivalent 20/63), 0.84 logMAR (Snellen equivalent 20/140), 0.93 logMAR (Snellen equivalent 20/170), 1.68 logMAR (Snellen equivalent 20/940). Each group showed a significant improvement in BCVA postoperatively at the six-month follow-up, with P -values of 0.016, 0.029, 0.024, 0.011, and 0.025, respectively. Mean postoperative BCVA in Groups 1-5 were 0.16 logMAR (Snellen equivalent 20/28), 0.22 logMAR (Snellen equivalent 20/34), 0.29 logMAR (Snellen equivalent 20/40), 0.65 logMAR (Snellen equivalent 20/89), 1.27 logMAR (Snellen equivalent 20/375). These results suggest that personalized ILM peeling combined with PPV surgery is effective for ERM. Furthermore, the changes in BCVA before and after surgery across the five groups are presented in Figure 5. By comparing the BCVA across the groups, we found a significant difference between Groups 1 and 5 both before and after surgery ($P=0.041$, $P<0.001$), although the differences in BCVA between Groups 1 and 4 were not significant at the six-month follow-up, the BCVA in Group 4 was significantly worse than in Group 1 compared to Groups 2 and 3. The BCVA of the Group 5 at 6mo postoperatively showed a significant difference compared to each of the other groups ($P<0.05$). Several features may affect postoperative BCVA, including baseline BCVA, IS/OS integrity, and macular degenerative changes. This suggests that earlier intervention, particularly before the fourth stage, could result in better visual outcomes.

Anatomical Outcomes After Surgery Meanwhile, the anatomical outcomes after surgery were evaluated using

Table 3 Postoperative macular anatomic outcomes					n (%)
Parameters	Group 1	Group 2	Group 3	Group 4	Group 5
Number of eyes	8	7	6	14	15
Central retinal reattachment	8 (100)	7 (100)	6 (100)	9 (64.3)	13 (86.7)
Integrity of IS/OS	8 (100)	7 (100)	4 (66.7)	4 (28.6)	4 (26.7)

IS/OS: Inner-segment/outer-segment.

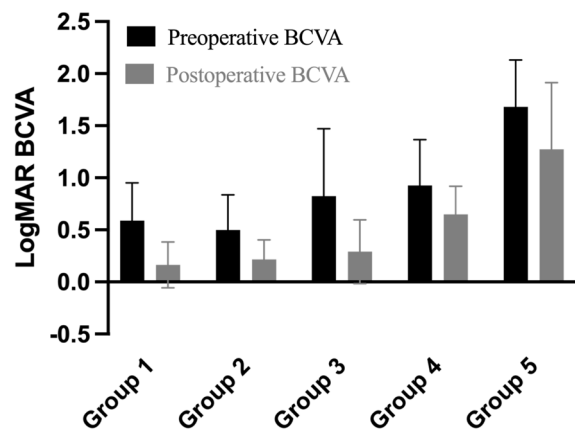


Figure 5 Changes in preoperative and postoperative BCVA across five groups Preoperative Group 1 vs preoperative Group 5 ($P=0.041$), preoperative Group 2 vs preoperative Group 5 ($P=0.020$), postoperative Group 4 vs postoperative Group 5 ($P=0.002$), postoperative Group 5 vs postoperative Group 1/2/3 ($P<0.001$). Using Bonferroni correction for multiple comparisons, $P<0.05$ was considered statistically significant. BCVA: Best-corrected visual acuity.

OCT. The integrity of the IS/OS junction and macular central retinal reattachment rate were assessed at 6mo postoperatively. Among these, the rate of macular central retinal reattachment in Groups 4 and 5 was lower at 6mo post-operation than in Groups 1 to 3. At the 6-month follow-up, Groups 3 to 5 showed a decrease in the integrity of the IS/OS junction compared to the Groups 1 and 2, as shown in Table 3. All patients in Groups 1 to 3 achieved 100% central retinal reattachment postoperatively. In contrast, the reattachment rates for Groups 4 and 5 were significantly lower, at 64.3% and 86.7%, respectively. Additionally, the integrity of the IS/OS junction showed that Groups 1 and 2 maintained 100% integrity postoperatively, whereas the integrity in Groups 4 and 5 significantly declined to 28.6% and 26.7%, respectively. This also reflects the anatomical disruption of the retinal photoreceptors, with lower recovery rates correlating with disease severity.

DISCUSSION

The results of this retrospective observation illustrated, for the first time, that highly myopic patients with ERM were classified into five groups based on different characteristic levels associated with MTM. We focused on the role of PPV surgery for ERM in highly myopic eyes. PPV and ERM peeling are well-established surgical treatments for

ERMs^[23-24]. In our observation, all patients demonstrated improved BCVA at 6mo postoperatively compared to their preoperative BCVA. As reported in current research, the ILM peeling during vitrectomy for ERM in highly myopic eyes is an effective surgical method^[7,25]. Although PPV surgery has proven to be an effective method for managing ERM, ILM peeling is thought to ensure complete removal of the overlying residual vitreous cortex and ERM and to alleviate tangential traction of the ERM^[26-27]. However, ILM stripping may be challenging in highly myopic eyes due to special anatomic factors such as severe abnormally thin retinas, posterior staphyloma, or choroidal retinal atrophy. Therefore, ILM peeling during vitrectomy in HM eyes remains controversial. Our observations suggest that surgical technique details should be individualized, with personalized ILM peeling approaches based on patient characteristics and retinal anatomy. These approaches may involve complete ILM peeling, fovea-sparing ILM peeling, or inverted ILM flap covering, depending on the clinical scenario. For instance, in patients with posterior staphyloma, inverted ILM flap covering may be considered based on the postoperative retinal anatomy and traction analysis. For patients with special factors, such as the relationship between the inner nerve fiber layer and the outer choroid and sclera of posterior scleral staphyloma, as well as thickness of the macular nerve fiber layer thickness, we opt for fovea-sparing ILM to avoid iatrogenic MH. Furthermore, the choice of appropriate endotamponade, such as balanced salt solution, air, gas or oil, should be based on the patient’s specific condition. Overall, a personalized approach to ILM peeling is necessary. This may include complete peeling, fovea-sparing ILM, inverted ILM flap covering, or other tailored techniques. The selection of tamponade should also be individualized. The difference in BCVA between preoperative and 6mo postoperative in each group was statistically significant. We observed worse BCVA as the disease progressed, with BCVA in Groups 4 and 5 being worse compared to the previous three groups at 6mo postoperatively. Several factors are known to influence postoperative outcomes, including baseline BCVA, IS/OS integrity, macular degenerative changes, macular traction and so on. These findings suggest that the progression of ERM associated with MTM is both accelerated and more intricate. The surgical plans and postoperative recovery vary depending on the different conditions. Parolini *et al*^[17]

described MTM as a progressive disorder, initially affecting the innermost retinal layers and gradually extending to the outer layers, eventually leading to MHs. Myopic MHs are frequently associated with macular schisis^[28]. As macular schisis progresses, it can result in foveal RD and full-thickness MHs, significantly impacting BCVA. Furthermore, during the follow-up period of our study, the integrity of the IS/OS junction and central foveal reattachment were still affected. Patients in Groups 4 and 5 had more advanced stages of MTM, including the presence of outer lamellar holes, full-thickness MHs, and macular RD. The lower rates of retinal reattachment and decreased IS/OS integrity in Groups 4 and 5 underscore the challenges of ERM associated with different stages of MTM. Previous studies have shown that the integrity of the IS/OS junction is closely correlated with poor BCVA improvement, further emphasizing the difficulty in achieving significant visual recovery^[29-31]. The presence of ERM with an outer lamellar hole or macular RD represents a critical stage for surgery, as substantial retinal damage makes full anatomical restoration more difficult, and persistent retinal traction is common in advanced stages. This is due to the more intricate and widespread ERM and the underlying pathophysiology of MTM. Early surgical intervention is crucial, particularly before reaching this stage. It can alleviate abnormal macular traction and restore the normal structure of the macula. This leads to more durable recovery, better maintenance of visual function, and improved long-term outcomes for patients with ERM associated with MTM.

Our study has some limitations: 1) it lacks long-term results beyond 6mo, which would help us better understand the natural progression of the disease. We hope that future studies will consider a longer follow-up period to assess long-term outcomes, which will provide more insights into the sustainability of the results and the potential risks or benefits over an extended duration. 2) The study was retrospective, and the choice of surgical procedure depended on the time of patient admission. Therefore, more prospective, long-term studies are needed to identify further anatomical and functional changes. 3) Although several classification systems for MTM have been proposed, there is still no consensus on the complete terminology and treatment strategies. The classification system used in this study is based on the existing MTM evolution grading system, with special consideration for the pathological changes caused by HM. As our understanding of the disease improves, more systematic and accurate grading systems are expected to be developed.

Above all, the management of ERM in patients with HM requires a multidisciplinary approach involving ophthalmologists, optometrists, and researchers. Early detection and timely surgical intervention are crucial for preserving visual

function and preventing irreversible vision loss. Continued advancements in surgical techniques and understanding of pathogenic mechanisms will further improve outcomes for these challenging cases.

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