Original Article

Vitrectomy with inner limiting membrane peeling effectively reduces ellipsoid zone defect diameter in patients with idiopathic macular holes

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Abstract: Objective: To comparatively assess the clinical outcomes of vitrectomy combined with either inner limiting membrane (ILM) peeling or ILM flap insertion for treatment of an idiopathic macular hole (IMH). Methods: A total of 116 IMH patients were enrolled, who underwent vitrectomy plus ILM peeling or vitrectomy with ILM flap insertion. They were divided into a peeling group (n=55, vitrectomy combined with ILM peeling) and an insertion group (n=61, vitrectomy plus ILM flap insertion). Intergroup differences were analyzed in postoperative lens status, best-corrected visual acuity (BCVA), intraocular pressure (IOP), hole closure rate/morphology, ellipsoid zone defect diameter, nasal/temporal inner retinal cyst (IRC) thickness, P1 wave amplitude (1-2 rings) of the first-order function in multifocal electroretinography (mfERG), safety, and vision-specific quality of life. Results: No significant intergroup differences were observed in postoperative lens status, hole closure rate, closure morphology, BCVA, IOP, nasal/temporal IRC thickness, P1 wave amplitude (1-2 rings) of mfERG first-order function, or vision-specific quality of life (all P > 0.05). However, the peeling group exhibited a smaller ellipsoid zone defect diameter than the insertion group (P < 0.05). No complications occurred in either group. Conclusion: Although vitrectomy combined with ILM peeling and that with ILM flap insertion yield comparable therapeutic effects and clinical safety, the former is more effective in reducing the size of ellipsoid zone defects in IMH treatment.

Keywords: Vitrectomy, inner limiting membrane peeling/flap insertion, idiopathic macular hole, surgical outcomes

Introduction

An idiopathic macular hole (IMH) is defined by a full-thickness retinal defect, predominantly occurring in the central macula. Unlike secondary macular holes, it is not associated with diabetic retinopathy, pathological myopia, or other ocular disorders [1]. IMH arises from macular traction-either anterior-posterior traction due to abnormal posterior vitreous detachment (PVD) or tangential traction caused by abnormal proliferation and contraction of the inner limiting membrane (ILM). Accounting for approximately 64.4% of all macular holes, it predominantly affects individuals over 60 years of age and females [2-5]. In the early stages, IMH is often asymptomatic; however, as the disease progresses, patients may experience gradual visual acuity loss, metamorphopsia, and central scotomas, which can impair their daily

activities, work, and study to varying degrees [6]. Vitrectomy is the primary treatment for IMH, often combined with ILM peeling or ILM flap insertion (inverted ILM flap technique) [7]. Reported macular hole closure rates exceed 90% with this surgical strategy [7]. However, surgical complications still exist, and postoperative incomplete anatomical closure or poor visual recovery may occur [8]. Thus, there is still room for optimizing vitrectomy for IMH, and improving these therapeutic strategies would significantly enhance the clinical outcomes and quality of life for affected patients.

The ILM is composed of the basal lamina of Müller cells and their expanded terminal footplates [9]. It is significantly thicker in the macular area and gradually thins toward the peripheral retina. A specialized conical thickening, known as the "Müller cone", is present at the

junction of the ILM and the external limiting membrane [9]. Abnormal vitreoretinal adhesions in eyes with IMH cause avulsion of the Müller cell cone. Furthermore, shortening of the ILM edges and proliferation of glial cells and Müller cells on the ILM further promote IMH progression [10]. ILM peeling, commonly performed in conjunction with vitrectomy, is used to treat macular holes, chronic macular edema secondary to epiretinal membranes, and vitreoretinal traction disorders. For IMH, in particular, it enhances retinal compliance, facilitating hole closure [11]. However, this procedure may adversely affect retinal structure and function: surgical instruments can induce temporary arcuate nerve fiber layer edema, and trauma from Müller cell detachment may lead to delayed dissociation of the inner retinal layers, which can be observed months postoperatively [12]. ILM flap insertion, a modified form of ILM peeling, involves placing an inverted temporal ILM flap and tamponading with perfluoropropane (C3F8). It induces glial cell proliferation on the ILM, reduces tangential traction around the macular hole, and promotes hole closure. This technique is preferred for patients with large, chronic macular holes or poor predicted preoperative closure rates [13].

The relative effectiveness of ILM peeling versus ILM flap insertion during vitrectomy for IMH remains inadequately investigated. This study aims to evaluate these two techniques to improve clinical understanding, optimize surgical decision-making, and refine patient management protocols.

Materials and methods

General data

The data of 116 patients with IMH treated at Liyang Hospital of Chinese Medicine from April 2022 to April 2024 were retrospectively analyzed. According to the surgical procedures, patients were divided into a peeling group (n=55, vitrectomy combined with ILM peeling) and an insertion group (n=61, vitrectomy plus ILM flap insertion). This study was approved by the Ethics Review Board of Liyang Hospital of Chinese Medicine.

Parameters for study participant selection

Inclusion criteria: Patients with symptomatic visual impairment and metamorphopsia of

varying degrees; IMH staged III-IV confirmed by optical coherence tomography (OCT) per the Gass classification [14]; surgeries performed exclusively by experienced vitreoretinal surgeons; stable refractive status (myopia \leq -6.00 diopters [D], axial length < 26 mm); no prior treatment for IMH; no significant proliferative retinopathy; and complete medical records.

Exclusion criteria: High myopia (spherical equivalent [SE] \leq -6.00 D or axial length [AL] \geq 26 mm); retinal detachment; age-related macular degeneration; ocular trauma; choroidal detachment; severe systemic diseases; concomitant severe cataracts, glaucoma, uveitis, retinal vascular diseases, or proliferative vitreoretinopathy (PVR) \geq grade B; prior ocular surgery; diabetes mellitus; hepatic or renal dysfunction; cardiovascular or cerebrovascular contraindications to surgery; autoimmune diseases; malignancies; and pregnancy or lactation.

Treatment methods

Patients in the peeling group underwent vitrectomy combined with ILM peeling, while those in the insertion group received vitrectomy plus ILM flap insertion. All surgeries were performed by the same experienced vitreoretinal surgeon under local anesthesia, using the Constellation system for 23-gauge triple-port pars plana vitrectomy, with intraoperative visualization assisted by ophthalmic surgical contact lenses.

ILM flap insertion procedure: The surgery started with standard three-port pars plana vitrectomy. If PVD was not clearly present, 0.1 mL triamcinolone acetonide was injected to improve vitreous visualization and facilitate PVD. After central vitrectomy, the ILM was stained with 0.25% indocyanine green (ICG) dye. Following complete ICG removal, an ILM flap was elevated starting from the temporosuperior region relative to the macula using microforceps, with a diameter approximately twice the width of the optic disc. The flap was then inverted and placed into the macular hole. If the ILM flap exhibited insufficient stability, a siliconetipped flute needle was used to gently tamponade the edges of the macular hole toward the center. Subsequent steps included fluid-air exchange with drainage of intraocular irrigation fluid, followed by intravitreal injection of 13% C3F8 gas to complete the surgery.

ILM peeling procedure: This approach differed from the ILM flap insertion technique only in

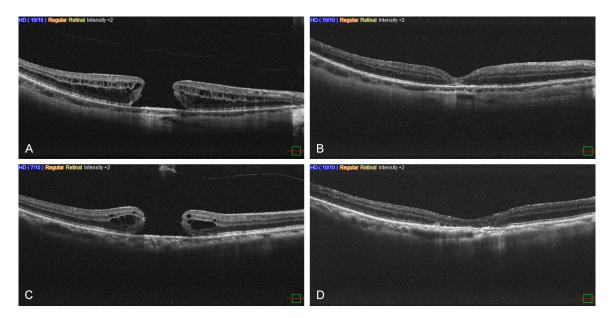


Figure 1. Pre- and post-intervention optical coherence tomography (OCT) images of a patient. A. Prior to intervention with inner limiting membrane (ILM) peeling, the OCT demonstrates a classic idiopathic macular hole (IMH), featuring a full-thickness retinal defect, cystoid edema at the hole's edges, and ellipsoid zone interruption. B. Post-ILM peeling, the macular hole is closed, and the neurosensory retina exhibits anatomical continuity. C. Prior to intervention with ILM flap insertion, similar characteristic findings of an IMH are observed. D. Post-ILM flap insertion, the macular hole is closed, demonstrating successful re-apposition of the neurosensory retinal layers.

ILM handling, involving standard peeling of a 2-disc-diameter ILM segment without the flap insertion step. **Figure 1** shows a comparison of OCT images from a representative case before and after treatment.

Endpoints

Postoperative lens status: Cases were categorized by lens status, including aphakia, intraocular lens (IOL) implantation, and mild/moderate cataracts.

Best-corrected visual acuity (BCVA) and intraocular pressure (IOP): BCVA was measured using logMAR charts following standardized refraction. IOP was assessed via handheld applanation tonometry. Data were collected preoperatively and at 6 months postoperatively.

Hole closure rate/morphology: The closure rate was calculated, and closure morphology was classified. Type I closure was defined as complete macular hole resolution with intact neuroepithelial continuity on OCT; Type II closure was characterized by focal neuroepithelial loss in the macula (exposing the retinal pigment epithelium [RPE]) but reattachment between the neuroepithelial layer and RPE at the hole site.

Ellipsoid zone (EZ) defect diameter: Horizontal distances between the discontinuities of the EZ in the photoreceptor layer were recorded preoperatively and 6 months postoperatively.

Nasal/temporal inner retinal cyst (IRC) thickness: IRC thickness (ranging from the nerve fiber layer to the inner plexiform layer) was measured 1,750 µm nasally and temporally from the foveal center preoperatively and 6 months postoperatively. Multifocal electroretinogram (mfERG) first-order kernel P1 wave amplitude (Rings 1-2): Measurements were performed preoperatively and at 6-month followup using the ERIS-420 system. Prior to testing, pupils were dilated with compound tropicamide. Electrodes were configured as follows: corneal Jet contact lens electrode, forehead ground electrode, and lateral canthus reference electrode. The non-tested eye was fully covered, and participants maintained fixation on the central target. P1 wave amplitudes of the firstorder kernel were measured for Ring 1 (foveal, 0°) and Ring 2 (5.44° eccentricity). Artifacts caused by eye movement, bubbles under the contact lens, blinking, or eyelid twitching were excluded. Safety: Ocular complications (e.g., lens damage, vitreous hemorrhage, retinal detachment, ocular hypertension, endophthalmitis, oculocardiac reflex) and systemic complica-

Table 1. Comparison of baseline data

Indicators	Peeling group (n=55)	Insertion group (n=61)	χ^2/t	Р
Sex (male/female)	20/35	21/40	0.048	0.828
Age (years)	57.31±7.70	55.80±6.07	1.179	0.241
Disease duration (months)	5.85±2.21	5.74±2.14	0.272	0.786
Macular hole diameter (µm)	651.29±37.37	654.79±43.28	0.464	0.644
Macular hole staging (III/IV)	28/27	29/32	0.131	0.717
Affected eye (left/right)	29/26	31/30	0.042	0.837

Table 2. Comparison of postoperative lens status

Indicators	Peeling group (n=55)	Insertion group (n=61)	χ²	Р
Aphakia	3 (5.45)	8 (13.11)	4.579	0.205
Intraocular lens implantation	22 (40.00)	30 (49.18)		
Mild lens opacity	21 (38.18)	18 (29.51)		
Moderate lens opacity	9 (16.36)	5 (8.20)		

tions (e.g., ischemic stroke, myocardial infarction) were documented in both groups. Vision-related quality of life (VRQoL): Assessments were conducted preoperatively and 6 months postoperatively using the Chinese version of the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) [15]. The questionnaire consists of 31 items across 12 subscales, with each item scored 0-4. Higher scores indicate better visual function and quality of life.

Among the above endpoints, postoperative lens status, hole closure rate/morphology, EZ defect diameter, IRC thickness, and safety were primary endpoints; mfERG first-order kernel P1 wave amplitude (Rings 1-2) and VRQoL were secondary endpoints.

Statistical methods

Data were analyzed using SPSS 25.0 software. Categorical data were presented as frequencies (percentages) and compared between groups using the χ^2 test. Continuous data were expressed as mean \pm standard error of the mean (SEM). Intergroup differences were analyzed using independent samples t-tests, and intragroup preoperative-postoperative changes were evaluated using paired samples t-tests. Statistical significance was set at P < 0.05.

Results

Comparison of baseline data

The two groups had comparable baseline characteristics (**Table 1**). No significant intergroup

differences were observed in sex distribution, mean age, disease duration, macular hole diameter, staging, or affected eye (all P > 0.05).

Comparison of postoperative lens status

Evaluation of postoperative lens status (aphakia, IOL implantation, mild/moderate cataracts) showed no significant differences between the two groups (all P > 0.05), as detailed in **Table 2**.

Comparison of ocular metrics (BCVA and IOP)

Table 3 presents the comparison of BCVA (LogMAR) and IOP between the groups. Preoperatively, no significant differences were found in either indicator (both P > 0.05). Postoperatively, both indicators decreased significantly in both groups (P < 0.01), but intergroup differences remained non-significant (both P > 0.05).

Comparison of hole closure rate and morphology

A comparison of hole closure rate and morphology is shown in **Table 4**. No significant differences were observed in either closure rate or closure morphology between the two groups (both P > 0.05).

Comparison of EZ defect diameter

As detailed in **Table 5**, baseline EZ defect diameters were comparable between the two groups (P > 0.05). Postoperatively, the peeling group showed a significant reduction in defect diameter (P < 0.01), whereas the insertion group

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Table 3. Comparison of ocular metrics (BCVA and IOP)

Indicators	Peeling group (n=55)	Insertion group (n=61)	t	Р
BCVA (LogMAR)				
Preoperative	1.18±0.51	1.26±0.59	0.777	0.439
Postoperative	0.76±0.37**	0.78±0.47**	0.253	0.801
IOP (mmHg)				
Preoperative	14.92±4.36	16.20±4.95	1.471	0.144
Postoperative	11.80±3.96**	12.47±4.29**	0.871	0.386

Note: BCVA, best-corrected visual acuity; IOP, intraocular pressure; Compared with pre-operative measurement, **P<0.01.

Table 4. Comparison of hole closure rate and morphology

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Indicators	Peeling group (n=55)	Insertion group (n=61)	χ^2	Р
Hole closure			0.029	0.864
Yes	50 (90.91)	56 (91.80)		
No	5 (9.09)	5 (8.20)		
Hole closure morphology			0.100	0.752
Type I closure	48 (87.27)	52 (85.25)		
Type II closure	7 (12.73)	9 (14.75)		

Table 5. Comparison of ellipsoid zone defect diameter

Ellipsoid zone defect diameter (µm)	Peeling group (n=55)	Insertion group (n=61)	t	Р
Preoperative	1014.15±183.85	1043.08±255.57	0.693	0.490
Postoperative	591.36±347.24**	925.03±407.76	4.719	< 0.001

Note: Compared with pre-operative measurement, **P < 0.01.

had a slight and non-significant reduction (P > 0.05). Intergroup comparison postoperatively confirmed superior outcomes in the peeling group (P < 0.01).

Comparison of nasal and temporal IRC thickness

Figure 2 displays the comparison of nasal and temporal IRC thickness between the two groups. Preoperatively, no significant differences were found in either nasal or temporal IRC thickness (P > 0.05). Postoperatively, both nasal and temporal IRC thicknesses decreased significantly in both groups (P < 0.01), with no significant intergroup differences (P > 0.05).

Comparison of mfERG first-order kernel P1 wave amplitude (Rings 1-2)

Figure 3 shows the comparison of mfERG first-order kernel P1 wave amplitudes (Rings 1-2) between the two groups. Preoperatively, no significant differences were observed in either Ring 1 or Ring 2 amplitudes (both P > 0.05).

Postoperatively, both groups showed significant improvements in both amplitudes (both P < 0.01), with no significant intergroup differences (both P > 0.05).

Comparison of safety profiles

No major perioperative complications including ocular complications (lens damage, vitreous hemorrhage, retinal detachment, ocular hypertension, endophthalmitis, oculocardiac reflex) and systemic complications (ischemic stroke, myocardial infarction) were observed in either group.

Comparison of VRQoL

Figure 4 presents the comparison of VRQoL assessed by the NEI-VFQ-25 between the two groups. Preoperatively, no significant difference was found in VRQoL scores (P > 0.05). Postoperatively, scores improved significantly in both groups (P < 0.01), but intergroup comparison showed no significant difference (P > 0.05).

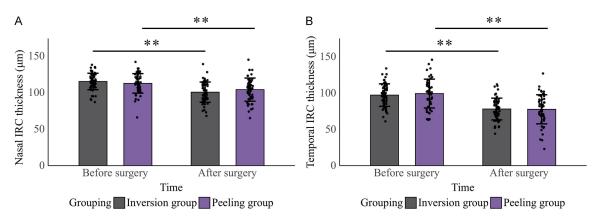


Figure 2. Comparison of Nasal and Temporal IRC Thickness. Changes in nasal IRC thickness pre- and post-surgery for both groups. A. Nasal IRC thickness pre- and post-operation. B. Temporal IRC thickness before and after surgery. Note: IRC, inner retinal cyst; **P < 0.01.

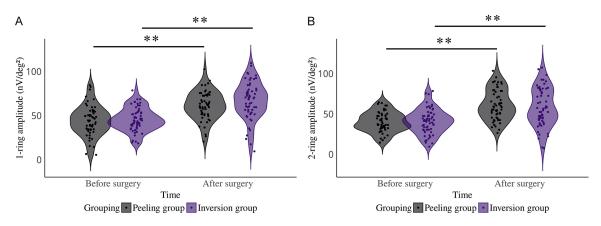


Figure 3. Comparison of mfERG First-Order Kernel P1 Wave Amplitude (Rings 1-2). A. Pre- vs. post-surgical P1 amplitude (ring 1) in the first-order mfERG function. B. Pre- vs. post-surgical P1 amplitude (ring 2) in the first-order mfERG function. Note: mfERG, multifocal electroretinogram; **P<0.01.

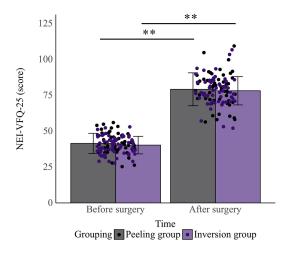


Figure 4. Comparison of VRQoL. Note: NEI-VFQ-25, National Eye Institute Visual Functioning Questionnaire-25; **P < 0.01.

Discussion

An idiopathic macular hole (IMH) is a full-thickness circular defect involving all layers of the foveal sensory retina, leading to visual impairment and metamorphopsia [16]. Vitrectomy is the primary treatment for IMH; however, preoperative mild lens opacities often progress to nuclear sclerotic cataracts postoperatively due to gas tamponade and other surgical factors, increasing the difficulty of subsequent interventions [17]. To optimize IMH treatment strategies, this study compared the clinical outcomes of vitrectomy combined with either ILM peeling or ILM flap insertion.

In this study, postoperative lens status did not differ significantly between the two groups. This

may be attributed to the similarity of the two techniques in all surgical steps except ILM handling, resulting in comparable effects on the lens. Additionally, both ILM peeling and ILM flap insertion achieved similar improvements in BCVA, LogMAR and reductions in IOP, indicating equivalent efficacy in visual recovery and IOP control. The macular hole closure rates were 90.91% in the peeling group and 91.80% in the insertion group, with Type I closure accounting for 87.27% and 85.25%, respectively. These results demonstrate that the two techniques have comparable effects on hole closure rate and morphology. Previous studies have shown that closure type affects postoperative vision in IMH patients, with Type I closure associated with better visual outcomes, improved visual function, and lower hole re-opening rates [18, 19]. Ma et al. [20] also reported that ILM flap insertion achieved a 93% closure rate and improved vision, which is consistent with our findings. The comparable efficacy may be related to the high proportion (92.24%) of large macular holes (> 600 µm) in our cohort, which may have masked potential differences in BCVA, IOP, closure rate, or morphology between the two techniques.

Regarding EZ defect diameter, ILM peeling significantly reduced defect size, whereas ILM flap insertion had no significant effect. This discrepancy may be due to the inserted ILM flap interfering with the natural healing of the macular hole, possibly via scar tissue formation. Both techniques significantly reduced nasal and temporal IRC thickness, with similar reduction effects. Further assessment of mfERG firstorder kernel responses showed that both techniques equally improved P1 wave amplitudes in the 1-ring and 2-ring regions. Additionally, the two procedures had equivalent safety profiles, with no ocular or systemic adverse events reported in either group. Finally, evaluations using the NEI-VFQ-25 indicated that both techniques achieved comparable improvements in VRQoL. ILM peeling releases tangential traction by completely removing a 2-disc-diameter ILM segment, promoting rapid centripetal closure of the macular hole. In contrast, ILM flap insertion relieves traction by inverting the peeled ILM flap into the defect and mechanically supporting the hole bottom. Despite differences in ILM handling, both techniques effectively reestablish retinal-choroidal reattachment in the macula, resulting in similar overall clinical outcomes.

Previous studies have explored various surgical treatments for IMH. One study [21] found that vitrectomy with ILM flap insertion achieved better hole closure and BCVA improvement than conventional ILM peeling. Fallico et al. [22] reported that the inverted ILM flap technique achieved equivalent visual recovery and anatomical closure rates to ILM peeling in patients with small IMH but was associated with adverse effects on postoperative outer retinal layer repair. Jia et al. [23] demonstrated that vitrectomy combined with single-layer inverted ILM flap coverage outperformed ILM flap insertion in patients with high myopia complicated by macular hole and retinoschisis, achieving better foveal reconstruction and significantly improved visual outcomes.

This study has several limitations. First, the small single-center sample size limits generalizability; future studies should include expanded multi-center samples to enhance representativeness. Second, long-term efficacy (5-10 years) of the two techniques requires further validation through extended follow-up. Finally, this study did not analyze anxiety, depression, or sleep quality in patients; incorporating these assessments could help clarify the potential clinical advantages of vitrectomy combined with ILM peeling. These limitations will be addressed in future research.

In conclusion, vitrectomy combined with ILM peeling and that with ILM flap insertion achieve comparable efficacy in IMH treatment, including postoperative lens status, visual recovery, IOP control, hole closure rate and morphology, nasal/temporal IRC thickness, mfERG P1 wave amplitude (1-2 rings), safety, and VRQoL. However, ILM peeling is superior in significantly reducing EZ defect size.

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Disclosure of conflict of interest

None.

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