Comparative Evaluation of Standard ILM Peel With Inverted ILM Flap Technique In Large Macular Holes: A Prospective, Randomized Study

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BACKGROUND AND OBJECTIVE: To compare the outcomes of inverted internal limiting membrane (ILM) flap technique (IFT) with the standard ILM peel (SIP) for large macular holes (MHs).

PATIENTS AND METHODS: This is a prospective, randomized study in which 100 patients with idiopathic MHs with minimum linear dimension of 600 µm or greater were recruited. Group 1 underwent SIP and group 2 underwent IFT. Best-corrected visual acuity (BCVA), type of MH closure, and multifocal electroretinogram (mfERG) were evaluated at presentation, 1 week, 1 month, and 3 months postoperatively.

RESULTS: Mean postoperative BCVA was 0.86 ± 0.19 in group 1 and 0.67 ± 0.3 in group 2 at 3 months postoperatively (P = .001). Type 1 closure was observed in 34.04% of patients in group 1 and in 62.79% of patients in group 2 (P = .02). mfERG showed improvement in both groups.

CONCLUSION: IFT provides superior outcomes compared to SIP and, hence, could be considered as the surgical modality of choice in large MH.

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INTRODUCTION

A full-thickness macular hole (FTMH) is defined as an anatomic defect in the fovea featuring interruption of all neural retinal layers from internal limiting membrane (ILM) to the retinal pigment epithelium (RPE).[1] The role of vitreous cortex in the pathogenesis of macular hole (MH) was better understood with the biomicroscopic observations of Gass.[2] MHs have been known since the 19th century[3] and were thought to be an untreatable condition until Kelly and Wendell proved the benefit of pars plana vitrectomy (PPV) combined with vitreous cortex detachment and fluid-gas exchange in a significant proportion of cases.[4] The success rate of MH surgery increased with the introduction of ILM peeling by Eckardt et al.[5] and now it is one of the most successful vitreoretinal surgeries.

The functional success of MH surgery depends upon the anatomical closure. Various types of anatomical closures of MHs have been defined. Postoperatively, if the MH is observed to close without a foveal defect in the neurosensory retina, it is considered to be a type 1 closure. If the foveal defect of neurosensory retina is found to persist, with flattening of surrounding cuff of fluid and the rim attached to the underlying RPE with a reduction in hole diameter, it indicates a type 2 closure.[7] The type 1 closure corresponds to the "u" and "v" pattern of closure and type 2 corresponds to the "w" pattern.[8] Non-closure is different from type 2 closure[9] of MH as it has elevated edges, which may be detached from surrounding RPE.

However, large MHs still pose a surgical challenge with poor anatomical and functional outcomes.

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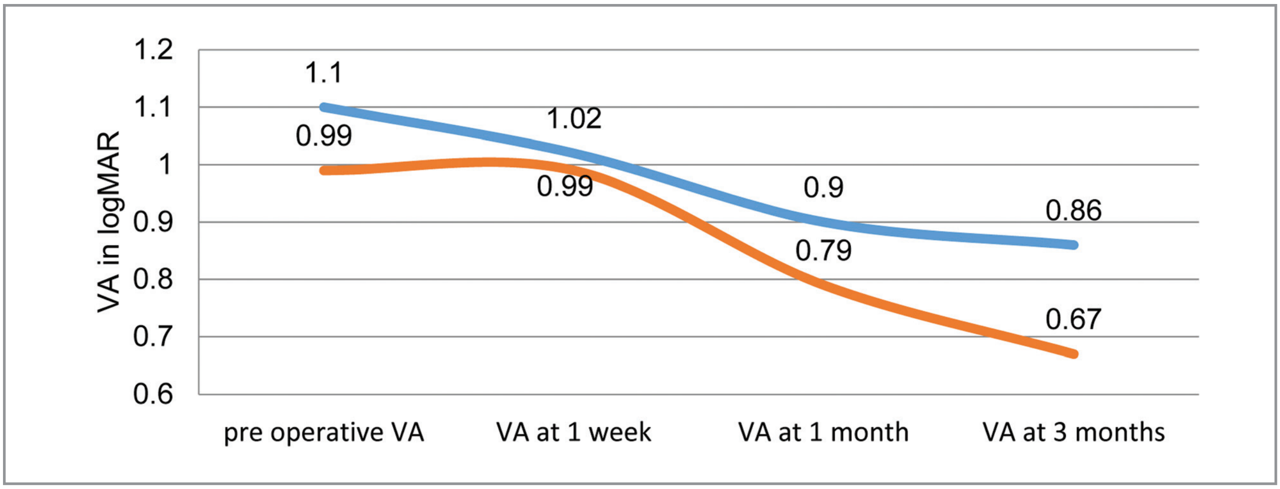

Figure 1. Line diagram showing visual acuity (VA) gain in each group (blue: group 1, red: group 2)

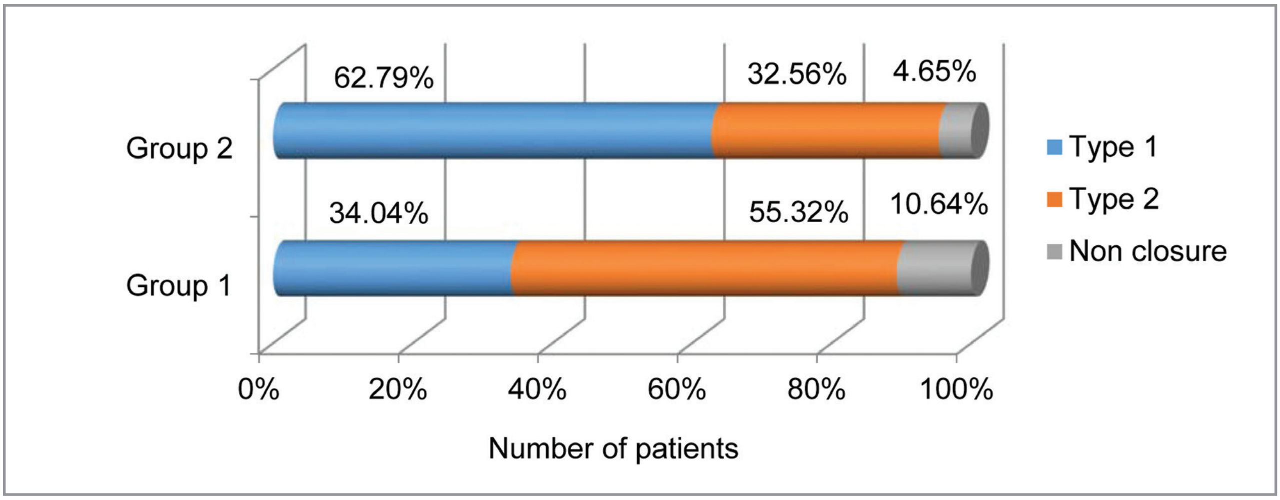

Figure 2. Type of macular hole closure in each group.

Michalewska et al. have proven the superiority of the inverted ILM flap technique over the standard ILM peel in patients with large MHs.[6] The outcome measures considered were anatomical closure of holes and visual acuity (VA). The current study compares the anatomical and detailed functional outcomes of inverted ILM flap technique with that of conventional MH surgery in large MHs.

PATIENTS AND METHODS

This is a prospective, randomized, interventional, comparative study. The study was carried out at a tertiary eye hospital in North India and was approved by the Institute Ethics Committee. One hundred patients with idiopathic FTMH with minimum linear diameter (MLD) of 600 µm or greater were randomized into two groups after excluding patients with traumatic MHs and associated ocular conditions, such as diabetic retinopathy, age-related macular degeneration, high myopia, retinal detachment, or glaucoma. Randomization was done using the computer-generated random number tables and the envelope method. In group 1, patients underwent standard ILM peeling, and in group 2 patients underwent inverted ILM flap technique.

Demographic profiles of the patients and duration of symptoms were noted. Best-corrected VA (BCVA) was measured using the standard ETDRS chart and converted to logMAR for statistical analysis. Detailed ocular examination was performed in all patients. Spectral-domain optical coherence tomography (SD-OCT) (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany) using the radial scan with 125 µm spacing through the center of the hole was used to measure the MLD and to assess postoperative hole closure. Multifocal electroretinogram (mfERG) (Metrovision, Perenchies, France) was done in all visits

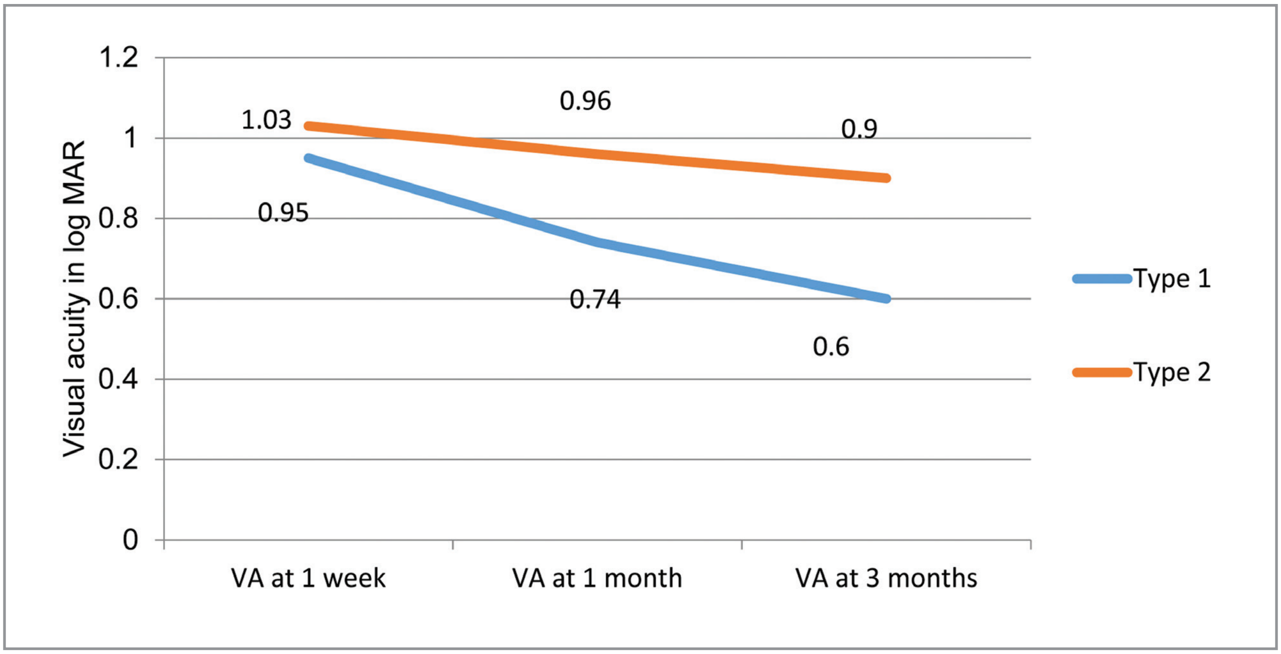

Figure 3. Type of closure and visual acuity (VA) gain.

in a fully dilated light adapted state for 5 minutes with monocular stimulation and a stimulus pattern of 61 regular scaled hexagons at a viewing distance of 33 cm.

Preoperatively, all patients underwent peribulbar block with a monitored anesthesia care. After core vitrectomy, triamcinolone assisted posterior vitreous detachment was done with active aspiration. ILM was stained with ILM-Blue 0.025% (DORC International, The Netherlands) dye. In group 1, the ILM was peeled subsequently and was confirmed by a second application of dye.

Inverted ILM Flap Technique

Instead of completely peeling off the ILM, a pedicle of the flap was left attached to the margins of the MH. The margins of the flap were trimmed with cutter under low suction, low cut rate, and shave mode duty cycle. The ILM flap was inverted and placed over the hole with a soft-tipped cannula or a diamond-dusted membrane scraper. The position of the flap was reconfirmed after fluid-air exchange.

In both groups, a nonexpansile mixture of 20% SF6 with air was left in the vitreous cavity. Postoperatively, face-down positioning was prescribed for 3 days, along with topical broad-spectrum antibiotics and anti-inflammatory therapies.

Postoperative Follow-Up

All patients were followed up at 1 week, 1 month, and 3 months postoperatively.

Outcome Measures

VA and postoperative MH closure were taken as the primary outcome. mfERG was considered as the secondary outcome measure. The outcome parameters were monitored on all visits.

Statistical Analysis

After attrition, 91 eyes were included for analysis: 48 eyes in group 1 and 43 eyes in group 2. The power of study was 0.989. Group 1 comprised 26 women and 22 men, and group 2 comprised 23 women and 20 men. All baseline parameters (Table 1) were comparable in both the groups.

Data analysis was done using SPSS Strata (Version 12.1; IBM, Armonk, NY). Nonparametric data were subjected to Mann-Whitney test and parametric data were subjected to two sample *t*-test. A *P* value less than .05 was deemed to be statistically significant.

RESULTS

VA measurement at 1 week was hampered by the residual gas bubble. Postoperative VA gain at 1 month (P = .01) and 3 months (P = .001) was significantly higher in group 2 than in group 1 (Figure 1).

In group 1, anatomical closure of the MH was observed in 42 of the 48 eyes, including 26 patients with type 2 closure and 16 patients with type 1 closure. In group 2, 41 of the 43 eyes had anatomical closure, including 14 eyes with type 2 closure and 27 eyes with type 1 closure. The difference in anatomical closure

TABLE 1

Baseline Parameters in Both Groups With Their *P* Values

Parameter	Group 1	Group 2	*P* Value
Age (Years)	60.95	63.41	.1
Duration (Months)	12.58	11.39	.1
Preoperative VA	1.1 ± 0.28	0.99 ± 0.25	.07
Preoperative MLD	657.5	673	.06
Preoperative MHI	0.34 ± 0.05	0.339 ± 0.06	.6

VA = visual acuity; MLD = minimum linear diameter; MHI = macular hole index

rates between the two groups was not statistically significant (P = .4). The type 1 closure rate observed in group 2 was higher than that seen in group 1, and the difference was statistically significant (P = .001) (Figure 2). The mean VA was higher in patients with type 1 closure than in those with type 2 closure (P = .02), indicating the functional superiority of type 1 closure (Figure 3).

There was no statistically significant difference in amplitude and implicit time of P1 wave between group 1 and group 2 at any stage (Table 2). A statistically significant difference between preoperative and postoperative value in group 2 indicates a better functional outcome in group 2 (Table 3).

DISCUSSION

PPV has been the gold standard of MH surgery since 1991.[4] The initial success rate described was 58%. The closure rate of MHs was 68% when ILM peeling-assisted PPV was first introduced[5] to manage idiopathic MH and has recently improved to between 86% and 100% with the aid of ILM staining.[10] The most important prognostic factor deciding the rate of MH surgical closure is the macular hole size.[11,12] Despite the good results reported, OCT demonstrates a flat, open appearance, also described as type 2 closure in 19% to 39% of large MHs. The eyes undergoing type 2 closure have limited VA.[13] Therefore, surgical closures of large MHs with improved functional outcomes continued to be challenging.

Multiple surgical modalities, including tapping of macular hole edges[14] and arcuate partial retinotomy,[15] were described previously for large MHs. But despite good anatomical success (86% to 92%), they result in poor functional outcomes owing to their traumatic nature. The aim is to obtain a type 1 anatomical closure in large MHs and, thus, obtain improved functional outcomes. All of the above mentioned surgical procedures and the inverted ILM flap technique induce glial cell proliferation, thereby resulting in filling of the tissue defect.[16,17] Tucking of the flap into the hole is not recommended due to the risk of injury to the RPE.

Any retinal damage will incite the migration of macrophage like cells into retina that secrete tumor necrosis factor alpha and induce gliosis by activating Müller cells. ILM peeling alone can induce gliosis, but when the ILM is left attached to the edge of MH, it acts as a scaffold and provides a basement membrane for cells to proliferate, thereby providing an environment for photoreceptors to align to a new position in direct proximity to the fovea. Müller cells also aid in transferring light from the retinal surface to the photoreceptor cell layer.[18] Besides gliosis, the ILM flaps create a closed compartment enabling the RPE to pump out fluid effectively, preventing further seepage of fluid and, hence, keeping the hole dry. This explains the functional and anatomical superiority of the inverted ILM flap over ILM peeling.

The inverted ILM flap technique is described with satisfactory results in patients with large MH[19] or high myopia.[20] In previous studies, BCVA was the only index used to compare the functional outcomes of the two surgical procedures. In our study, mfERG — which provides an objective measure of the functional outcome of MH surgery — was also considered. Both VA and mfERG response improved incrementally after surgery, but they do not adequately represent each other.[21] In our study, there is an increase in amplitude and a decrease in implicit time in group 2 postoperatively, but this was not statistically significant when compared to group 1. The improvement in mfERG takes a longer time than VA. Therefore, a study with a longer duration of follow-up may show statistically significant changes in mfERG. The BCVA is a subjective measurement, whereas mfERG provides an objective measurement of the functional outcomes.

In conclusion, the inverted ILM flap has a high incidence of type 1 closure with improved functional outcome in large MHs as compared to the standard ILM peel.

TABLE 2

Amplitude of P1 Wave in Group 1

	< 2°		2° to 5°		5° to 10°		10° to 15°		> 15°	
Parameter	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**
Median	536	694	469	590	547	857	689	897	765	1,090
Minimum	281	461	392	110	346	456	456	439	487	521
Maximum	1,206	1,568	932	1,481	1,507	1,368	1,464	1,360	1,361	1,781
P Value Wilcoxon Signed-Rank Test	.05		.02		.1		.3		.03	

TABLE 3

Amplitude of P1 Wave in Group 2

	< 2°		2° to 5°		5° to 10°		10° to 15°		> 15°	
Parameter	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**	**Preop**	**3 Months**
Median	557	917	498	678	515	844	637	873	687	986
Minimum	267	384	367	423	261	462	176	414	423	448
Maximum	1,277	1,610	870	1,104	1,076	1,267	1,464	1,433	1,284	1,564
P Value Wilcoxon Signed-Rank Test	.008		.006		.003		.002		.002	

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