Conventional Internal Limiting Membrane Peeling Versus Temporal Inverted Internal Limiting Membrane Flap Technique for Large Macular Holes: A Comparative Study

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Research Article

Keywords: large macular hole, internal limiting membrane, temporal inverted internal limiting membrane flap technique, vitrectomy

Posted Date: July 7th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-645284/v1

Abstract

Purpose: To compare the anatomical, morphological, and functional outcomes of the conventional internal limiting membrane (ILM) peeling versus temporal inverted internal limiting membrane flap technique for large full-thickness macular holes (FTMHs).

Subjects and Methods: Forty-six eyes of 44 patients with a minimum base diameter > 600 μm were included in this retrospective interventional study. The patients were divided into Group 1 (conventional ILM peeling) and Group 2 (temporal inverted ILM flap). The hole closure rate, best-corrected visual acuity (BCVA), ellipsoid zone (EZ), and external limiting membrane (ELM) defects were analyzed at baseline and 6 months after surgery.

Results: Hole closure was achieved in 17/25 (68%) cases of Group 1 and 20/21 (95.2%) cases of Group 2. The hole closure rate was significantly higher in the temporal inverted ILM flap group ($p = 0.022$). The mean BCVA (logMAR) changed from 1.12 ± 0.43 to 0.72 ± 0.31 in Group 1 and from 1.07 ± 0.34 to 0.51 ± 0.26 in Group 2 at six months ($p < 0.001$ in both cases). U-shaped closure was observed in 3 (12%) eyes in Group 1 and 15 (71.4%) eyes in Group 2 ($p < 0.001$). The total restoration rates of ELM and EZ were significantly higher in the temporal inverted ILM flap group ($p = 0.009$, $p = 0.001$, respectively).

Conclusion: The temporal inverted ILM flap technique is more effective than conventional ILM peeling for larger than 600 μm macular holes and improves anatomical, morphological, and functional outcomes.

Introduction

A full-thickness macular hole (FTMH) is a retinal defect that develops in the foveolar region and occurs most often in the elderly, with a prevalence ranging from 0.2–0.8% [1–3]. In 1991, the first successful surgery in patients with idiopathic FTMH was described by Kelly and Wendel [4]. Since then, vitrectomy with internal limiting membrane (ILM) peeling is commonly used as a gold standard treatment, and has been associated with an anatomical success rate of more than 90% [5–8]. However, the literature has reported relatively low anatomical success rates (i.e. closure rates of 40–80%) in complicated cases, such as those involving large (minimum diameter > 400 μm), myopic, or recurrent macular holes (MHs) [9–11]. Although several studies have investigated the new surgical approaches to improve the anatomical and functional results of these MHs, no effective treatment was found until recently.

Michalewska et al. [12] first described the inverted ILM flap technique (IFT), which improved both the anatomical and functional outcomes of large idiopathic MHs and myopic MHs. In this technique, the ILM is not completely peeled; a small remnant is retained on the margin of the MH. However, IFT has been associated with inner retinal layer defects [13, 14]. Tadayoni et al. [15] were the first to report the presence of a dissociated optic nerve fiber layer (DONFL) or inner retinal dimples after ILM peeling. These changes were demonstrated to be deeper and more prevalent in temporal macular areas [16]. In addition, some complications related to the IFT, such as worse post-operative visual acuity than the pre-operative level and expansion of retina pigment epithelial (RPE) atrophy have been reported [17–19]. Michalewska et al.

later introduced the temporal inverted ILM flap, a modified form that preserves the nasal part of the ILM. This technique not only decreases the risk of iatrogenic surgical trauma and DONFL appearance, but also provides anatomical and visual outcomes similar to those of the original inverted ILM flap technique [20]. ILM peeling was limited to the temporal side of the MH in an area of about two diameters of the optic nerve, and the MH was covered with an inverted single-layered flap.

This study aimed to compare anatomical, morphological, and visual outcomes of the conventional ILM peeling vis-à-vis single-layered temporal inverted ILM flap technique for the initial treatment of idiopathic and large macular holes with minimum diameter > 600 μm.

Subjects And Methods

This retrospective interventional study was conducted at Ondokuzmayıs University Hospital, Samsun, Turkey, from October 2018 to September 2020. The study protocol was approved by the Institute's Ethics Committee of Ondokuzmayıs University (2020/693), and the study adhered to the tenets of the Declaration of Helsinki. Each patients was informed about the risks and benefits of the surgery, and written informed consent was obtained.

The minimum and maximum diameters of the MHs were measured, and only those patients with MH symptom duration less than one year and whose minimum diameter exceeding 600 μm were included in the study. Patients with idiopathic FTMH and a minimum follow-up of 6 months were included. Patients with a retinal disease other than MH, traumatic and myopic macular holes, presence of co-existing ocular pathologies affecting vision, a history of previous surgery except for phacoemulsification, and inability to remain in a prone position after surgery were excluded. Patients were divided into two groups: conventional ILM peeling (Group 1) and temporal inverted ILM flap (Group 2).

Ocular parameters

All patients underwent a comprehensive ophthalmological examination, including refraction (KR8900, Topcon, Japan), best-corrected visual acuity (BCVA) using the Snellen chart, slit-lamp biomicroscopy, Goldman applanation tonometry, axial length measurement with IOLMaster (Zeiss Meditec AG, Jena, Germany), indirect ophthalmoscopy, and spectral-domain optical coherence tomography (SD-OCT; Heidelberg Engineering, Heidelberg, Germany), at baseline and 6 months after surgery. The BCVA values from the Snellen chart were converted into the logarithm of the minimum angle of resolution (logMAR). The foveal closure type, minimum and base diameters of the MHs, pre-operative and post-operative sizes of the ellipsoid zone (EZ), and external limiting membrane (ELM) defects were assessed using SD-OCT. The MH diameters and EZ and ELM defects were measured using a manual caliper placed parallel to the RPE on the horizontal and vertical SD-OCT B-scans through the fovea. The MH base diameter was defined as the longest distance of the base of the MH, while the minimal diameter was defined as the shortest distance between the edges of the MH. The post-operative foveal closure types were categorized as type 1 (U-shaped), type 2 (V-shaped), and type 3 (W-shaped) [21–24]. The U- and V-shaped closures were defined as a contour similar to that of a healthy fovea and a steep contour with a thin fovea centralis, respectively. The W-shaped closure was a closed but irregular contour that could not be defined as U- or V-shaped.

Surgical Procedure

All surgeries were performed by one experienced vitreoretinal surgeon (x.x) using retrobulbar anesthesia. Standard small-incision phacoemulcification (Alcon Centurion) and intraocular foldable lens implantation were performed in eight patients in each group in the same session with vitrectomy. A complete pars-plana vitrectomy was performed with an Enhancing Visual Acuity vitrectomy system (DORC, The Netherlands) using 23- gauge instrumentation. Following the removal of the core and cortical vitreous, the ILM was stained with Membrane Blue dye (DORC, The Netherlands) for 30 s. The dye was removed with a backflush needle, and then in the conventional ILM peeling group, the ILM was peeled completely in a circular fashion about two disc diameters from the edges of the MH. In Group 2, after the dye was removed, a large drop of PFCL was slowly injected into the posterior pole to stabilize the flap. Subsequently, ILM forceps was used to grasp and peel the ILM off from the temporal side of the MH in an area of about two diameters of the optic nerve. The peeled ILM was inverted and gently coaxed over the MH until adequate coverage was achieved [20]. If an epiretinal membrane (ERM) was present, it was peeled. Fluidair exchange was conducted, and octafluoropropane (C_3F_8, 14%) gas tamponade was used in all eyes. The patients were instructed to remain in the prone position at least for 3 days after the surgery.

Statistical analysis

All the quantitative measurements were expressed as the mean ± standard deviation. The Statistical Package for the Social Sciences (SPSS) software (v21.0 for Windows; SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses. For each continuous variable, the normality test was determined using the Kolmogorov-Smirnov test. Student’s t-test / Mann-Whitney *U* test was used to analyze the significant difference of continuous variables between the groups. BCVA, ellipsoid zone (EZ), and external limiting membrane (ELM) defect sizes were compared at baseline and 6 months post-operatively using Wilcoxon sign-rank test. The categorical variables between the groups were analyzed using the Chi-square / Fisher’s exact test. $P < 0.05$ was considered to be statistically significant.

Results

Twenty-five eyes of 24 consecutive patients operated with conventional ILM peeling and twenty-one eyes of 20 consecutive patients operated with temporal inverted ILM flap technique were included in the study. Eight patients in both groups underwent phacovitrectomy, while the remaining eyes underwent vitrectomy alone ($p = 0.665$). The mean ages of the patients were 69.1 ± 9.8 years and 67.7 ± 8.1 years in Group 1 and Group 2, respectively. The mean minimal and base MH diameters were higher in the conventional ILM peeling group, but the differences were not statistically significant ($p = 0.240$, $p = 0.234$, respectively). There were no significant differences in terms of age, sex, and baseline ocular findings, including BCVA, EZ defect size, and ELM defect size between the groups ($p > 0.05$ for all). The baseline characteristics of the patients are presented in Table 1.

The MH closure rate after a single surgery was 68% ($n = 17/25$) in Group 1 and 95.2% ($n = 20/21$) in Group 2. The hole closure rate was significantly higher in the temporal inverted ILM flap group ($p = 0.022$). Initial surgical failure was detected in eight eyes in Group 1 and only one eye in Group 2. Additional surgery was performed for four patients in Group 1 and one patient in Group 2, but surgical success was not achieved in any of these eyes. U-shaped closure was achieved in 3 (12%) eyes in Group 1 while 15 (71.4%) eyes in Group 2 ($p < 0.001$). V-and W-shaped closures were detected in 12 (45%) eyes and 2 (8%) eyes in Group 1, and 3 (14.3%) eyes and 2 (9.5%) eyes in Group 2, respectively.

The mean pre-operative ELM and EZ defects were significantly reduced in both groups at 6 months after surgery ($p < 0.001$ in both cases). Post-operative mean ELM defect sizes reduced to 512.8 ± 294.1 μm and 324.0 ± 276.9 μm in Group 1 and Group 2, respectively ($p = 0.032$). Post-operative mean EZ defect sizes in Group 1 and Group 2 were 634.5 ± 312.1 μm and 404.2 ± 279.0 μm, respectively ($p = 0.124$). The restoration of the ELM was always preceded by that of the EZ. Complete restoration of ELM rate was significantly higher in Group 2 ($n = 12/21$, 57.1%) than in Group 1 ($n = 5/25$, 20%) at six month postoperatively ($p = 0.009$). Similar to ELM, the total EZ restoration rate was significantly higher in Group 2 than in Group 1 ($p = 0.001$). A representative case of 66 -year-old man with a U-shaped MH closure and total restoration of the ELM and EZ is shown in Fig. 1.

The mean BCVA (logMAR) changed from 1.12 ± 0.43 to 0.72 ± 0.31 in Group 1 and from 1.07 ± 0.34 to 0.51 ± 0.26 in Group 2 at six months. The difference between the pre-operative and post-operative BCVA was statistically significant within Group 1 and Group 2. ($p < 0.001$ in both cases). The mean improvement in BCVA was significantly higher in Group 2 (logMAR 0.59 ± 0.38) than in Group 1 (logMAR 0.29 ± 0.19)($p = 0.004$). Patients with the total restoration of ELM and EZ defects had significantly better mean BCVA than those without ($p < 0.005$). Surgical outcomes of two groups 6 months after surgery are shown in Table 2. The illustration of a 73-year-old woman with a V-shaped closure and lasting ELM and EZ defects is shown in Fig. 2. None of the eyes presented deterioration in visual acuity in both groups, and no serious complications such as endophthalmitis, retinal tear or detachment, and glaucoma were encountered in the study.

Discussion

ILM peeling has been the main surgical approach for treating MH since its introduction in 1991 [4]. The surgery aims to relieve tractional forces responsible for the hole development and trigger reparative gliosis using the Müller cells [25, 26]. Although the MH closure rates can reach up to 90% with the standard surgical procedure, some cases (e.g., large, chronic, or myopic MHs) are more challenging and display a worsened prognosis [9–11]. Michalewska et al. first presented the inverted ILM flap technique for the treatment of large idiopathic MHs (diameter > 400 μm) and myopic MHs [12, 27]. The exact mechanism behind the improved anatomical and functional results remains unclear. One theory is that the inverted ILM flap provides a smooth and gap-free natural scaffold for glial cells and photoreceptors towards the fovea [12, 20]. Another proposes that the ILM acts as a barrier preventing the entry of fluid from the vitreous cavity into the MH [28]. Moreover, the activated Müller cells secrete neurotrophic and growth factors on the surface of the ILM, which may promote the survival of retinal neurons and photoreceptors cells and may contribute to the closure of the MH [28]. In her first description of this technique, Michalewska et al. reported an anatomical success rate of 98%. In addition, the post-operative BCVA was significantly higher in the inverted flap group compared to the standard surgery group (p = 0.001). However, despite its advantages, the appearance of dark striae on autofluorescence imaging in areas of previous ILM peeling has been reported by several authors [29]. These striae correspond to the swelling of the inner retinal layers, which is followed by the formation of small dimples in the retinal nerve fiber layer (RNFL). Various modifications of the original IFT, such as filling the hole with a folded ILM, a free ILM flap, and a pedicle ILM transposition flap, have been reported to minimize the surgical trauma and maximize the hole closure rates [30–32].

Michalewska et al. subsequently introduced the novel technique of the temporal inverted ILM flap, which included peeling off the ILM only from the temporal side of the fovea and inverting the flap nasally to cover MH. In their study, they compared the MH closure rates between the classic IFT (n = 43) and the temporal IFT, and they reported that the temporal inverted ILM flap technique was non-inferior to the classic inverted technique for MHs > 400 µm. In addition, the post-operative inner retinal dimplings was significantly lower in this modified technique [20]. MH closure was reported in 93% of the patients with temporal IFT after the initial surgery in this study. A second surgery was performed in 3 patients between 1 and 7 months after the initial surgery and, a hole closure rate of 100% was achieved. Takai et al. retrospectively analysed the outcomes of temporal IFT in chronic, large, and highly myopic patients and found a 100% hole closure rate in their study [33]. In another comparative study, Avci et al recently reported a 100% MH closure rate with temporal IFT in patients with a minimum hole diameter > 400 µm [34]. The study showed significantly higher MH closure rates in the temporal IFT group than the conventional ILM peeling group (100% vs. 72.2%). Similar to these results, we also observed a high MH closure rate in the temporal IFT group compared to the conventional ILM peeling group in the current study. The difference between our study and these studies was that only patients with minimal MH diameter larger than 600 µm were included in the study.

Previously, three types of successful MH closures have been described: U-, V-, and W-shaped. The first type is defined as a contour similar to that of a healthy fovea; The V-shaped closure is described as the RPE covered by the retinal layers with a steep notch; The last closure is defined as the RPE covered by the retinal tissue with an irregular surface. Michalewska et al. reported that the post-operative closure type and foveal contour could influence the BCVA, and the best results were achieved in eyes with U-shaped closures [35]. In another work using the temporal IFT, Michalewska et al. reported the rates of U-, V-, and W-shaped closures at the end of the 6 months to be 64%, 14%, and 16%, respectively [20]. Avci et al. observed the U- and V-shaped closure rates of 80% and 20%, respectively, at 12 months after surgery.[34] However, in the same study, the rate of U-shaped closure was reported to be only as %5 percent in the conventional ILM peeling group. In the current study, the U-, V-, and W-shaped closures were achieved in

15 (71%) eyes, 3 (14%) eyes, and 2 (5%) eyes in the temporal IFT group, respectively. In addition, similar to Avci et al.'s study, we observed a decrease in U-shaped closure rate in the conventional ILM peeling group. Thus, the higher BCVA values in the temporal IFT group can be explained by the higher rate of the U-shaped MH closure.

The post-operative structural analysis showed that patients with U-shaped closures had smaller ELM and EZ defects as well as normal retinal thickness at the end of the follow-up.[24, 35] The restoration of those structures can reportedly predict good post-operative visual outcomes. Michalewska et al. [20], Wakabayashi et al. [36], and Ramtohul et al. [37] reported that the integrity of ELM and EZ significantly correlated with the post-operative final BCVA. In her first description of temporal IFT, Michalewska et al. reported significantly worsened BCVA in patients with lasting ELM and EZ defects [20]. In the current study, both the statistically significant reduction in ELM and EZ defect sizes and higher post-operative complete restoration rates of ELM and EZ contributed to the better BCVA in the temporal IFT group compared to the conventional ILM peeling group. Our study results are consistent with those of previous studies that showed that ELM and EZ are critical structural features significantly correlated with BCVA.

Several researchers have suggested that a single-layered flap provides superior morphological and functional results compared with the multilayered flap or insertion technique [30, 38]. Michalewska et al. and Avci et al. found significant visual acuity improvement in cases undergoing temporal IFT surgery [20, 34]. Similar to their results, we found significant improvement in terms of BCVA (1.07 ± 0.34 logMAR vs. 0.51 ± 0.26 logMAR) at 6 months after surgery. None of the eyes underwent deterioration in visual acuity. A challenging part in the original temporal IFT technique is the flap detachment during the fluid–air exchange. To overcome this, we applied PFCL to the flap and gently massaged it on the edges to create a proper, single-layered, and unwrinkled covering over the hole. This modification may have contributed to the good anatomical and morphological results of the current study. No serious complications were observed in the study. The retrospective design, small sample size, and the follow-up period of six months, which was relatively short for evaluating the restoration of the outer retinal layers and visual outcomes, could be considered as some of the study limitations. However, to the best of our knowledge, this is the first study comparing conventional ILM peeling vis-à-vis single-layered temporal inverted ILM flap technique for the initial treatment of idiopathic and large macular holes with a minimum diameter larger than 600 μm.

In conclusion, large MHs are challenging cases with low surgical success rates. The temporal inverted ILM flap technique is more effective than conventional ILM peeling for larger than 600 μm macular holes and improves anatomical, morphological, and functional outcomes. Recovery of the outer retinal layers significantly correlated with better final visual outcomes. Further studies with larger sample sizes and longer follow-up times are needed to evaluate this surgical technique in more detail.

Declarations

Declaration of Interest

The authors declare that there is no conflict if interest

Funding Statement

The authors received no financial support for the research, authorship, and/or publication of this article.

Ethical Approvel

The study protocol was approved by the Institute’s Ethics Committee of Ondokuzmayıs University (2020/693)

References

References

1. Casuso LA et al (2001) Long-term follow-up of unoperated macular holes. Ophthalmology 108(6):1150–1155
2. Ezra E (2001) Idiopathic full thickness macular hole: natural history and pathogenesis. Br J Ophthalmol 85(1):102–108
3. Jackson TL et al (2013) United Kingdom National Ophthalmology Database study of vitreoretinal surgery: report 2, macular hole. Ophthalmology 120(3):629–634
4. Kelly NE, Wendel RT (1991) Vitreous surgery for idiopathic macular holes. Results of a pilot study. Arch Ophthalmol 109(5):654–659
5. Rahimy E, McCannel CA (2016) IMPACT OF INTERNAL LIMITING MEMBRANE PEELING ON MACULAR HOLE REOPENING: A Systematic Review and Meta-Analysis. Retina 36(4):679–687
6. Lai MM, Williams GA (2007) Anatomical and visual outcomes of idiopathic macular hole surgery with internal limiting membrane removal using low-concentration indocyanine green. Retina 27(4):477–482
7. Park DW et al., *Macular hole surgery with internal-limiting membrane peeling and intravitreous air.* Ophthalmology, 1999. **106**(7): p. 1392-7; discussion 1397-8
8. Yao Y et al (2019) The impact of extent of internal limiting membrane peeling on anatomical outcomes of macular hole surgery: results of a 54-week randomized clinical trial. Acta Ophthalmol 97(3):303–312
9. Salter AB et al (2012) Macular hole surgery prognostic success rates based on macular hole size. Ophthalmic Surg Lasers Imaging 43(3):184–189
10. Scott RA et al (2000) Visual and anatomical results of surgery for long standing macular holes. Br J Ophthalmol 84(2):150–153
11. Suda K, Hangai M, Yoshimura N (2011) Axial length and outcomes of macular hole surgery assessed by spectral-domain optical coherence tomography. Am J Ophthalmol 151(1):118–127.e1
12. Michalewska Z et al (2010) Inverted internal limiting membrane flap technique for large macular holes. Ophthalmology 117(10):2018–2025

13. Alkabes M et al (2011) En face optical coherence tomography of inner retinal defects after internal limiting membrane peeling for idiopathic macular hole. Invest Ophthalmol Vis Sci 52(11):8349–8355
14. Christensen UC et al (2009) Value of internal limiting membrane peeling in surgery for idiopathic macular hole stage 2 and 3: a randomised clinical trial. Br J Ophthalmol 93(8):1005–1015
15. Tadayoni R et al (2001) Dissociated optic nerve fiber layer appearance of the fundus after idiopathic epiretinal membrane removal. Ophthalmology 108(12):2279–2283
16. Nukada K et al (2013) Tomographic features of macula after successful macular hole surgery. Invest Ophthalmol Vis Sci 54(4):2417–2428
17. Deshpande R, Narayanan R, *Surgical repair of a giant idiopathic macular hole by inverted internal limiting membrane flap.* BMJ Case Rep (2015) **2015**
18. Hirano M et al (2015) Case report: successful closure of a large macular hole secondary to uveitis using the inverted internal limiting membrane flap technique. BMC Ophthalmol 15:83
19. Imai H, Azumi A (2014) The Expansion of RPE Atrophy after the Inverted ILM Flap Technique for a Chronic Large Macular Hole. Case Rep Ophthalmol 5(1):83–86
20. Michalewska Z et al (2015) TEMPORAL INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE VERSUS CLASSIC INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE: A Comparative Study. Retina 35(9):1844–1850
21. Shin MK et al (2014) Perfluoro-n-octane-assisted single-layered inverted internal limiting membrane flap technique for macular hole surgery. Retina 34(9):1905–1910
22. Andrew N et al (2016) Modification of the Inverted Internal Limiting Membrane Flap Technique for the Treatment of Chronic and Large Macular Holes. Retina 36(4):834–837
23. Michalewska Z, Nawrocki J, SWEPT-SOURCE OPTICAL COHERENCE TOMOGRAPHY *ANGIOGRAPHY REVEALS INTERNAL LIMITING MEMBRANE PEELING ALTERS DEEP RETINAL VASCULATURE*. Retina, 2018. 38 **Suppl 1**: p. S154-s160
24. Bonińska K, Nawrocki J, Michalewska Z, *MECHANISM OF "FLAP CLOSURE" AFTER THE INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE*. Retina, 2018. 38(11): p. 2184–2189
25. Smiddy WE, Feuer W, Cordahi G, *Internal limiting membrane peeling in macular hole surgery.* Ophthalmology (2001) **108**(8): p. 1471-6; discussion 1477-8
26. Gupta D (2009) Face-down posturing after macular hole surgery: a review. Retina 29(4):430–443
27. Michalewska Z et al (2014) Inverted internal limiting membrane flap technique for surgical repair of myopic macular holes. Retina 34(4):664–669
28. Shiode Y et al (2017) The Role of Inverted Internal Limiting Membrane Flap in Macular Hole Closure. Invest Ophthalmol Vis Sci 58(11):4847–4855
29. Clark A et al (2012) Swelling of the arcuate nerve fiber layer after internal limiting membrane peeling. Retina 32(8):1608–1613
30. Song Z et al., *Viscoat Assisted Inverted Internal Limiting Membrane Flap Technique for Large Macular Holes Associated with High Myopia.* J Ophthalmol, 2016. **2016**: p. 8283062

31. Morizane Y et al (2014) Autologous transplantation of the internal limiting membrane for refractory macular holes. Am J Ophthalmol 157(4):861–869.e1
32. Reis R, Ferreira N, Meireles A (2012) Management of Stage IV Macular Holes: When Standard Surgery Fails. Case Rep Ophthalmol 3(2):240–250
33. Takai Y et al., *The Role of Single-Layered Flap in Temporal Inverted Internal Limiting Membrane Flap Technique for Macular Holes: Pros and Cons.* J Ophthalmol, 2019. **2019**: p. 5737083
34. Avci R, Mavi A, Yildiz, Yilmaz S, *Conventional internal limiting membrane peeling versus temporal inverted internal limiting membrane flap for large macular holes*. Eur J Ophthalmol, 2019: p. 1120672119892427
35. Michalewska Z et al (2008) Correlation between foveal structure and visual outcome following macular hole surgery: a spectral optical coherence tomography study. Graefes Arch Clin Exp Ophthalmol 246(6):823–830
36. Wakabayashi T et al (2018) Inverted internal limiting membrane insertion versus standard internal limiting membrane peeling for macular hole retinal detachment in high myopia: one-year study. Graefes Arch Clin Exp Ophthalmol 256(8):1387–1393
37. Ramtohul P et al (2020) Inverted internal limiting membrane flap technique versus complete internal limiting membrane peeling in large macular hole surgery: a comparative study. BMC Ophthalmol 20(1):11
38. Hillenkamp J et al (2007) Retreatment of full-thickness macular hole: predictive value of optical coherence tomography. Br J Ophthalmol 91(11):1445–1449

Tables

Table 1
The baseline characteristics of the two groups

	Conventional ILM peeling	Temporal inverted ILM flap	p value
Number of eyes	25	21	-
Age, mean ± SD, years	69.1 ± 9.8	67.7 ± 8.1	0.332[a]
Gender (female/male), n (%)	14 / 10	13 / 7	0.651[b]
Mean BCVA ± SD, logMAR	1.12 ± 0.43	1.07 ± 0.34	0.438[c]
Duration of symptoms, mean ± SD, months	4.8 ± 1.4	4.1 ± 1.1	0.520[c]
Preoperative lens status **Phakic / Pseudophakic**	14/11	11 / 10	0.806[b]
Minimum FTMH diameter, mean ± SD, μm	692.6 ± 228.0	673.7 ± 182.5	0.240[c]
Base FTMH diameter, mean ± SD, μm	1318.2 ± 324.6	1234.8 ± 315.1	0.234[a]
ELM defect size, mean ± SD, μm	1344.3 ± 352.9	1295.6 ± 350.6	0.152[a]
EZ defect size, mean ± SD, μm	1321.0 ± 339.3	1271.7 ± 348.5	0.181[a]

SD: Standard deviation, BCVA: best-corrected visual acuity, logMAR: logarithm of minimal angle of resolution, ERM: epiretinal membrane, ILM: internal limiting membrane, FTMH: full-thickness macular hole, EZ: ellipsoid zone, ELM: external limiting membrane

[a]Independent *t*-test.

[b]Chi-square test.

[c]Mann-Whitney *U* test.

Table 2
Surgical outcomes of two groups 6 months postoperatively

	Conventional ILM peeling	Temporal inverted ILM flap	p value
Primary hole closure rate, n (%)	17/25 (%68)	20/21 (%95.2)	0.022[a]
U-shaped closure, n (%)	3/25 (%12)	15/21 (%71.4)	< 0.001[b]
V-shaped closure, n (%)	12/25 (%48)	3/21(%14.3)	0.015[b]
W-shaped closure, n (%)	2/25 (%8)	2/21 (%9.5)	0.626[a]
ELM defect size, mean ± SD, µm	512.8 ± 294.1	324.0 ± 276.9	0.032[c]
EZ defect size, mean ± SD, µm	634.5 ± 312.1	404.2 ± 279.0	0.124[c]
Complete restoration of ELM, n (%)	5/25 (%20)	12/21 (%57.1)	0.009[b]
Complete restoration of EZ, n (%)	3/25	12/21 (%57.1)	0.001[b]
Mean BCVA, logMAR	0.72 ± 0.31	0.51 ± 0.26	0.016[c]
Mean improvement in BCVA, logMAR	0.29 ± 0.19	0.59 ± 0.38	0.004[c]

SD: Standard deviation, BCVA: best-corrected visual acuity, logMAR: logarithm of minimal angle of resolution, ILM: internal limiting membrane, EZ: ellipsoid zone, ELM: external limiting membrane

[a]Fischer's exact test

[b]Chi-square test

[c]Mann-Whitney *U* test

Figures

Figure 1

a. Pre-operative and post-operative cross-sectional B-scan images of a 66-year-old man with macular hole (MH). The pre-operative minimal and maximal MH diameters are 616 µm and 1381µm, respectively. Pre-operative best-corrected visual acuity (BCVA) was 0.2 b One month post-operatively. An inverted temporal ILM flap technique was performed. Macular hole closure was observed, but there was an incomplete restoration in outer retinal layers (between yellow arrowheads) c. Six months after surgery. SD-OCT showed a persistent U-shaped closure of the MH. There was a complete restoration of the ellipsoid zone and external limiting membrane lines. The BCVA increased to 0.4.

Figure 2

a. SD-OCT images for a 73-year-old woman with a large FTMH. The pre-operative minimum and base diameters of the macular hole were 746 μm and 1893 μm, respectively. The sizes of the ellipsoid zone (EZ) and external limiting membrane (ELM) lines were 2016 μm and 2090 μm, respectively. Pre-operative BCVA was 0.05 b. At six months after surgery, V-shaped MH closure and partially defective EZ (between red arrowheads) and ELM (between yellow arrowheads) lines were observed (The sizes of EZ and ELM were 1227 μm and 1282 μm, respectively). BCVA did not change (BCVA=0.05).