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RETINAL DISORDERS

Foveola nonpeeling internal limiting membrane surgery to prevent inner retinal damages in early stage 2 idiopathic macula hole

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Abstract

Purpose The purpose of this study was to investigate and present the results of a new vitrectomy technique to preserve the foveolar internal limiting membrane (ILM) during ILM peeling in early stage 2 macular holes (MH).

Methods The medical records of 28 consecutive patients (28 eyes) with early stage 2 MH were retrospectively reviewed and randomly divided into two groups by the extent of ILM peeing. Group 1: foveolar ILM nonpeeling group (14 eyes), and group 2: total peeling of foveal ILM group (14 eyes). A donut-shaped ILM was peeled off, leaving a 400-μm-diameter ILM over foveola in group 1.

Results Smooth and symmetric umbo foveolar contour was restored without inner retinal dimpling in all eyes in group 1, but not in group 2. The final vision was better in group 1 (P=0.011). All eyes in group 1 (100 %) and seven of 14 eyes in group 2 (50 %)regained the inner segment/outer segment (IS/OS) line. Restoration of the umbo light reflex was found in 12 of 14 eyes in group 1 (86 %) but none in group 2 (0 %).

Conclusions Nonpeeling of the foveolar ILM in early stage 2 idiopathic MH surgery prevented inner retinal damages, restored umbo light reflex, achieved better foveolar microstructures, and led to better final visual acuity.

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Keywords Fovea · Foveola · Internal limiting membrane · macular hole · Müller cell · Vitrectomy

Introduction

It is generally agreed that internal limiting membrane (ILM) peeling is important in achieving closure of macular holes (MH) [1]. An autopsy study of a patient who had undergone successful MH closure showed an area of absent ILM surrounding the sealed MH [2].

The present ILM peeling surgery of idiopathic MH includes total removal of foveolar ILM. However, removal of all the ILM over the foveola causes anatomical changes of the macula [3, 4]. They consisted primarily of dimpling or damages of the inner retina, paracentral scotoma observed by scanning laser ophthalmoscopy microperimetry, retinal pigment epithelial changes, dissociated optic nerve fibers layer (DONFL), focal dehiscence, concentric macular dark spots, and asymmetric elongation of foveal tissue [5–9]. A reduction of the ganglion cell complex thickness was observed after vitrectomy with ILM peeling for idiopathic MH [10]. In addition, after the removal of ILM there will be no impediment to the flow of fluid into the inner retina [11]. These factors may contribute to the traditional concept that there is no positive effect in ILM peeling for MH smaller than 400 μm [12]. Thus, small early stage 2 MH was chosen to perform the present foveola nonpeeling surgery, which is less invasive and protective than traditional total peeling ILM surgery.

In fact, during the natural course of the development of an early MH, there is only a small full-thickness retinal hole seen either centrally within the yellow ring or eccentrically at the margin of the ring at the foveal center. The foveolar ILM tissue still exists before the ILM peeling surgery [13, 14]. The preservation of the foveolar ILM during ILM peeling of MH surgery can maintain the integrity of the foveolar structure

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and may benefit the outcome of MH surgery. Besides, total ILM peeling for small or early MH may be too damaging to the foveolar tissue, hence there was no visual outcome benefit in the small hole after ILM for the whole foveola in previous reports [15].

We previously described a surgical technique [16] to preserve the central 400 μm ILM over the foveola in myopic traction maculopathy by combined usage of microscissors and ILM peeling forceps, which successfully released the tangential traction and restored the foveal contour. We aimed to apply this foveola nonpeeling technique to such stage 2, small, full-thickness MH. Thus, the present study was conducted to evaluate the result of the novel vitrectomy technique in early stage 2 MH.

Patients and methods

All of the patients had undergone surgery at the Department of Ophthalmology, National Taiwan University Hospital, and all were diagnosed with early stage 2 idiopathic MH according to the Gass classification. The preoperative data recorded included age, sex, right or left eye, spectral domain optical coherence tomography (SD-OCT), and Snellen best-corrected visual acuity (BCVA). All of the patients had comprehensive ophthalmologic examinations pre-operatively, and then 1 month and every 3 months postoperatively. The examinations included BCVA, binocular indirect ophthalmoscopy, non-contact lens slit-lamp biomicroscopy, fundus photography, and SD-OCT examination. The SD-OCT images were evaluated to determine the integrity of the external limiting membrane (ELM), IS/OS junction.

The medical records of 24 patients (28 eyes) with early stage 2 MH were retrospectively reviewed. They were divided randomly into two groups by the extent of ILM peeing. Group 1: foveolar ILM nonpeeling group (14 eyes) and group 2: total peeling of foveal ILM group (14 eyes). A donut-shaped ILM was peeled off, leaving a 400-μm-diameter ILM over foveola in group 1. All surgeries were performed after the patients received a detailed explanation of the surgical and SD-OCT procedures. The surgery was performed by a single surgeon, one of the authors (T.-C. Ho). A standard 3-port pars plana vitrectomy was used to close the MH under 2 % lidocaine retrobulbar anesthesia. An intravitreal injection of triamcinolone acetonide (Kenacort-A; Bristol Pharmaceuticals KK, Tokyo, Japan) or indocyanine green (ICG)(Santen Pharmacy, Osaka, Japan) was used to make the vitreous gel and ILM more visible. ICG (0. 5 mg/ml) was used to stain the ILM before ILM peeling. Approximately 0.1–0.2 ml of dye was applied to the ILM surface for 30 seconds. Core vitrectomy was performed and the partially detached posterior hyaloid membrane adhered to the margin of the MH was removed. Then, the ILM was removed with preservation of the central 400-μm-diameter ILM in group 1 and was totally removed in group 2. Nonexpansive 15 % C3F8 was used to tamponade the retina, and patients were instructed to maintain a facedown position for 3–4 days postoperatively. Anatomic success was defined as the presence of a flat or closed MH at 1 month postoperatively, confirmed by biomicroscopy and SD-OCT. Microstructural images of the fovea were obtained by the SD-OCT (OCT4000; Cirrus HD-OCT, Carl Zeiss Meditec Inc, Dublin, California, USA). The entire macular area was scanned, and high-quality images of 6-mm scans were obtained with the 5-line raster mode. We used the horizontal or vertical 6-mm scans to evaluate the IS/OS junction and ELM line. A recovered foveal microstructure in the photoreceptor layer was defined as a recovery of the continuous backreflecting lines corresponding to the IS/OS junction and the ELM line.

Statistical analyses were performed with SPSS for Windows version 11.5 (SPSS Inc, Chicago, Illinois, USA). The significance of differences between the hole diameter, preoperative and postoperative BCVA, and BCVA improvement in each group was determined by Mann-Whitney U tests. A P value<.05 was considered statistically significant.

Institutional review board approval was obtained, and all patients were provided written informed consent in accordance with institutional guidance, according to the Declaration of Helsinki.

Results

Intraoperatively, after removal of the posterior hyaloid membrane we were able to perform a donut-shaped peel of the foveal ILM surrounding the central foveola in the group 1 eyes. The foveal ILM was complete preoperatively except for the small linear crescent or central defect in the macular hole. Approximately two-fifths of the ILM was peeled off in the beginning and microscissors were used to make tangential cuts superior or inferior to the foveola. Repeated microscissor cuts and peeling with ILM forceps were needed. The remaining ILM could then be peeled off without damaging the central foveola (Fig. 1). Scissors should be used more carefully than in eyes with myopic traction maculopathy, because the neurosensory retina is less flexible in idiopathic MH than in myopic traction maculopathy. At the end of the operation, a donut-shaped ILM was peeled off with a remaining central epifoveolar membrane 300–400 μm in diameter. A video supplement of the technique submitted along would better demonstrate the technique. Shimada et al. [17] reported a fovea-sparing method by vitrector trimming in myopic traction maculopathy, which was different from our method and most likely cannot be applied to early stage 2 MH. Their vitrector trimming method trimmed ILM to the size of one

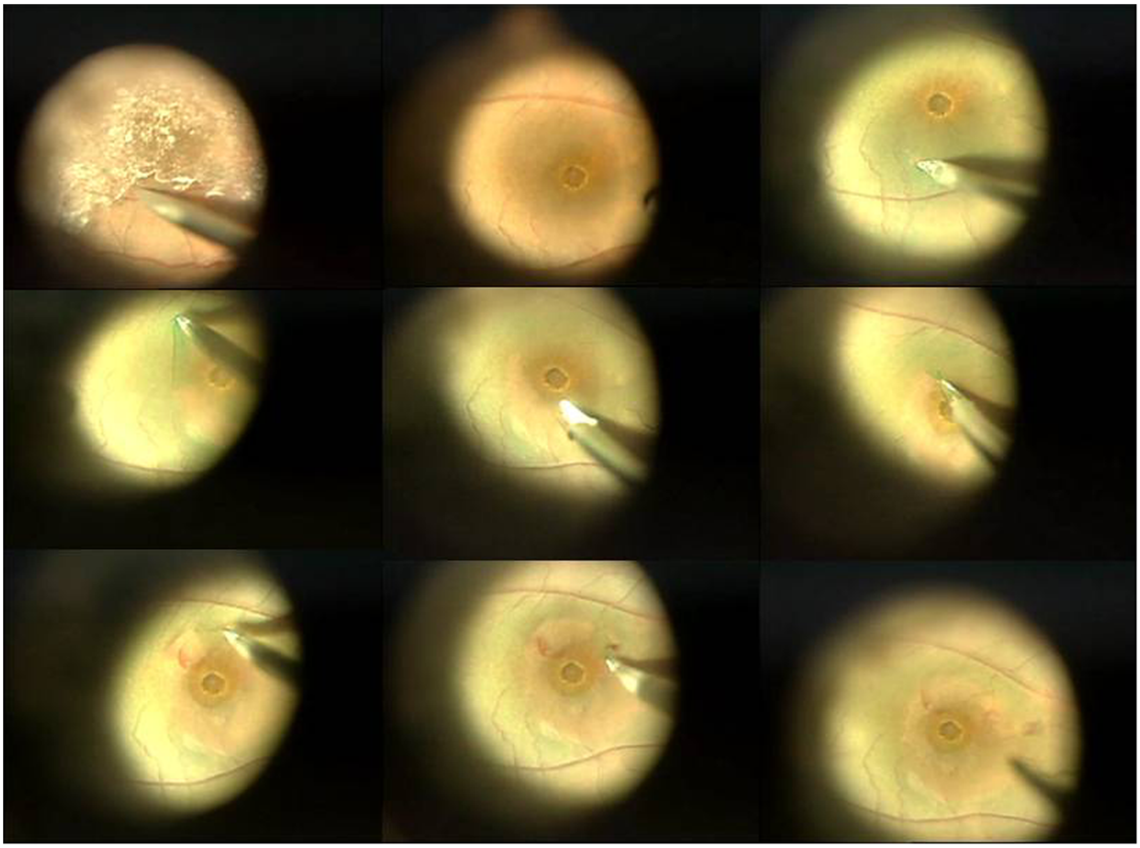

Fig. 1 Step-by-step photos of the foveola nonpeeling surgery in early stage 2 macular hole. Removal of the posterior hyaloid membrane was performed gently. Care was taken not to apply too much traction to the margin of the hole. Approximately two-fifths of the ILM was peeled off in the beginning and microscissors were used to make tangential cuts superior or inferior to the foveola. Repeated microscissor cuts and peeling with ILM forceps were needed. The remaining ILM could then be peeled off without damaging the central foveola and leaving a 400-μm-diameter ILM over the foveola. ILM=internal limiting membrane

disc diameter with a curly edge, which may not be small enough to release tangential traction in early stage 2 MH.

A total of 15 females and 13 males comprised the two groups. Ages ranged from 60 to 86 years (mean, 64 years). The mean follow-up periods were 16.8 months (range, 14 to 19 months) in group 1 and 17 months (range, 14 to 19) in group 2. The sizes of the holes in both groups were comparable (P= 0.301) and the vitreomacular adhesions were present in all eyes in both groups. All the MHs in both groups were closed after operation. LogMAR BCVA improved from 0.76 LogMAR to 0.30 LogMAR in group 1 and from 0.73 LogMAR to 0.39 LogMAR in group 2 (Table 1). There was more improvement of logMAR BCVA in group 1 (0.46) than in group 2 (0.34), which was statistically significant (P=0.0489). The mean preoperative logMAR BCVAs were comparable (P=0.474) and the mean postoperative logMAR BCVA was significantly better in group 1 (P=0.011)(Table 1). The OCT microstructures studies showed a regain of the IS/OS line in all 14 cases in group 1 (100 %) and in seven of 14 cases in group 2 (50 %). Recovered ELM lines were found in all 14 cases in group 1

Table 1 Anatomical and visual outcomes before and after surgery in group 1: Foveola-nonpeeling (FN) group, and group 2: total peeling (TP) group

	FN group(n=14)	TP group(n=14)	*P* value
Hole diameter	103±8	100±7	*P*=0.301
Vitreomacular adhesion	Presence in all	Presence in all	NA
Preoperative BCVA in logMAR, mean±SD	0.76±0.11	0.73±0.15	*P*=0.474
Postoperative BCVA in logMAR, mean±SD	0.30±0.10	0.39±0.08	*P*=0.011
BCVA improvement in logMAR, mean±SD	−0.46±0.16	−0.34±0.17	*P*=0.049

BCVA=best-corrected visual acuity; FN=foveola-nonpeeling; TP=total peeling; logMAR=logarithm of minimal angle of resolution; SD=standard deviation

(100 %) (Fig. 2) and seven of 12 cases in group 2 (50 %) (Fig. 4). Restoration of umbo light reflex was found in 12 of 14 eyes in group 1 (86 %) (Fig. 3), but was not found in group 2 (0 %). Group 1 eyes achieved restoration of smooth and symmetric umbo foveolar contour without postoperative retinal dimpling in group 1 (0 %)(Fig. 2); however, there was retinal dimpling in all eyes in group 2 (Fig. 4). Figures 5 and 6 showed the preoperative and four-month postoperative SD-OCT images of five more cases of the foveola-nonpeeling group (Fig. 5) and another five more cases of the total peeling group (Fig. 6).

Fig. 3 Recovery of umbo light reflex in foveola nonpeeling group eye. Umbo light reflex was recovered (yellow arrow) after foveola nonpeeling surgery in the patient shown in Fig. 2

Discussion

The present surgical method to preserve the central 400-μm-diameter foveolar ILM prevents postoperative foveal inner retinal dimpling, dissociated optic nerve fiber layer and asymmetric elongation of the foveola. Closure of MHs and smooth foveolar contours were achieved. IS/OS and ELM line were restored more. Our study also showed that total removal of foveolar ILM over the early stage 2 MH causes inner retinal dimpling and retinal thinning with significantly worse postoperative visual acuity and less foveolar microstructures improvement. It has been suggested that the presence of a continuous IS/OS line was a sign of well-restored photoreceptor

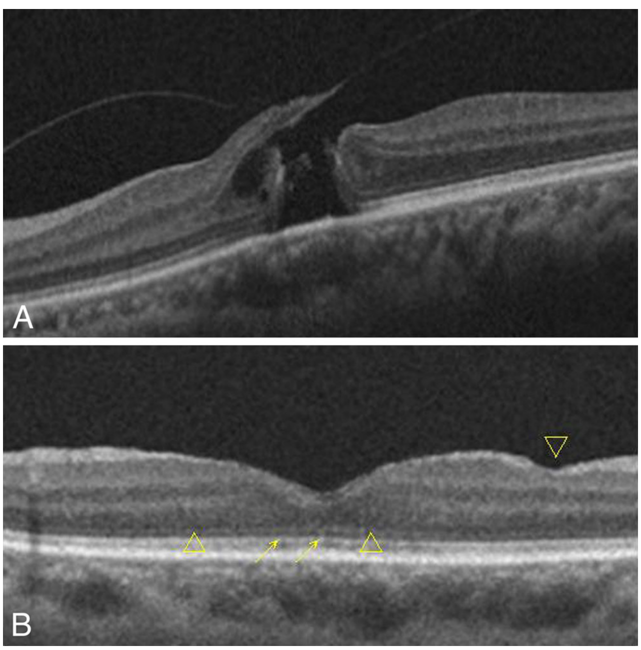

Fig. 2 Preoperative and postoperative SD-OCT images of foveola nonpeeling group eye. A 63-year-old female who had an early stage 2 macular hole with a 20/200 preoperative visual acuity underwent foveolar nonpeeling ILM surgery. **a**. Foveal ILM was complete preoperatively except for a linear crescent defect. **b**. Six months after foveola nonpeeling surgery the hole was closed and the external limiting membrane line (yellow arrowheads) and IS/OS line (yellow arrows) were restored. The visual acuity improved to 20/50 postoperatively. The dimpling of the inner retina (white arrowhead) was located in the ILM peeled area. The foveola contour was smooth and symmetric with good umbo depression. ILM=internal limiting membrane. IS/OS=inner segment/ outer segment

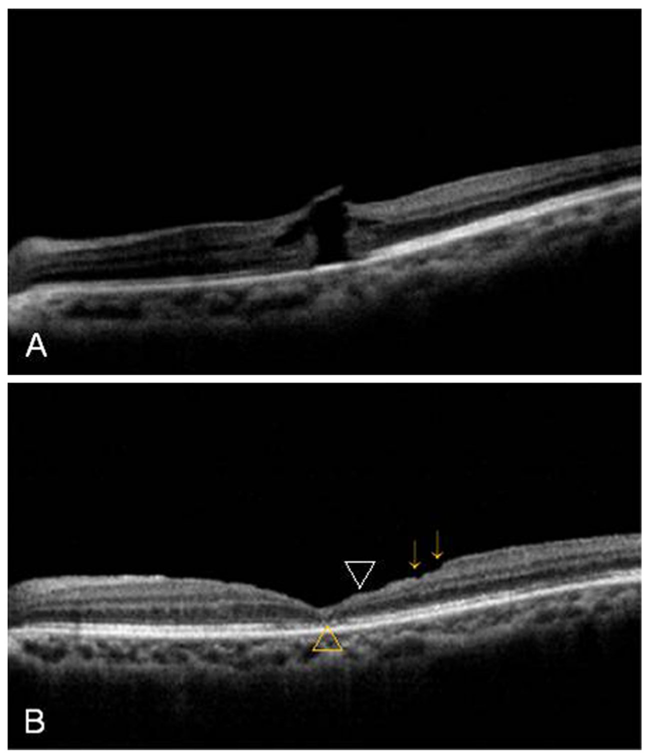

Fig. 4 Preoperative and postoperative SD-OCT images of total peeling group eye. **a** 64-year-old female who had an early stage 2 macular hole with a 2/20 preoperative visual acuity underwent foveolar total peeling ILM surgery. **a**. Foveal ILM was complete preoperatively except for a linear crescent defect. **b**. Six months after total foveola ILM peeling the hole was closed, but the external limiting membrane line and IS/OS line were not restored (yellow arrowhead). The postoperative visual acuity was 20/100. Inner retinal dimpling (yellow arrow) and foveola thinning (white arrowhead) were present. ILM=internal limiting membrane. IS/OS=inner segment/ outer segment

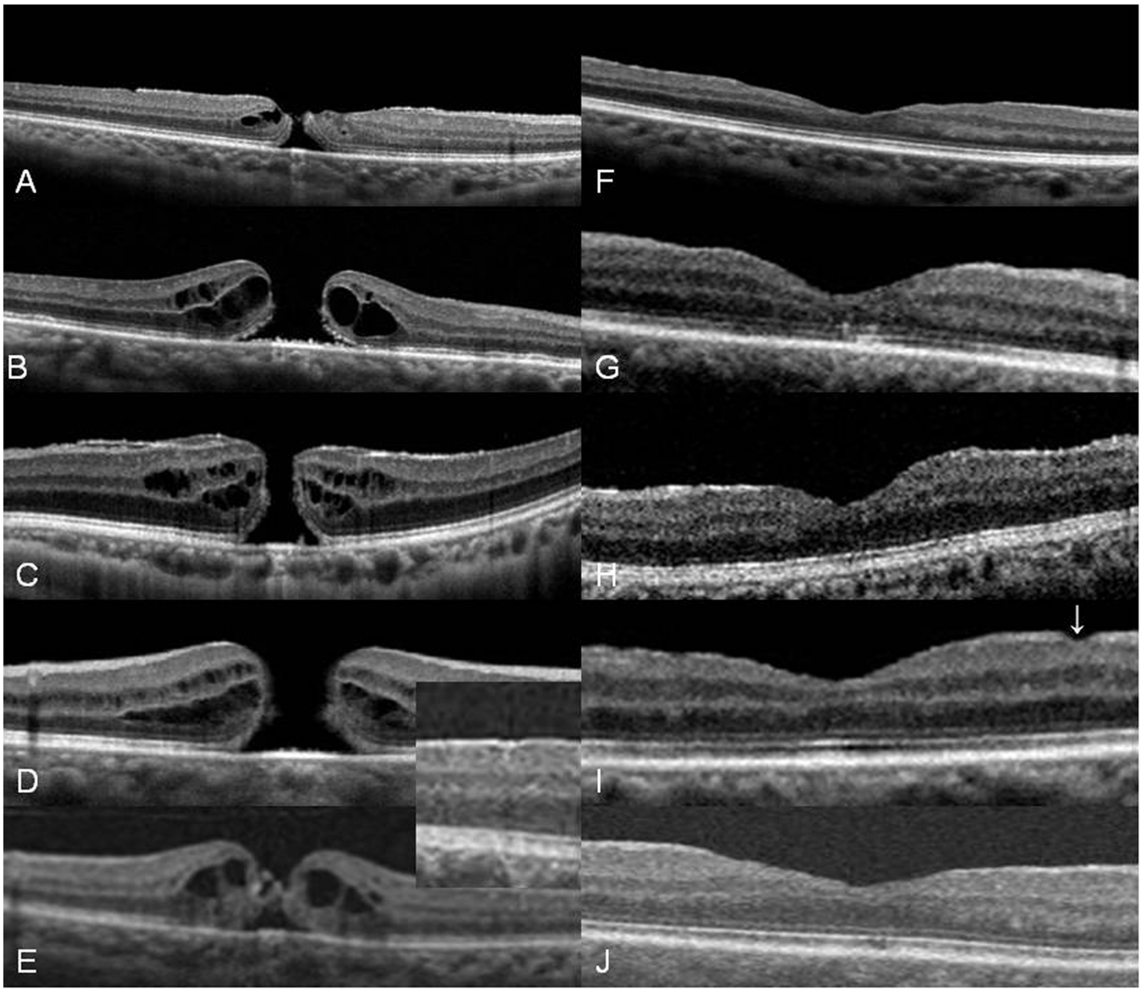

Fig. 5 Preoperative and four-month postoperative SD-OCT images of five more cases of foveola nonpeeling group eyes. **a**, **b**, **c**, **d**, and **e** showed preoperative images of cases 2–6. **f**, **g**, **h**, **i**, and **j** showed postoperative images from cases 2–6 respectively. **a** and **f**. Early stage 2 macular hole was found preoperatively and smooth contour of foveal depression with recovery of external limiting membrane line and IS/OS line were found postoperatively. **b** and **g**. Recovery of smooth foveal contour, external limiting membrane line, and IS/OS line postoperatively. **c** and **h**. Recovery of smooth foveal depression, external limiting membrane line, and IS/OS line postoperatively. **d** and **i**. Recovery of symmetric and smooth foveal contour, external limiting membrane line, and IS/OS line. The dimpling of the inner retina (arrow) was located in the ILM peeled area. **e** and **j**. Recovery of smooth foveal contour, external limiting membrane line, and IS/OS line. IS/OS=inner segment/ outer segment

cells, and a continuous ELM was a sign of intact photoreceptor cell bodies and Müller cells [18, 19].

There were controversies in terms of the effect of ILM removal in idiopathic MH. Although Lois et al. reported that there was no evidence of a difference in distance visual acuity after the ILM peeling and no-ILM peeling techniques, the authors favored ILM peeling for stage 2 to 3 MH because of higher anatomic closure and lower reoperation rates [20]. Chan et al. reported that MH surgery may be associated with a late-onset DONFL appearance, which does not appear to affect postoperative BCVA, gain in BCVA, or OCT central macular thickness. Chan et al. reported that patients who underwent brilliant blue G (BBG)-assisted ILM removal showed a greater frequency of dimpling, which may be a reflection of a more thorough removal of the ILM scaffold, since eyes without this appearance tended to demonstrate persistent ILM, regardless of the use of intraoperative BBG. Final postoperative BCVA among those with dimpling was 0.24 logMAR, a gain of 0.39 logMAR from baseline, as compared to 0.18 logMAR (0.32 logMAR gain) among those without dimpling ($p>0.410$) [21]. Concerning the effect of ILM removal, Chang et al. [22] found that there was a greater proportional decrease in central macular thickness in the single-peeling group (peeling off only the epiretinal membrane) than in the double-peeling group (peeling off both the epiretinal membrane and the ILM) in eyes that underwent surgery for idiopathic epiretinal membrane.

However, Pilli et al. reported that inner macular volume in eyes with surgically closed idiopathic MH correlated best with visual outcome. The authors found that routine total foveolar ILM peeling reduced total and inner macular volume, and limited visual acuity outcome. In this series, macular surface

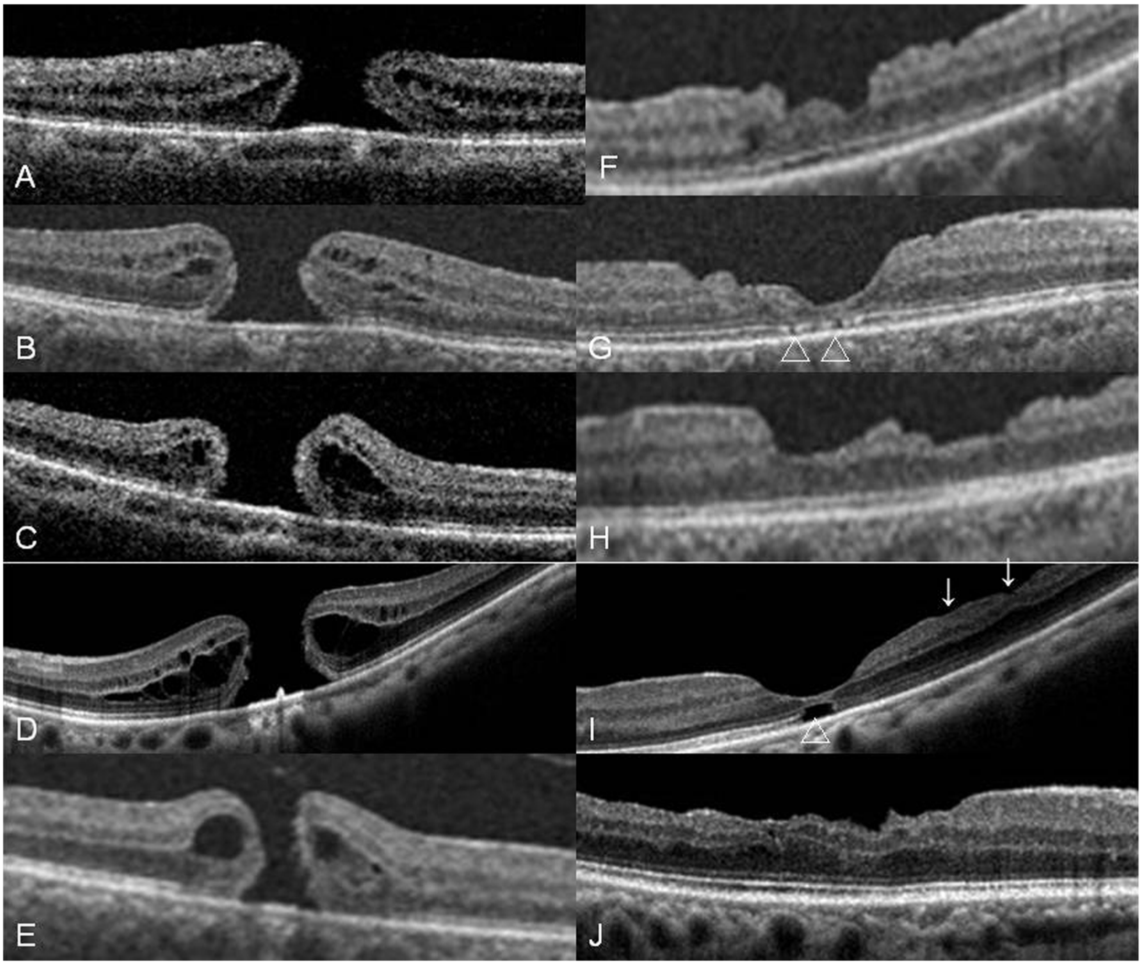

Fig. 6 Preoperative and four-month postoperative SD-OCT images of five more cases of total peeling group eyes. **a**, **b**, **c**, **d**, and **e** showed preoperative images of cases 2–6. **f**, **g**, **h**, **i**, and **j** showed postoperative images from cases 2–6, respectively. **a** and **f**. Stage 2 macular hole was found preoperatively. Sealed macular hole but with inner retinal dimpling, foveal thinning and recovered IS/OS line were found postoperatively. **b** and **g**. Sealed hole but with inner retinal dimpling and recovery of external limiting membrane and some IS/OS line defect (arrowheads) postoperatively. **c** and **h**. Sealed hole but with severe inner retinal dimpling, foveal thinning, and recovery of IS/OS line postoperatively. **d** and **i**. Sealed hole but with inner retinal dimpling (arrow) and large IS/OS line discontinuity (arrowhead) postoperatively. **e** and **j**. Sealed hole with poor foveal contour, inner retinal dimpling but recovered external limiting membrane line and IS/OS line postoperativley. IS/OS=inner segment/outer segment

rregularities were noted in 66.7 % of eyes with ILM peeling but in none of the non-ILM peeled eyes. The authors concluded that the possible effect of ILM peeling on visual outcome needs to be further investigated [12]. Our study demonstrated that preservation of foveolar ILM prevents inner retinal dimpling and had better visual improvement than total removal of ILM.

Tadayoni et al. [15] showed that the need for ILM peeling may depend on the size of the hole. ILM peeling had a positive effect on MH closure for sizes larger than 400 um, but this effect did not apply to MHs smaller than 400 um. Our study showed that total ILM peeling for small or early MH may be too damaging to the foveolar tissue, hence there was no visual outcome benefit in small holes after ILM peeling for the whole foveola.

The asymmetric elongation of foveal tissue after MH surgery causes postoperative metamorphopsia as reported by Kim et al [9]. Both the horizontal and vertical inter-outer plexiform layer (OPL) distances were increased during the follow-up period. Horizontal inter-OPL distances were significantly longer than vertical distances. Further nasal and superior elongation was noted on the horizontal and vertical planes. The distance between the parafoveal edges of the outer plexiform layer was elongated asymmetrically, showing destruction of the Müller cell integrity after total peeling of the ILM. The skeleton system that held the foveolar structure together may be damaged due to the removal of the foveolar ILM, which constructed the inner surface of the Müller cell cone. Also, macular migration toward the optic disc after ILM peeling for diabetic macular edema was noted by Yoshikawa et al [23]. Kim et al. [9] postulated that a thicker retina is tauter, and traction to the direction of the thicker retina will be greater than to the thinner retina. Hence, the preservation of the foveolar ILM by the present technique may hold the integrity of the Müller cell cone, restore the symmetric umbo foveolar depression, and prevent the asymmetric elongation of the foveal tissue after MH surgery.

Gaudric et al. described the early change in foveal tissue in stage 0 MH [24]. In stage 0 MH it is possible to detect a slight focal elevation of the inner curvature of the foveal center, subtle changes in the foveal contour, and reflectivity of the center of the foveola. The umbo foveal reflex is then lost during the development of stage 2 MH. However, in traditional total ILM peeling eyes, the foveal reflex can never be restored postoperatively. Our present technique recovered the foveal reflex by preserving the foveolar ILM.

The restoration of smooth foveolar contour may be crucial in the management of idiopathic MH. On the surface of the foveola the endfeet are crucial in capturing divergent rays of light and guiding them toward the photoreceptors. They also have a lower refractive index than other parts of the Müller cell and other cells in the retina, and serve to minimize reflection of incident light as it passes from the vitreous humor into the uppermost layers of the retina [25]. Müller cells have an extended funnel shape, a higher refractive index than their surrounding tissue, and are oriented along the direction of light propagation [25]. Transmission and reflection confocal microscopy of retinal tissue in vitro and in vivo showed that these cells provide a low-scattering passage for light from the retinal surface to the photoreceptor cells. Müller cells act as optical fibers. Müller cells seem to mediate the image transfer through the vertebrate retina with minimal distortion and low loss [25].

However, after repair of MH by total removal of ILM the foveal contour usually does not recover as a smooth surface. Spaide [8] reported that a high proportion of eyes with ILM peeling develop inner retinal dimples that course along the path of the nerve fiber layer. The dimples seem to be the result of an interplay between trauma and healing processes constrained by the nerve fiber layer and do not appear to be because of the dissociation of optic nerve fibers. The true nature of the abnormalities induced is still under investigation in order to evaluate the long-term risks and benefits of routine ILM peeling. Hence, the smooth contour of the foveola and the restoration of the umbo light reflex rendered a more physiological state of the foveola and are probably a factor of the final visual outcomes in our cases.

Regarding the use of ICG in ILM peeling, a comparative study has been reported in MH ILM peeling surgery. No differences were found in the incidence of a dissociated optic nerve fiber layer between the eyes with and without the use of ICG, and between ICG-peeled and trypan blue-peeled eyes [26, 27]. Nukada et al. found that no significant differences were found in the frequency of the deep inner retinal defects between eyes treated with ICG and triamcinolone acetonide [28]. Thus, ILM peeling rather than ICG toxicity is the cause of the inner retinal dimpling in the peeled area in both total peeling and foveola nonpeeling eyes in our cases.

The usage of microplasmin in intravitreal injection may release the posterior hyaloid traction to early stage 2 MH [29–35]. In a randomized study in which the MH closure rates were compared after intravitreal injection of ocriplasmin and after placebo, MHs smaller than 250 μm had a closure rate of 58.5 % [36]. However, its effect on the ILM and formation of inner retinal dimpling remains to be determined. Since the average successful rate of ocriplasmin to achieve MH closure is 40.6 % by day 28, surgical intervention to the ILM is still necessary in the unsuccessful eyes after ocriplasmin treatment.

In conclusion, to our knowledge this is the first article to present the surgical technique and the beneficial effects of this novel approach to early stage 2 idiopathic MH. Various studies have shown that ILM peeling during macular hole surgery is associated with increased primary hole closure rate [1, 37]. Our study suggested that ILM peeling benefits the foveolar contour and microstructure recovery even when the hole is small, as long as the foveola ILM can be preserved during the operation. The ILM does not need to be totally removed in order to close the early stage 2 MH. The preservation of the foveolar ILM prevents inner retinal dimpling, achieves symmetric umbo foveolar depression and better foveolar microstructures, and better visual outcomes. The limitation of the study would be its small number of examined cases. However, the present study aimed to introduce a new perspective in MH surgery by preserving the integrity of the Müller cell cone. Long-term tomographic features and visual outcomes are currently under investigation.

Conflicts of interest None.

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