Efficacy of Fovea-Sparing Internal Limiting Membrane Peeling for Epiretinal Membrane Foveoschisis

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Keywords

Epiretinal membrane foveoschisis · Fovea-sparing internal limiting membrane peeling · Microincision vitrectomy surgery

Abstract

Introduction: The aim of the study was to investigate the outcomes of vitrectomy with fovea-sparing internal limiting membrane (ILM) peeling (FSIP) for epiretinal membrane (ERM) foveoschisis based on new optical coherence tomography definitions. **Methods:** Twenty-three eyes of 22 patients (69.7 ± 9.9 years old) who underwent vitrectomy with FSIP without gas tamponade for ERM foveoschisis were analyzed. All patients underwent follow-up examinations for at least 12 months. In the FSIP technique, the ILM is peeled off in a donut shape, preserving the foveal ILM. The logarithm of the minimal angle of resolution best-corrected visual acuity (BCVA), central macular thickness (CMT), and surgical complications were examined. **Results:** The BCVA at 12 months improved significantly from baseline ($p < 0.001$). Baseline ellipsoid zone defects were found in 2 eyes (9%), and all defective eyes had recovered at 12 months. CMT decreased significantly from baseline ($p < 0.001$). Acute macular edema, full-thickness macular hole, and recurrence of

ERM were not observed during follow-up. **Discussion/Conclusion:** FSIP achieved good visual outcome and retinal morphological change. Moreover, FSIP might avoid acute macular edema in ERM foveoschisis surgery.

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Introduction

The lamellar macular hole (LMH) was first described by Gass [1] in 1976. He reported a case of LMH secondary to cystoid macular edema (CME) after cataract surgery which was identified with slit-lamp biomicroscopy. However, several reports suggested that lamellar holes usually result from an abortive process of macular hole formation [2, 3]. Other studies proposed that anteroposterior and tangential forces exerting centripetal or centrifugal traction on the fovea might be involved in the pathogenesis of LMH [4, 5]. However, more recent spectral-domain optical coherence tomography (OCT) studies challenged those assumptions, suggesting that true LMH might be the result of remodeling of the foveal tissue occurring in the absence of overt epiretinal tractional forces [6–10]. Previous reports gave criteria for the differential diagnosis between a macular pseudohole (MPH) and an LMH,

both of which have lamellar intraretinal cleavage at the edges of non-full-thickness macular holes (FTMHs) [11]. Govetto et al. [12] reported that LMHs consist of 2 subtypes, tractional and degenerative, based on the structural variation observed on OCT imaging. While tractional LMHs are characterized by a sharp-edged, “schisis-like” appearance and tractional epiretinal membrane (ERM), degenerative LMHs have round-edged cavitation, a foveal bump, and are often seen in conjunction with lamellar hole-associated epiretinal proliferation.

More recently, Hubschman et al. [10] have updated the definition of LMH and differentiated it from other similar morphology. ERM foveoschisis is the most common reason for diagnostic error of LMH. ERM foveoschisis was previously distinguished but referred to as “tractional” LMH and MPH with stretched edges. One main aspect differentiating LMH from ERM foveoschisis and MPH resides in the assumption that only LMH is associated with loss of tissue. Presumed signs of retinal cell loss on OCT in the presence of LMH are the undermined edges, foveal thinning, and a posterior vitreous detachment associated with pseudo-operculum [13].

Presently, the technique proposed by most vitreoretinal surgeons for ERM foveoschisis and LMH is pars plana vitrectomy to release vitreomacular adhesions by removing the ERM and internal limiting membrane (ILM), promoting reconstruction of the normal foveal profile [14]. It remains controversial whether degenerative LMHs and tractional LMHs result in differences in postoperative visual acuity [15, 16]. We focused on the surgical technique of

fovea-sparing ILM peeling (FSIP) originally proposed by Shimada et al. [17]. Surgery with the FSIP procedure has been reported to reduce the rate of severe postsurgical complications, such as FTMH or retinal atrophy compared with complete peeling for treating myopic foveoschisis and degenerative LMH [17–20]. Russo et al. [21] suggested that complete ILM peeling for ERM may reduce retinal sensitivity and significantly increase the incidence of microscotomas compared with the FSIP surgical technique. We considered that these surgical benefits of FSIP might be useful for a new entity recently defined as ERM foveoschisis. However, the efficacy of FSIP has not been confirmed in the treatment of ERM foveoschisis. The aim of the current study was to examine the FSIP method for the treatment of ERM foveoschisis in emmetropic or mildly myopic eyes and to analyze the morphologic and functional changes and postsurgical complications of this procedure.

Methods

This retrospective study was approved by the Institutional Review Board of St. Marianna University School of Medicine (Kanagawa, Japan) and adhered to the tenets of the Declaration of Helsinki. Informed written consent to participate in the current study was obtained from all patients. This study was registered in the University Hospital Medical Information Network (<https://www.umin.ac.jp>) (UMIN:UMIN000046063). We examined 23 eyes of 22 patients with ERM foveoschisis who were available for follow-up for >12 months after surgery from January 2018 through May 2020.

All patients underwent an ophthalmological examination including best-corrected visual acuity (BCVA), slit-lamp biomicros-

Table 1. Baseline characteristics

Baseline characteristics	ERM foveoschisis (23 eyes, 22 patients)
Age: mean $\pm$ SD, years	69.7 $\pm$ 9.9
Sex, <i>n</i> (%)	
Male	7 (32)
Female	15 (68)
BCVA: logMAR, mean $\pm$ SD	0.09 $\pm$ 0.10
Combined cataract surgery, <i>n</i> (%)	22 (96)
Without combined cataract surgery, <i>n</i> (%)	
Pseudophakia	1 (4)
Curvature evocative of mild posterior staphyloma, <i>n</i> (%)	10 (43)
EZ defect, <i>n</i> (%)	2 (9)
CMT: mean $\pm$ SD, μ m	369 $\pm$ 33
Complete posterior detachment, <i>n</i> (%)	17 (74)
Intraretinal cystoid spaces located in the INL, <i>n</i> (%)	10 (43)
Wrinkling, <i>n</i> (%)	18 (78)

SD, standard deviation; BCVA, best-corrected visual acuity; logMAR, logarithm of minimum angle of resolution; CMT, central macular thickness; EZ, ellipsoid zone; INL, inner nuclear layer; ERM, epiretinal membrane.

copy, and OCT anatomic examination using spectral-domain OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA, USA) performed at baseline and at 1, 3, 6, and 12 months after surgery. BCVA was measured using the Landolt C acuity test and converted into logarithm of the minimal angle of resolution (logMAR) units. Central macular thickness (CMT) was defined as the mean distance between the ERM and retinal pigment epithelium within a 3-mm central sub-field. CMT measurements were derived from the software (Cirrus 3.0; Carl Zeiss Meditec, Inc.) provided by the manufacturer.

Eyes with media opacities resulting in insufficient OCT signals were excluded from the analysis. Other exclusion criteria were severe cataract of higher than grade 3; vitrectomized eye; high myopia defined by an axial length longer than 26 mm; secondary ERM (due to diabetic retinopathy, uveitis, and retinal vascular disease); central retinal vein occlusion; uveitis; and other chorioretinal diseases such as diabetic retinopathy, hypertensive retinopathy, and choroidal neovascularization.

The preoperative OCT images were diagnosed by one expert ophthalmologist (J.K.) based on the previous reports for the classification of ERM foveoschisis [10]. The mandatory criteria for the diagnosis of ERM foveoschisis was based on the presence of (1) contractile ERM (arrowhead) and (2) foveoschisis at the level of Henle's fiber layer, typically between the outer nuclear layer and outer plexiform layer (Fig. 1). The optional criteria were the presence of (1) microcystoid spaces in the inner nuclear layer (INL); (2) retinal thickening; and (3) retinal wrinkling.

Fig. 1. Diagnostic criteria of ERM foveoschisis. The diagnosis of ERM foveoschisis was made based on the presence of (1) contractile ERM (arrowhead) and (2) foveoschisis at the level of Henle's fiber layer, typically between the ONL and OPL (arrow). ERM, epiretinal membrane; ONL, outer nuclear layer; OPL, outer plexiform layer.

Fig. 2. Time course change in OCT findings after surgery. Changes in OCT findings after vitrectomy with FSIP for ERM foveoschisis. **a** Preoperative OCT image of the left eye of a 51-year-old woman with an axial length of 25.97 mm. The logMAR BCVA was 0.04. ERM (arrowhead) and foveoschisis (arrow) can be seen. CMT was 362 μ m. **b** At 1 month after surgery, the foveoschisis, which remained at the level of Henle's fiber layer, decreased. **c** At 3 months after surgery, an additional decrease in the foveoschisis was seen, and an intraretinal cystoid space on the INL was detected. **d** At 6 months after surgery, the logMAR BCVA was -0.07. Foveoschisis and intraretinal cystoid spaces were diminished. OCT, optical coherence tomography; FSIP, fovea-sparing internal limiting membrane peeling; ERM, epiretinal membrane; logMAR, logarithm of the minimal angle of resolution; BCVA, best-corrected visual acuity; CMT, central macular thickness; INL, inner nuclear layer.

Fig. 3. Time course change in logMAR BCVA. The paired-sample *t* test was used to determine the correlation between baseline and postoperative logMAR BCVA. The BCVA significantly improved at each time point (** $p < 0.005$, *** $p < 0.0005$ compared with the baseline). logMAR, logarithm of the minimal angle of resolution; BCVA, best-corrected visual acuity.

Fig. 4. Time course change in CMT. The paired-sample *t* test was used to determine the correlation between preoperative and postoperative CMT. In ERM foveoschisis patients who underwent surgery with the FSIP technique, CMT increased significantly postoperatively (* $p < 0.05$, ** $p < 0.005$ compared with the baseline). CMT, central macular thickness; ERM, epiretinal membrane; FSIP, fovea-sparing internal limiting membrane peeling.

The presence of remaining intraretinal cystoid spaces and the occurrence of acute postoperative CME were assessed on the postoperative B-scan images at 1, 3, 6, and 12 months. Diagnostic criteria for acute postoperative CME were an increase in intraretinal cystoid spaces and a macular thickness increase.

Surgical Technique

All patients agreed to undergo 27-gauge microincision vitrectomy at the St. Marianna Medical University Hospital. All surgical procedures were performed by a single expert surgeon using the FSIP technique as previously reported [17]. In this procedure, the ILM was grasped with an ILM forceps and peeled off in a circular fashion, but the ILM was not completely removed and was left attached to the fovea. After the ILM was peeled from the macula excluding the foveal area (in a circular area with a diameter approximately 1/3 of the vertical extent of the optic disc), the peeled ILM was trimmed with a vitreous cutter. Cataract surgery combined with vitrectomy was performed in 22 eyes. One eye already had pseudophakia. No fluid-air exchange was performed, and prone positioning was not required.

Statistical Analysis

All statistical analyses were performed using JMP pro 13 software (SAS Institute Inc., Cary, NC, USA). The differences between the preoperative and postoperative logMAR BCVA and CMT were analyzed using the paired-sample *t* test. *p* values of < 0.05 were considered to represent statistically significant differences. Data are presented as mean $\pm$ SD.

Results

The baseline characteristics and clinical data of the patients are shown in Table 1. Representative OCT images of the postoperative course of ERM foveoschisis eyes treated with FSIP surgery are shown in Figure 2. The preoperative mean logMAR BCVA improved from 0.09 ± 0.10 to -0.01 ± 0.09 at 1 month, -0.03 ± 0.06 at 3 months,

Fig. 5. Time course change in OCT findings after surgery in eyes with intraretinal cystoid space remaining. **a** Baseline OCT image of the left eye of a 58-year-old woman with an axial length of 25.51 mm. The logMAR BCVA was 0. ERM (arrowhead). Foveoschisis (arrow) and intraretinal cystoid spaces (circle) can be seen. CMT was 395 μ m. **b** At 1 month after surgery, the foveoschisis, which remained at the level of Henle's fiber layer, decreased. The intraretinal cystoid spaces on the INL increased (circle). **c** At 6 months after surgery, an additional decrease in foveoschisis was seen, and an intraretinal cystoid space on the INL was still detected. **d** At 12 months after surgery, the logMAR BCVA was -0.07 . Foveoschisis and intraretinal cystoid spaces remained. LogMAR, logarithm of the minimal angle of resolution; BCVA, best-corrected visual acuity; OCT, optical coherence tomography; ERM, epiretinal membrane; CMT, central macular thickness; INL, inner nuclear layer.

-0.04 ± 0.09 at 6 months, and -0.04 ± 0.08 at 12 months postoperatively ($p < 0.001$, respectively) (Fig. 3). The baseline CMT did not change significantly (from 369 ± 33 μ m to 358 ± 23 μ m at 1 month, $p = 0.25$), although it decreased significantly to 346 ± 22 μ m at 3 months ($p =$

0.02), 340 ± 25 μ m at 6 months ($p = 0.002$), and 334 ± 20 μ m at 12 months ($p < 0.001$) (Fig. 4).

Preoperative EZ defects were observed in 2 eyes (9%), and all recovered after surgery. Remaining foveoschisis at the level of Henle's fiber layer was observed in 9 eyes

(39%) at 1 month, 8 eyes (34%) at 3 months, 6 eyes (26%) at 6 months, and 1 eye (4%) at 12 months postoperatively. The number of eyes with an intraretinal cystoid space located in the INL was 6 (26%) at 1 month, 3 (13%) at 3 months, 3 (13%) at 6 months, and 2 (9%) at 12 months postoperatively. However, the 2 eyes with remaining intraretinal cystoid showed slight visual improvement from logMAR BCVA of 0.15 ± 0.21 to -0.07 ± 0.0 . Only one eye had both an intraretinal cystoid space and remaining foveoschisis at 12 months. OCT images of the postoperative course of the remaining eyes are shown in Figure 5. One of 18 eyes with wrinkling at baseline continued to show wrinkling 12 months postoperatively, although the wrinkling diminished in 17 eyes at 1 month postoperatively. There were no recurrences of ERM during 12-month follow-up. No severe complications, such as FTMH, retinal detachment, or CME, were observed in any patient.

Discussion

We retrospectively reviewed emmetropic or mildly myopic eyes with ERM foveoschisis after FSIP surgery. ERM foveoschisis was defined as the presence of stretched hyporeflective cystoid spaces splitting the foveal retinal layers at the level of Henle's fiber layer [22]. Lam et al. [22] noted that the emmetropic ERM foveoschisis images were similar to the images of myopic foveoschisis on OCT B-scans. We observed 10 eyes with a slight curvature of the retina and the sclera suggestive of mild staphyloma, despite the exclusion of eyes with high myopia, defined as having an axial length >26 mm. However, the defined criteria of curvature of the retina and sclera are unclear and not described in the reports by Lam et al. [22]. They reported that 7 of 17 eyes (41%) with ERM foveoschisis had mild curvature similar to those in our study (43%). Moreover, there was no difference between the axial length and the posterior curvature in their series. However, the rate of posterior curvature suggestive of staphyloma was higher in the ERM foveoschisis group (41%) compared with the control group (23%) [22]. That report and our results suggest that the role of anteroposterior traction in retinal stretching could not be ruled out in foveoschisis formation [23].

The term "ERM foveoschisis" has also recently been referred to as a differential diagnosis of LMH in an OCT-based consensus and distinguished from MPH [10]. The relationship between morphological and functional recovery after FSIP is contentious. In this study, we found

significant visual improvement after FSIP (Fig. 3). It was reported that total ILM peeling for tractional LMH, which is similar to ERM foveoschisis, achieved BCVA improvement [24]. It was also reported that the FSIP technique improved VA for eyes with idiopathic ERM or myopic foveoschisis [21, 25]. ERM foveoschisis was defined as a subtype of idiopathic ERM with features similar to those of myopic foveoschisis [10]. Due to that similarity, our data showing significant visual improvement with FSIP appear valid. However, most patients in our study underwent combined cataract surgery, and it was reported that VA improvement after ERM surgery was greater in those who with combined cataract surgery [20]. The preoperative to postoperative improvement of BCVA in our study might be partially associated with the effect of combined cataract surgery.

In terms of CMT, many eyes in the present study became significantly thinner throughout the 12-month follow-up period (Fig. 4), in agreement with previous results showing that the postoperative CMT was thinner than preoperatively after total ILM peeling for ERM foveoschisis and FSIP for idiopathic ERM [21, 22]. Our CMT data were similar to those in previous studies. The CMT decrease might be due to a reduction in foveal traction related to the ERM [21, 22]. It remains controversial whether decreased retinal thickness is beneficial in terms of VA [26].

Several reports showed that the condition of the outer retina correlates with visual function [24, 26, 27]. In our present study, preoperative EZ defects were observed in 2 eyes (9%). Lam et al. [22] found that preoperative EZ disruption occurred in significantly more patients with ERM foveoschisis (58%) than in the ERM control group (5%). The rate of EZ disruption in our patients was lower than that reported by Lam et al. [22] (58%), although it was greater than in the ERM control group (5%). Another report on tractional LMH mentioned that the EZ disruption rate was 15% [28].

When examining our patients' postoperative retinal morphology, OCT showed that ERM foveoschisis construction tended to result in recovery of the regular foveal outlines. Although Lam et al. [22] assumed that alterations of the outer retina could be artifacts caused by the shadowing of the cystoid spaces in some cases, their report showed that total peeling for ERM foveoschisis improved the outer retinal disruption. Similarly, in a study that included both ERM foveoschisis and MPH in the "tractional" group with total ILM peeling, Figueroa et al. [24] also reported functional and anatomic outcomes with foveal restoration in 93% of cases. In addition, pre-

operative disruption of the EZ can be repaired after FSIP for myopic foveoschisis [29]. Michalewska et al. [30] reported that the regeneration of the EZ which appeared in spectral domain-OCT may be caused by gliosis. Bulging of the glial cells may move the photoreceptors, with those new positions then making it possible to recover visual function [31]. Thus, glial cells may play a role in this morphologic normalization, and the same mechanism may be exerted in ERM foveoschisis.

The resolution of foveoschisis occurred after surgery in 22 eyes (96%) at 12 months postoperatively in our study. Lam et al. [22] found that the resolution of foveoschisis occurred in 77% of patients at the final follow-up visit and hypothesized that tangential traction caused the foveoschisis. These results might suggest that the FSIP technique improved the retinal morphology to a greater extent than total peeling [22]. Opinions published on total macular ILM peeling have focused on morphological macular changes, including dimpling or damage to the inner retina and a high risk of the postoperative development of full-thickness MHs [18]. FSIP might contribute to a greater reduction in iatrogenic foveal traction than total ILM peeling and thereby reduce Muller cell damage.

The presence of intraretinal cystoid spaces was gradually reduced during follow-up in our patients. Lam et al. [22] found that the cystoid spaces in the INL were less likely to disappear after peeling, which supports the hypothesis of Muller cell damage in ERM foveoschisis, as their nuclei are located in the INL. Surgical removal of the ERM and ILM may cause detachment and disruption of adhering Muller cell end-feet and subsequent persistence of an increase in CME [32, 33]. The percentage of patients with intraretinal cystoid spaces 12 months after FSIP was lower than that after total ILM peeling in previous reports [22]. These results suggest that the FSIP technique induces less tractional Muller cell injury of the macula. Lam et al. [22] reported that ERM foveoschisis had a higher prevalence of CME than ERM without intraretinal cystoid spaces after total peeling of the ILM. The absence of CME complications in our study after FSIP also supports this hypothesis. Moreover, we showed the beneficial result of no complications of FTMH. Surgery with the FSIP procedure was reported to reduce the rate of severe postsurgical complications, such as MH or retinal atrophy, compared with total ILM peeling for myopic foveoschisis and degenerative LMH [18, 34, 35]. All eyes with intraretinal cystoid remaining showed a tendency toward visual improvement (logMAR BCVA: -0.07). It was also reported that no significant changes in the VA of postoperative idiopathic ERM patients were observed between those

with and without foveal hyporeflexive zones, as our data also showed [36]. Wrinkling is the one of the optional diagnostic criteria. Wrinkling was decreased after FSIP in most eyes in our patients, indicating that it was due to traction from the ERM [10].

No recurrence of ERM was seen in our patients after surgery using the FSIP technique. Previously, it was reported that patients who did not undergo ILM peeling had a higher ERM recurrence rate than those with ILM peeling [37]. However, Russo et al. [21] did not find a difference in the ERM recurrence rate in patients who underwent the FSIP procedure and ILM peeling. They left the ILM over the foveal region with a diameter of approximately one optic disc intact. However, we left the ILM with a diameter of approximately 1/3 of the optic disc intact. This difference might be due to the size of the residual ILM in the patients treated by Russo et al. [21] and our group.

Conclusion

In conclusion, the FSIP technique may be beneficial to both surgeons and patients by reducing complications such as CME and FTMH. In addition, leaving the ILM 1/3 of the size of the optic disc during FSIP may lower the risk of recurrence.

Limitations

The limitations of this study were that there were no controls consisting of patients who underwent total ILM peeling. In addition, this study was retrospective. Additional surgical data must be collected and further functional studies must be conducted to determine whether it is safe to leave a portion of the ILM in front of the retina in patients with ERM foveoschisis.

Statement of Ethics

This retrospective study was approved by the Institutional Review Board of St. Marianna University School of Medicine (Kanagawa, Japan) and adhered to the tenets of the Declaration of Helsinki (Approval number 5346). Informed written consent to participate in the current study was obtained from all patients. This study was registered in the University Hospital Medical Information Network (<https://www.umin.ac.jp>) (UMIN:UMIN000046063).

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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The entire study was performed and completed at the Department of Ophthalmology, St. Marianna University School of Medicine, Kanagawa, Japan, without any support from grants or other funding.

Author Contributions

R.S., H.T., and J.K. designed the study, and J.K. performed surgery; T.J., K.S., I.A., and T.K. collected the data; R.S. and J.K. generated the figures and tables; R.S., J.K., N.T., Y.K., and H.T. drafted and revised the manuscript; and all approved the final manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available because they contain information that could compromise the privacy of research participants but are available from J.K. upon reasonable request.

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