Extent of Internal Limiting Membrane Peeling and its Impact on Macular Hole Surgery Outcomes: A Randomized Trial

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• PURPOSE: To identify whether and how outcomes of macular hole (MH) surgery are influenced by the extent of internal limiting membrane (ILM) peeling.
• DESIGN: Randomized clinical trial.
• METHODS: This study involved 65 eyes from 65 patients who underwent surgery for idiopathic MH. ILM was peeled with a radius of either 0.75 disc diameter (small-extent group, SEG) or 1.5 disc diameter (large-extent group, LEG), according to the randomization. Anatomic success, visual acuity, and metamorphopsia score (M-score) were measured at 2- and 6-month postoperative visits. The distance between the foveal center and the parafoveal edge of the outer plexiform layer on optical coherence tomography was measured in 4 directions, and further distance increases in certain directions were defined as asymmetric elongation of foveal tissue.
• RESULTS: Complete closure of the MH was observed after initial operation in 97.0% of eyes in both groups. The mean visual improvement at 6 months after surgery was 20.4 ± 12.8 and 19.1 ± 10.8 ETDRS letters in SEG and LEG, respectively ($P = .452$). The mean amount of improvement in M-score was 0.26 ± 0.55 in SEG and 0.50 ± 0.53 in LEG ($P = .039$). There was a difference in the mean degree of asymmetric elongation between the 2 groups (22.5% ± 10.8% in SEG vs 13.4% ± 5.8% in LEG, $P = .001$). And there was inverse correlation between the mean degree of asymmetric elongation and the amount of improvement in M-score at 6 months postoperatively ($P < .001$).
• CONCLUSION: Larger extent of ILM peeling during MH surgery is beneficial with respect to reduction of metamorphopsia, alleviating asymmetric elongation of foveal tissue. (Am J Ophthalmol 2016;169:179–188. © 2016 Elsevier Inc. All rights reserved.)

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SINCE KELLY AND WENDEL INTRODUCED THE VITRECTOMY technique to reattach the macular hole (MH),[1] considerable advances in surgical treatment have been achieved. As a consequence, MH has now become a surgically treatable disease with standardized techniques incorporating vitrectomy, induction of posterior vitreous detachment, internal limiting membrane (ILM) peeling, and gas tamponade.[2] Although there was a debate on ILM peeling in the past, ILM peeling has been established to improve surgical success rates.[3–6] In addition, retinal ILM peeling has been facilitated by staining dye such as indocyanine green.[7,8]

The rationale for ILM peeling is that MH can occur and enlarge owing to contraction of perifoveal vitreous and cellular constituents with myofibroblastic differentiation on the surface of the ILM.[2,9] Although ILM has no inherent contractile properties, it does act as a scaffold for contractile tissue to exert tangential traction on fovea.

Several studies using optical coherence tomography (OCT) have reported the dynamic sealing process after MH surgery.[10–13] Foveal tissue elongation and macular migration have been noted following ILM peeling after surgery for MH and diabetic macular edema.[14–17] In addition, there is a significant correlation between these morphologic changes and visual function such as metamorphopsia.[14]

Although ILM peeling has become a widely accepted surgical technique since the introduction of MH surgery, the optimal extent of ILM peeling is not known and the anatomic and functional outcomes according to peeling extent have not been investigated. The purpose of this study was to investigate the influence of the extent of ILM peeling on anatomic and functional outcomes of MH surgery.

METHODS

THIS PROSPECTIVE RANDOMIZED CLINICAL TRIAL WAS performed at a single center according to the tenets of the Declaration of Helsinki. The study protocol (Supplementary Text; Supplemental Material available at AJO.com) was approved by the institutional review board and ethics committees (Samsung Medical Center IRB no. 2013-07-083, ClinicalTrials.gov identifier NCT02010138).

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Subjects were recruited between July 12, 2013 and March 23, 2015. Trial follow-up of the last enrolled subject was completed in November 2015. All patients provided written informed consent before enrollment.

The study population consisted of subjects 18 years of age or older diagnosed with idiopathic MH before undergoing vitrectomy. Idiopathic MH was defined as a defect of the foveal retina involving its full thickness from the ILM to the outer segment of the photoreceptor layer without other accompanying ophthalmic disorders.

Exclusion criteria included eyes with traumatic MH, evidence of ocular inflammation, diabetic retinopathy, hypertensive retinopathy, retinal vasculitis, media opacity that would influence visual acuity or preclude acquisition of clear spectral-domain OCT images, −6.0 diopters or more of spherical equivalent, presence of staphyloma, history of intraocular surgery other than uncomplicated cataract surgery, and other ocular diseases that could influence macular microstructure or visual function. Patients who declined to participate in the study were also excluded.

At baseline, a detailed demographic and medical history was collected, and all subjects underwent a complete preoperative evaluation, including examination for best-corrected visual acuity (BCVA) using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart (Lighthouse International, New York, New York, USA), M-chart (Inami Co, Tokyo, Japan) test, anterior segment examination, and dilated fundus examination with a 90 diopter lens. Horizontal and vertical OCT scans through the fovea were performed with a combined confocal scanning laser ophthalmoscope and spectral-domain OCT (Spectralis HRA-OCT; Heidelberg Engineering, Heidelberg, Germany). Metamorphopsia score (M-score) measurement was performed using the M-chart according to a previously described method.[18]

• **RANDOMIZATION AND TREATMENT:** The block randomization method was designed by an independent clinical trial consultant. Subjects were randomized based on preallocated codes placed in sealed envelopes that were opened during the randomization visit by a trial coordinator. Based on the code, each subject was randomized to either the small-extent group (SEG) or the large-extent group (LEG). Participants and examiners who were assessing outcomes were masked to the assignment of groups.

A standard 3-port pars plana vitrectomy was performed by a single surgeon (S.W.K.) using the Constellation (Alcon Laboratories Inc, Fort Worth, Texas, USA) or Associate (Dutch Ophthalmic Research Center, Inc, Zuidland, The Netherlands) 23 gauge vitrectomy system. After core vitrectomy, the posterior hyaloid membrane was removed using the vitreous cutter. In cases without posterior vitreous detachment, partial posterior hyaloidectomy was performed to prevent the risk of triggering peripheral break.[19] Then, peeling of the retinal ILM was performed using vitreous forceps with the assistance of indocyanine green dye staining. Scrapers were never used. With reference to the size of the optic nerve, the ILM was pinched with end-gripping forceps (Grieshaber Maxgrip 723.13; Alcon Laboratories Inc, Fort Worth, Texas, USA) at the point of desired radius (0.75 or 1.5 disc diameter). Then, the strand of ILM was peeled off radially toward the foveal center. Then another short strand of ILM was peeled off circumferentially toward the initial pinching point to create an L-shaped slit for starting round-shaped laminorrhexis (Supplemental Figure; Supplemental Material available at AJO.com). The operator then pulled the ILM flap and lifted several times at its mid-edge, paying special attention to create a round-shaped laminorrhexis (Figure 1). This was followed by a complete fluid–gas exchange using either 25% sulfur hexafluoride gas or 14% perfluoropropane gas. The selection of gas was dependent on the size and duration of MH. That is, we used 25% sulfur hexafluoride gas if the MH was smaller than 400 μm with a symptom duration shorter than 3 months. Otherwise, we used 14% perfluoropropane gas. Combined cataract surgery was conducted in patients with visually significant cataracts or incipient cataracts in subjects older than 60 years. All patients were encouraged to maintain a face-down position for at least 5 days postoperatively. Subjects with persistent MH at the first postoperative visit or reopened MH were supposed to undergo additional fluid–gas exchange along with intravitreal injection of autologous platelet concentrate.

• **OUTCOME MEASURES:** Postoperative measurements of BCVA and M-score were conducted at 2- and 6-month follow-up visits by independent, masked observers. The amount of improvement in BCVA and M-score values between the preoperative visit and the postoperative 6-month follow-up were defined as the Δ BCVA and Δ M-score, respectively.

The first postoperative OCT scanning was usually conducted 1–2 weeks after operation according to intraocular gas status. After that, OCT scans were conducted at follow-up visits 2 and 6 months postoperatively. The same experienced examiner conducted all OCT scans on all subjects.

OCT images of 1:1 μm setting, rather than 1:1 pixel setting, were used for measurement.[14] The measurements were performed manually using the contained Heidelberg Eye Explorer software (version 1.5.12.0; Heidelberg Engineering). MH size was calculated as the mean of the horizontal and vertical diameters. Two independent observers (K.B., J.M.Y.) analyzed the images in a masked fashion.

To evaluate postoperative elongation of the foveal tissue, the distance between the edges of the outer plexiform layer (OPL) was measured and defined as the inter-OPL distance. The difference in inter-OPL distance between horizontal and vertical images was defined as horizontal-vertical asymmetry. The horizontal-vertical percent asymmetry (H-V % asy) was calculated as (horizontal inter-OPL