Ganglion Cell-Inner Plexiform Layer Thickness after Epiretinal Membrane Surgery

A Spectral Domain Optical Coherence Tomography Study

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Purpose: To investigate postoperative macular ganglion cell-inner plexiform layer (GCIPL) thickness, determine the factors related to GCIPL thickness, and evaluate the association of GCIPL thickness with postoperative visual outcomes in patients with idiopathic epiretinal membrane (ERM).

Design: Retrospective, cohort study.

Participants: Sixty-two patients with unilateral idiopathic ERM who were followed for ≥6 months after surgery.

Methods: Ophthalmologic evaluations included best-corrected visual acuity (BCVA) assessment, spectral-domain optical coherence tomography, and macular visual field (VF) mean sensitivity (MS) as measured by Humphrey VF test. Macular GCIPL thickness in eyes with ERM was compared with that of the normal contralateral eyes 6 months after surgery. The correlation between the interocular difference in GCIPL thickness and postoperative visual outcome was evaluated.

Main Outcome Measures: Postoperative macular GCIPL thickness, factors related to the interocular differences in GCIPL thickness, and correlations of GCIPL thickness with BCVA and macular VF MS 6 months after surgery.

Results: Macular GCIPL thickness was significantly lower in eyes with ERM 6 months after surgery (71.77±10.21 μm) than in the unaffected contralateral eyes (81.69±5.33 μm; $P<0.001$). Thirty-three subjects were followed for 1 year after surgery, and the macular GCIPL thickness in eyes with ERM did not significantly change between 6 and 12 months after surgery (71.77±10.21 vs 70.64±9.57 μm; $P = 0.179$). Preoperative central foveal thickness was the only factor significantly correlated with interocular differences in macular GCIPL thickness ($r = 0.3677$; $P = 0.0033$). Among patients with intact photoreceptor layers, a greater decrease in GCIPL thickness was correlated with a worse postoperative BCVA ($r = 0.5209$; $P<0.0001$) and a greater decrease in macular VF MS ($r = -0.2845$; $P = 0.0390$).

Conclusions: Macular GCIPL thickness decreased after vitrectomy to remove an idiopathic ERM. The decrease in GCIPL thickness was significantly correlated with postoperative visual outcomes in patients with intact photoreceptor layers. *Ophthalmology 2014;■:1–9 © 2014 by the American Academy of Ophthalmology.*

Idiopathic epiretinal membrane (ERM) is a frequently diagnosed macular pathology characterized by fibrocellular proliferation on the inner retinal surface of the macular area.[1,2] Patients are often asymptomatic, but the ERM can induce tangential traction on the retina, which often leads to various visual impairments and metamorphopsia. Standard treatment for an ERM is surgical removal. Numerous studies have investigated prognostic factors for visual outcome after ERM surgery.[3–9]

The introduction of spectral-domain (SD) optical coherence tomography (OCT) allowed for layer-by-layer evaluation of the retina. Previous studies using SD-OCT have mainly focused on the status of the outer retina—such as the photoreceptor inner segment/outer segment (IS/OS) junction and cone outer segment tips (COST) line—as the prognostic factors in patients with ERM.[6,10–12] We previously showed that photoreceptor status was significantly associated with surgical outcomes in patients with ERM.[13] However, only considering outer retinal influences seems insufficient to predict postoperative visual outcome, particularly because ERM tangential traction occurs on the inner retina. This can cause retinal wrinkling, subsequent retinal ganglion cell (RGC) damage, and impairment of inner retinal structural integrity.

Macular ganglion cell-inner plexiform layer (GCIPL) thickness could be a good diagnostic indicator of RGC damage or loss.[14] The GCIPL thickness represents the combined thickness of the ganglion cell layer (GCL) and the inner plexiform layer (IPL) and is less influenced by retinal nerve fiber layer (RNFL) thickness variation than the ganglion cell complex thickness (sum of RNFL, GCL, and IPL thicknesses). Several recent studies have demonstrated that measurements of macular GCIPL thickness can be used for early glaucoma detection and are correlated with macular sensitivity.[14–18] However, changes in macular GCIPL after ERM removal and the relationship between postoperative macular GCIPL thickness and visual outcome have not yet been investigated.

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The aim of this study was to assess postoperative macular GCIPL thickness and identify factors related to macular GCIPL thickness in patients undergoing surgery to remove an idiopathic ERM. The association between macular GCIPL thickness and the postoperative visual outcome was also evaluated.

Methods

This retrospective study comprised 62 consecutive patients who underwent successful vitrectomy for a unilateral idiopathic ERM and who were followed for ≥6 months after surgery. All procedures took place at Seoul National University Hospital between April 2011 and March 2012. The diagnosis of ERM was made by the physician via indirect fundus examination. Patients were excluded if they had a secondary ERM (e.g., history of trauma, retinal detachment surgery, uveitis, venous occlusion), bilateral ERM, macular or lamellar hole, glaucoma, anisometropia >2.0 diopters, high myopia (spherical equivalent of ≥−6.0 diopters or axial length [AL] ≥26 mm), or other ocular pathology that could interfere with visual function (e.g., comorbid maculopathy). Patients with an optical media opacity that significantly disturb OCT image acquisition (e.g., cataract of more than Emery−Little classification grade III) were also excluded. The study protocol was approved by the Institutional Review Board of Seoul National University Hospital and adhered to the tenets of the Declaration of Helsinki.

Ocular Examination

All patients underwent comprehensive ophthalmologic examinations before surgery and 1, 3, and 6 months after surgery. Examinations included measurement of best-corrected visual acuity (BCVA), intraocular pressure (IOP; by Goldmann applanation tonometry), noncycloplegic refraction (Autorefractor KR-8900; Topcon Corporation, Tokyo, Japan), and AL (Axis II PR; Quantel Medical, Inc., Bozeman, MT). Slit-lamp biomicroscopy, indirect fundus examination, fundus photography (Vx-10; Kowa Optimed, Tokyo, Japan), fluorescein angiography (Vx-10; Kowa Optimed), SD-OCT (Cirrus; Carl Zeiss Meditec, Dublin, CA), and standard automated perimetry (Humphrey visual field Analyzer II with Swedish Interactive Threshold Algorithm standard 30-2; Carl Zeiss Meditec) were also performed. The BCVA measurements were made using a Snellen chart and were converted to logarithm of the minimum angle of resolution units for statistical analyses. Additionally, refraction data were converted to spherical equivalent for analyses.

We performed SD-OCT to obtain horizontal and vertical cross-sectional images of the macula using a 5-line raster scan mode with a length of 6 mm. Central foveal thickness (CFT), the distance between the inner surface of the retina and the inner border of the retinal pigment epithelium at the fovea, was measured using the macular cube 512 × 128 mode, which scans a retinal area of 6.0 × 6.0 mm (128 lines, 512 A-scans per line). Disruptions of the IS/OS junction and the COST line were defined as a loss in the corresponding line of hyperreflectivity at the fovea. The SD-OCT images were evaluated by 2 independent observers (E.K.L. and H.G.Y.) and a consensus was reached in each case. Two scans, including 1 macular scan (macular cube 200 × 200 protocol) and 1 peripapillary RNFL scan (optic disc cube 200 × 200 protocol), were also obtained using an SD-OCT device.

The built-in ganglion cell analysis (GCA) algorithm (Cirrus OCT software version 6.0) detects and measures macular GCIPL thickness within the 6 × 6 × 2-mm cube in an elliptical annulus around the fovea (dimensions: vertical inner and outer radii of 0.5 and 2.0 mm, respectively; horizontal inner and outer radii of 0.6 and 2.4 mm, respectively). The size of the inner ring was chosen so as to exclude the area where the GCIPL is thin and difficult to detect accurately, whereas the dimension of the outer ring was selected to include the area where the GCIPL is thickest in a normal eye.[17,19] The GCA algorithm identifies the outer boundary of the RNFL as well as the outer boundary of the IPL. The difference between the RNFL and the IPL outer boundary segmentations yields the combined thickness of the GCL and the IPL.[17] Images with a signal strength of <6, blinking artifacts, or algorithm segmentation failure were excluded from analyses (Fig 1A−D). Macular GCIPL thickness of eyes with ERM was compared with that of the normal contralateral eyes 6 months after surgery (Fig 1E). Preoperative measurements were not used for analyses because the GCA algorithm occasionally shows segmentation failures when severe retinal layer distortion is present.

Because the GCA thickness map covers a radial area between 2.1 and 8.3 degrees from the fovea, with the ellipse extending in the vertical direction between 1.7 and 7 degrees, the macular visual field (VF) was projected centrally on the Humphrey 30-2 Swedish Interactive Threshold Algorithm map. Macular VF mean sensitivity (MS), expressed in decibels, was determined using the Humphrey VF and was defined as the average of the differential light sensitivity obtained at a 12-point area representing the macula (Fig 1F).

Intraoperative Procedures

Surgery was performed in patients with visual acuity reductions or visual disturbances, such as metamorphopsia. All surgeries were performed by a single surgeon (H.G.Y.) under retrobulbar anesthesia. In each case, a Millennium 25-gauge transconjunctival sutureless vitrectomy system (Bausch & Lomb, St. Louis, MO) was used to perform a 3-port pars plana vitrectomy. A posterior vitreous detachment was mechanically induced using an ocutome if one was not already present. The ERM was peeled using end-gripping forceps (Alcon Surgical, Fort Worth, TX) with the assistance of triamcinolone acetonide. The ERM was directly engaged with the intraocular forceps to create a flap and then peeled from the nerve fiber layer plane, usually in a fashion similar to a capsulorhexis. Internal limiting membrane (ILM) peeling was performed based on the surgeon's discretion, with 0.03% indocyanine green (ICG) dye staining in some cases. The ERM and/or ILM peeling was started at the outer region around the fovea, usually in the parafoveal area. If a clinically significant cataract was present, phacoemulsification and aspiration with foldable intraocular lens implantation were performed during vitrectomy. Fluid−air exchange and endolaser photocoagulation were conducted to treat retinal breaks or lattice degeneration, when present.

Main Outcome Measures

Interocular difference in macular GCIPL thickness was determined by subtracting measurements in the ERM eye 6 months after surgery from those obtained in the normal contralateral eye. Main outcome measures included postoperative macular GCIPL thickness, factors influencing interocular differences in macular GCIPL thickness, and the association between interocular macular GCIPL thickness differences and postoperative visual outcomes. Postoperative visual outcomes were examined using BCVA and macular VF MS measurements obtained 6 months after surgery.

Statistical Analysis

A paired t test was used to compare ocular parameters and macular GCIPL thickness in the eye with the ERM and the contralateral eye