Longitudinal Changes in Retinal Nerve Fiber Layer Thickness After Vitrectomy for Epiretinal Membrane

Sung-Bok Lee,1,2 Yong-II Shin,1 Young-Joon Jo,1,2 and Jung-Yeul Kim1,2

1Department of Ophthalmology, Chungnam National University College of Medicine, Daejeon, Republic of Korea
2Research Institute for Medical Science, Chungnam National University, Daejeon, Republic of Korea

PURPOSE. We investigated longitudinal changes in retinal nerve fiber layer (RNFL) thickness following vitrectomy for epiretinal membrane (ERM).

METHODS. Thirty-one patients who underwent pars plana vitrectomy with internal limiting membrane (ILM) peeling for ERM were included. Average thickness and four quadrants of RNFL thicknesses were determined before and at 1, 3, 6, and 12 months after surgery by spectral-domain optical coherence tomography (SD-OCT). As macular lesions could affect RNFL thickness, we evaluated changes in RNFL thickness by dividing the RNFL into 12 o’clock hourly positions, defining pathologic area adjacent to the lesion and nonpathologic area.

RESULTS. Retinal nerve fiber layer thickness of the affected eyes increased at 1 month after vitrectomy and later decreased compared to baseline values. Temporal quadrant RNFL thickness was statistically significantly thicker in affected eyes at baseline and at 1 month after surgery and thinner after 12 months than fellow eyes. Retinal nerve fiber layer thickness in pathologic area decreased after surgery, and the RNFL was statistically significantly thinner at 3, 6, and 12 months postoperatively, compared to the baseline thickness. The RNFL thickness of pathologic area of affected eyes compared to fellow eyes was thicker both at baseline and 1 month after surgery but thinner at 12 months compared to baseline values.

CONCLUSIONS. Postoperative RNFL thickness after vitrectomy combined with ERM removal tended to decrease postoperatively. Retinal nerve fiber layer thicknesses in temporal pathologic area were significantly reduced at 3, 6, and 12 months postoperatively compared to baseline values, whereas RNFL thicknesses in nasal nonpathologic area exhibited no significant postoperative changes. We found that ERM itself and the removal procedure resulted in decreased RNFL thickness.

Keywords: epiretinal membrane, RNFL, vitrectomy

An epiretinal membrane (ERM) is a semitransparent membrane between the internal limiting membrane (ILM) and the vitreous which causes macular dysfunction. An ERM develops in the macular area without symptoms in early stages, although mild metamorphopsia or a decrease in the extent of central vision may occur. As the membrane contracts, it induces macular distortion or macular edema, leading to decreased and distorted vision. Surgical treatment is required. Vitrectomy for ERM removal with or without ILM removal is the standard treatment.1 Some complications in visual field defects and optic nerve pallor associated with high intraocular pressure during surgery have been reported.2

Optical coherence tomography (OCT) is used widely to assess the retinal nerve fiber layer (RNFL) because it allows non-invasive detection of changes in the RNFL, using low-coherence interferometry. The availability of cross-sectional images make OCT useful in many studies of ocular diseases, including glaucoma and optic neuropathy. Also, OCT is affected less by refractive state, axial length, nuclear sclerotic grade, and medium opacity.3

The recently developed spectral-domain OCT (SD-OCT) processes data 50-fold more rapidly and is more sensitive than time-domain OCT (TD-OCT) and offers high-resolution images.4,5 Many reports have shown that SD-OCT outperforms TD-OCT, affording excellent repeatability and reproducibility when used to measure RNFL thickness and to detect localized RNFL defects.6–8

In the present study, we used SD-OCT to evaluate longitudinal RNFL thickness changes in patients who underwent pars plana vitrectomy, ERM removal, and ILM peeling.

METHODS

Patients

This was a prospective cohort study. The protocol was approved by the Institutional Review Board of Chungnam National University Hospital. All participants signed informed consent forms, and the study adhered to the tenets of the Declaration of Helsinki.

In total, 41 patients with a diagnosis of ERM in a single eye at the Retina Clinic of Chungnam National University Hospital from January to December 2011 and who underwent vitrectomy with completion of 1-year follow-up were included. We excluded patients with histories of glaucoma or optic nerve disorder, optic disc abnormality, myopia > 6 diopters (D), and...
IOP > 21 mm Hg after surgery; patients who underwent fluid-air or fluid-gas exchange during vitrectomy; and those with other optic nerve or retinal dysfunctions that might affect the RNFL.

All fellow eye best-corrected visual acuity (BCVA) was better than 20/40, and the IOP, cup-to-disc ratio, and RNFL thickness were normal.

Study Protocol

The BCVA, IOP, and refraction were determined, and the anterior segment and fundus were examined using slit lamp biomicroscopy, in addition to OCT before surgery and at 1, 3, 6, and 12 months after surgery.

Pars Plana Vitrectomy

All 3-port 23-gauge pars plana vitrectomies were performed by one of the authors (J-YK), using an Acuvue machine (Alcon Surgical, Fort Worth, TX, USA) with a widefield viewing system (MiniQuad XL VIT contact lens; Volk, Mentor, OH, USA). Phacoemulsification was performed prior to vitrectomy in patients with cataract. Vitreous body removal was followed by ILM removal. After the ILM was stained with 0.25% indocyanine green (ICG) solution, it was removed from an area within 2 or 3 disc diameters around the fovea, using microforceps. A posterior chamber intraocular lens was inserted, and vitrectomy was completed.

Measurement of RNFL Thickness

Optical coherence tomography test was performed to determine RNFL thickness using the optic disc cube mode of the Cirrus HD-OCT unit (Carl Zeiss, Meditec, Dublin, CA, USA) before surgery and at 1, 3, 6, and 12 months after surgery; both eyes were dilated.

Images were acquired by a single technician experienced in the use of SD-OCT imaging. We excluded poor quality images with a signal strength less than 6 and any scans with visible eye movements or blinking artifacts or poor centration. Also, we discarded images with missing parts, misplacement of boundaries between retinal layers, or images showing seemingly distorted anatomy that resulted in readings of zero or otherwise abnormally low value to keep data from algorithm segmentation failure. We excluded 10 patients because of poor data quality. All eyes were scanned twice to evaluate reproducibility, and we believe good reproducibility was achieved because intraclass correlation coefficients (ICC) were 0.924 to 0.988.

The optic disc cube 200 × 200 scanning software achieves 200 A-scans from 200 linear B-scans evenly distributed in a 6 × 6-mm area centered over the optic nerve. This scanning mode was used to measure the average RNFL thickness and RNFL thicknesses of four quadrants. Retinal nerve fiber layer thickness was divided into 12 segments of 30° each and positioned on a 12-hour clock of RNFL thickness measurements.

Under the assumption that macular lesions could affect RNFL thickness, changes in the average RNFL thickness were evaluated by dividing 12 o’clock RNFL thicknesses into pathologic temporal 7 o’clock area (256°–105°), including the lesion and nonpathologic nasal 5 o’clock area (106°–255°) (Fig. 1).

Affected and fellow eyes were compared before and after surgery and during follow-up. Changes in RNFL thickness at 1, 3, 6, and 12 months after surgery were compared with baseline RNFL thicknesses.

Statistical Analysis

Statistical analysis was performed using SPSS version 18.0 software (SPSS, Inc., Chicago, IL, USA). Retinal nerve fiber layer thicknesses of affected and fellow eyes were compared using the paired t-test. We used repeated-measures ANOVA to explore the significance of differences before and after surgery. A P value of <0.05 indicated statistical significance.

Results

We enrolled 31 eyes of 31 patients, of whom 9 were males and 22 were females of a median age of 62.1 ± 9.7 years (range, 48–79 years of age). We operated on 19 right and 12 left eyes, of which 28 underwent vitrectomy with cataract surgery, whereas three received vitrectomy alone. Four patients (12.9%) had a history of diabetes, and 10 patients (32.3%) had a history of hypertension.

Changes in RNFL Thickness in the Average and Four Quadrants in Affected and Fellow Eyes

Comparisons between affected and fellow eyes showed that the RNFL thickness in the temporal quadrant was increased at baseline (100.71 ± 20.24 and 68.97 ± 9.86 μm, respectively, P < 0.001) and at 1 month after surgery (85.50 ± 14.28 and 69.14 ± 9.58 μm, respectively, P < 0.001) but was decreased at 12 months (61.53 ± 10.90 and 69.87 ± 9.57 μm, respectively, P = 0.034), to an extent that was statistically significant. The average RNFL thicknesses and the RNFL thicknesses in the superior, nasal, and inferior quadrants in
RNFL Thickness After Vitrectomy for ERM

TABLE 1. SD Changes in RNFL Thickness in the Average and Four Quadrants Using OCT in Affected and Fellow Eyes

<table>
<thead>
<tr>
<th>Location</th>
<th>6 months Post-OP</th>
<th>12 months Post-OP</th>
<th>12 months Pre-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>Affected Eye</td>
<td>Fellow Eye</td>
<td>Affected Eye</td>
</tr>
<tr>
<td>Superior</td>
<td>109.97 ± 20.32</td>
<td>118.32 ± 20.17</td>
<td>100.71 ± 20.24</td>
</tr>
<tr>
<td>Nasal</td>
<td>114.52 ± 20.02</td>
<td>117.95 ± 20.69</td>
<td>115.31 ± 20.48</td>
</tr>
<tr>
<td>Temporal</td>
<td>112.72 ± 20.59</td>
<td>117.75 ± 20.10</td>
<td>112.64 ± 20.66</td>
</tr>
<tr>
<td>Average</td>
<td>108.55 ± 19.54</td>
<td>115.17 ± 20.11</td>
<td>113.65 ± 20.69</td>
</tr>
</tbody>
</table>

TABLE 2. Mean SD Changes in RNFL Thickness in Pathologic and Nonpathologic Area Using OCT in Affected and Fellow Eyes

<table>
<thead>
<tr>
<th>Area</th>
<th>6 months Post-OP</th>
<th>12 months Post-OP</th>
<th>12 months Pre-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td></td>
<td>Affected Eye</td>
<td>Fellow Eye</td>
<td>Affected Eye</td>
</tr>
<tr>
<td>Pathologic</td>
<td>78.46 ± 12.40</td>
<td>83.94 ± 12.48</td>
<td>78.46 ± 12.40</td>
</tr>
<tr>
<td>Nonpathologic</td>
<td>78.46 ± 12.40</td>
<td>83.94 ± 12.48</td>
<td>78.46 ± 12.40</td>
</tr>
</tbody>
</table>

Changes in RNFL Thickness in Pathologic and Nonpathologic Area in Affected and Fellow Eyes

Comparison between the affected and fellow eyes showed that the mean RNFL thickness in the pathologic temporal 7 o’clock area was increased at baseline (112.88 ± 12.66 and 102.94 ± 11.58 μm, respectively, \( P = 0.023 \)) and at 1 month after surgery (112.63 ± 15.43 and 102.95 ± 11.49 μm, respectively, \( P = 0.023 \)) but decreased at 12 months (94.47 ± 13.53 and 103.57 ± 9.00 μm, respectively, \( P = 0.039 \)) and that the differences were statistically significant. In contrast, the mean RNFL thicknesses in the nonpathologic nasal 5 o’clock area were not significantly different from those of fellow eyes (Table 2).

Longitudinal Changes in Average and Four Quadrant Thicknesses of Affected Eyes

The RNFL thickness of the temporal quadrant of affected eyes exhibited a statistically significant decrease at 1 month postoperatively compared to the baseline RNFL thickness. Similarly, it showed a statistically significant decrease at 3, 6, 12 months, consecutively. In contrast, neither the average RNFL thickness nor the RNFL thickness in the superior, nasal, and inferior quadrants changed significantly after surgery compared to the corresponding baseline data (Fig. 2).

Longitudinal Changes in Mean RNFL Thickness in Pathologic and Nonpathologic Area of the Affected Eye

The mean RNFL thickness in the pathologic temporal 7 o’clock area of the affected eyes exhibited a statistically significant decrease at 3 months postoperatively compared to the baseline RNFL value. Similarly, it showed a statistically significant decrease at 6 and 12 months, consecutively. In contrast, the mean RNFL thickness in the nonpathologic nasal 5 o’clock area did not change significantly after surgery (Fig. 3).

Discussion

Epiretinal membrane development is common in older adults and causes decreased vision.9,10 This membrane results from cellular proliferation on the ILM,11 which causes the retina to wrinkle and distort, resulting in decreased visual acuity and metamorphopsia. Since the 1970s, vitrectomy has been used to remove an ERM. Recently, this surgical approach has been combined with ILM peeling to reduce ERM recurrence. Peeling an ILM is effective in reducing the risk of ERM recurrence by eliminating the area where cells, including myofibroblasts, can proliferate.12–14

The ILM is stained using Trypan Blue, triamcinolone, and ICG for better visualization during peeling. Since 2000, ICG has been used to selectively stain the ILM. Internal limiting membrane removal is therefore easy and safe to perform, with a reduced risk of retinal damage.15–17

Several studies have discussed structural changes in the RNFL after vitrectomy for macular disorders. Brazitikos et al.18 reported decreased RNFL thickness in the temporal quadrant in 35 eyes after macular surgery using Trypan Blue staining, although the changes were not statistically significant. Kim et al.19 demonstrated a decrease in RNFL thickness at 6 months after performing vitrectomy in patients with ERM, macular hole, or vitreous hemorrhage and suggested an association
between decreased RNFL thickness and ILM peeling, fluid-air exchange, and gas tamponade. Balducci et al.\textsuperscript{20} reported decreased temporal sector RNFL thickness in 30 eyes after vitrectomy including ILM peeling for both ERM and macular hole at 6 months postoperatively, a result similar to ours. However, we included ERM patients only, to reduce the effect of the fluid-gas exchange on RNFL thinning, which is another factor in RNFL thinning. Also, we gathered 1-year observational data and found that RNFL thickness was still decreasing gradually. Furthermore, we evaluated RNFL thickness by dividing eyes into pathologic and nonpathologic area to explore the effect of ILM peeling on RNFL thickness.

In the present study, we found that the average and temporal RNFL thicknesses of affected eyes were thicker than those of unaffected fellow eyes. Temporal quadrant RNFL thickness showed statistically significant thickening. Retinal nerve fiber layer thickness in the temporal quadrant showed statistically significant thickening at 1 month after surgery and thinning at 12 months, compared to those of unaffected fellow eyes. Postoperative thinning of the temporal RNFL is explained by the recovery from transitory RNFL swelling caused by traction forces of ERM, which causes increased RNFL thickness. After ERM removal, retinal edema diminished over time.

The RNFL thicknesses of nonpathologic area were somewhat thicker than baseline values but were not statistically significant. Disc edema caused by postoperative inflammation might have affected RNFL thickening.

Decreases in RNFL thickness after vitrectomy may be caused by various mechanisms, including increases in intraoperative IOP, phototoxic effect of the endoilluminator, mechanical damage induced by ILM peeling, toxicity of the ICG dye, and damage to the optic disc caused by induction of posterior vitreous detachment.\textsuperscript{21} In the present study, neither a gas tamponade nor fluid-air exchange was required, and there were no effects of these procedures on RNFL thickness.

During ILM removal, any morphological and functional damage to the RNFL may be caused by traction forces.\textsuperscript{22,23} Internal limiting membrane removal can also induce anatomical disruption under the ILM. Haritoglou et al.\textsuperscript{24,25} found RNFL defects in macular hole patients exhibiting central scotoma after ILM removal and cited mechanical damage during ILM peeling as a possible cause. Pichi et al.\textsuperscript{26} found that there are frequent postoperative inner retina layer modifications. After ILM peeling, there is swelling of the arcuate retinal nerve fiber layer, which disappears within 3 months, and then a dimple-shaped dissociated optic nerve fiber layer defect shows on inner retina layer of OCT. Uemura et al.\textsuperscript{27} attributed
postoperative visual field defects in patients with ERM to RNFL damage during ILM removal. As the temporal quadrant of the peripapillary RNFL is adjacent to the macular, ERM itself and surgical procedure including ERM removal and ILM peeling may affect RNFL thickness in this quadrant. Therefore, the RNFL thicknesses in the temporal quadrant and pathologic area were significantly decreased in our study.

This study has a few limitations. First, the number of patients who had completed the follow-up examinations for 1 year, 31, was small, and any long-term follow-up over 1 year was not possible to conduct. Further long-term study would be required on a larger scale, enrolling a higher number of patients. Second, the RNFL measuring software was developed for normal eyes, and the ERM may affect the RNFL thickness measurement. The ability of the software to accurately measure RNFL thickness in these eyes is uncertain because it was not possible to segment to original signals to determine the accuracy of RNFL measurements.

In conclusion, RNFL thickness displayed a tendency to decrease in patients who underwent vitrectomy combined with removal of an ERM and ILM. Retinal nerve fiber layer thicknesses in the pathologic area were significantly thinner at 3, 6, and 12 months postoperatively than the baseline RNFL thicknesses. In contrast, RNFL thickness in the nonpathologic area did not display a statistically significant postoperative change. The postoperative decreases in RNFL thickness after vitrectomy were closely associated with removal of the ILM and ERM. Further studies are required to explore the clinical effects of postoperative decreases in RNFL thickness on visual field defects and to compare patients who undergo ILM peeling with those who do not.

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References