Relationship of Dissociated Optic Nerve Fiber Layer Appearance to Internal Limiting Membrane Peeling

Yoshinori Mitamura, MD, Kenji Ohtsuka, MD

Purpose: The dissociated optic nerve fiber layer (DONFL) appearance features numerous arcuate striae after vitrectomy for idiopathic epiretinal membrane or macular hole. We studied the relation between the DONFL appearance and internal limiting membrane (ILM) peeling and performed static microperimetry to explore the possible mechanisms underlying the DONFL appearance.

Design: Prospective cohort study.

Participants: Ninety-five eyes of 88 consecutive patients undergoing vitrectomy for idiopathic macular hole.

Methods: Vitrectomy and gas tamponade were performed with or without ILM peeling. All eyes were examined postoperatively using fundus photography with blue filters. Static microperimetry was performed in 31 eyes with a clearly visible DONFL appearance.

Main Outcome Measure: The postoperative incidence of the DONFL appearance on blue-filtered fundus photographs. The secondary outcome measure included the microperimetry threshold value in the arcuate striae and the surrounding normal retina within the papillomacular bundle.

Results: On blue-filtered photographs, 46 (62.2%) of 74 eyes with ILM peeling exhibited the DONFL appearance, compared with 0 (0%) of 21 eyes without ILM peeling ($P = 0.0002$). The area of the DONFL appearance was limited to the area of ILM peeling. There was no difference in the microperimetry threshold value between the arcuate striae and the surrounding normal retina ($P = 0.9312$).

Conclusion: The present study indicates that the DONFL appearance might be related to ILM peeling and is not associated with the loss of optic nerve fibers. These results are consistent with the suggestion that the DONFL appearance might be caused by cleavage of the optic nerve fiber bundles due to damage to the Müller cells, which are in close contact with the ILM and act to maintain the close proximity of the nerve fiber bundles. Ophthalmology 2005;112:1766–1770 © 2005 by the American Academy of Ophthalmology.

Tadayoni et al reported that the fundus frequently has a particular appearance after pars plana vitrectomy (PPV) for idiopathic epiretinal membrane or macular hole and referred to this feature as a dissociated optic nerve fiber layer (DONFL) appearance. The DONFL appearance consists of numerous arcuate striae within the posterior pole in the direction of the optic nerve fibers and is slightly darker than the surrounding retina on blue-filtered photographs. The cause of the DONFL appearance, however, remains unclear. We studied the relationship of the DONFL appearance to internal limiting membrane (ILM) peeling and performed static microperimetry to explore the possible mechanisms underlying the DONFL appearance.

Patients and Methods

Ninety-five eyes of 88 consecutive patients (49 women and 39 men ranging in age from 48 to 81 years [mean, 63.6]) who underwent vitrectomy for idiopathic macular hole between January 2002 and June 2004 were included in the study. Six eyes undergoing additional vitrectomy due to failure of macular hole closure were excluded from the study. The surgical success rate was 94.1%. There were 13 eyes with a stage 2 macular hole, 66 eyes with stage 3, and 16 eyes with stage 4. Both biomicroscopy and optical coherence tomography (OCT) were used to classify the stage of the macular hole. Surgery consisted of PPV and gas tamponade with ILM peeling (74 eyes) or without ILM peeling (21 eyes). In 64 of the 74 eyes with ILM peeling, indocyanine green was used to peel the ILM. In the other 10 eyes, indocyanine green was not used. In the 21 eyes without ILM peeling, the macular hole was stage 2 or 3 and up to 0.1 disc diameter in size.

In the 64 eyes undergoing indocyanine green–assisted vitrectomy, indocyanine green autofluorescence fundus photographs were taken 2 weeks after the surgery to detect the area of ILM peeling. We used an infrared-sensitive video camera (50IA, Topcon, Tokyo, Japan) inserted with barrier and exciter filters with...
intensity of the emitting light set at maximum. All eyes were examined 3 to 6 months after the surgery using fundus photography with blue filters. Blue-filtered fundus photographs were taken using the blue exciter filter of the fundus camera (Topcon) for fluorescein angiography. To examine the functional effect of the DONFL appearance on vision, static microperimetry using MP-1 (Nidek Technologies Srl, Vigonza, Italy) was performed in 31 eyes with a clearly visible DONFL appearance. Each of 2 test stimuli was distributed in the arcuate striae area and in the surrounding normal retinal area around the midpoint between the papilla and macula (Fig 1). Distances from the macula to each stimulus point were made equal. The stimulus size was Goldmann I. This study was conducted in accordance with the institutional guidelines of Sapporo Medical University, and the institutional review board at Sapporo Medical University decided that approval was not required for this study. Informed consent was obtained from each patient.

Data were statistically analyzed with the Fisher exact probability test, chi-square test, or paired t test. The Fisher exact probability test or chi-square test was used for statistical comparison of categorical variables. A paired t test was used for continuous variables. A P value of <0.05 was considered to be statistically significant. Preoperative and postoperative visual acuities (VAs) were converted into the logarithm of the minimum angle of resolution (logMAR) for calculating the mean VA.

**Results**

On blue-filtered photographs, 46 (62.2%) of the 74 eyes with ILM peeling exhibited the DONFL appearance, compared with 0 (0%) of the 21 eyes without ILM peeling (Figs 2–4, Table 1). There was a significant difference between the 2 groups (P < 0.0001, Fisher exact probability test). With respect to indocyanine green usage during the surgery, 41 (64.1%) of the 64 eyes in which indocyanine green was used exhibited the DONFL appearance, compared with 5 (50.0%) of the 10 eyes in which indocyanine green was not used (Table 1). No significant difference was found between the 2 groups (P = 0.4890, Fisher exact probability test), although the number of eyes without use of indocyanine green was small. Of the 46 eyes with the DONFL appearance, the limits of the area of ILM peeling were clearly visible in 43 on blue-filtered photographs (13) (Fig 2) or indocyanine green autofluorescence fundus photographs (30) (Fig 5). The area of the DONFL appearance was limited to the area of ILM peeling in all 43 eyes.

In the static microperimetry, threshold values were 7.5 ± 2.6 (mean ± standard deviation) decibels in the arcuate striae area and 7.5 ± 2.8 decibels in the surrounding normal retinal area (Fig 1). No significant difference was found between the 2 areas (P = 0.9312, paired t test).

In all 95 eyes enrolled in the present study, the mean preoperative VA was 20/114 (logMAR, 0.76 ± 0.27), and the mean postoperative VA was 20/56 (logMAR, 0.45 ± 0.31). In the 74 eyes with ILM peeling, no difference was found between the eyes with and without the DONFL appearance in postoperative improvement of VA of ≥2 Snellen lines (32 [69.6%] of the 46 eyes with the DONFL appearance; 18 [64.3%] of the 28 eyes without the DONFL appearance; P = 0.6380, chi-square test).

**Discussion**

The cause of the DONFL appearance remains unclear. Tadayoni et al suggested that the DONFL appearance might be associated with the course of the optic nerve fibers, based on its shape and distribution. They reported that there was no difference between eyes with and without the DONFL appearance with regard to preoperative and post-
operative mean VAs or mean change in VA. Moreover, the visual field (VF) was normal in 3 eyes with the DONFL appearance. In the present study, there was no significant difference between the arcuate striae and the surrounding normal retina concerning the microperimetry threshold values. These findings suggest that the DONFL appearance is not associated with the loss of optic nerve fibers.

The DONFL appearance is clearly visible on blue-filtered photographs, which provide a good reflection of the inner retinal surface. Moreover, the DONFL appearance is clearly identified in short-wavelength illumination and poorly identified with long wavelengths using a scanning laser ophthalmoscope. Therefore, the DONFL appearance is caused by an abnormality of the inner retinal surface. Tadayoni et al described that the DONFL appearance might be caused by traction exerted on the retina during the removal of the ERM and ILM, although they could not prove this hypothesis. In the present study, 62.2% of the eyes with ILM peeling exhibited the DONFL appearance, compared with 0% of the eyes without ILM peeling. In addition, the area of the DONFL appearance was limited to the area of ILM peeling. These results suggest that the DONFL appearance is associated with ILM peeling, although the DONFL appearance is not always observed in eyes with peeling. In addition, there was no difference in the postoperative incidence of the DONFL appearance between

| Table 1. Relationship of the Dissociated Optic Nerve Fiber Layer Appearance (DONFL) to Internal Limiting Membrane (ILM) Peeling or Indocyanine Green (ICG) Staining |
|---------------------------------|-----------------|-----------------|
| ILM peeling (−)* (21 eyes)      | 0 (0%)          | 21 (100%)       |
| ILM peeling (+)† (74 eyes)      | 46 (62.2%)      | 28 (37.8%)      |
| ICG staining (−)* (10 eyes)     | 5 (50.0%)       | 5 (50.0%)       |
| ICG staining (+)† (64 eyes)     | 41 (64.1%)      | 23 (35.9%)      |

*P<0.001, Fisher exact probability test. †P = 0.4890, Fisher exact probability test.
the eyes with and without intraoperative indocyanine green exposure. This result suggests that the DONFL appearance is not related to indocyanine green use in the surgery.

We previously reported that OCT indicated dimples in the retinal nerve fiber layer (RNFL) corresponding to each stria of the DONFL appearance and that depths of all the dimples were limited to the RNFL thickness. On the other hand, OCT images revealed no distinct dimples in eyes without the DONFL appearance. Therefore, we believe the DONFL appearance is caused by dimples, the depths of which are limited to the RNFL thickness. Moreover, the present study suggests that the DONFL appearance is related to ILM peeling and is not associated with the optic nerve fiber loss. Taken together, the DONFL appearance might be created by cleavage (separation) of the optic nerve fiber bundles due to damage to the Müller cells, which are in close contact with the ILM and act to maintain the nerve fiber bundles close to each other. To support this hypothesis, focal electroretinogram is useful. Terasaki et al reported a limited and delayed recovery of the b-wave amplitude of the focal macular electroretinogram after ILM peeling during macular hole surgery. This finding suggests some damage to the Müller cells after ILM peeling. To prove damage of the Müller cells in eyes with the DONFL appearance, further investigations using multifocal electroretinograms are under way.

Tadayoni et al proposed another mechanism. The inner surface of the ILM is smooth and its outer surface is rough. The removal of the ILM exposes the rough surface composed of optic nerve fibers surrounded by Müller cell processes. The DONFL appearance might be due to this irregular surface. This suggestion, however, is not consistent with the results of previous reports. In our previous study using OCT, the mean depth of each dimple corresponding to the stria of the DONFL appearance was 28.6 μm. On the other hand, the ILM thickness was reported to be approximately 1.1 to 2.5 μm in the posterior pole.

In some cases, the limits of the area of ILM peeling are visible on postoperative blue-filtered fundus photographs. In the present study, the limits of the area of ILM peeling were clearly visible in 13 eyes on blue-filtered photographs. In eyes undergoing indocyanine green-assisted vitrectomy, indocyanine green autofluorescence fundus photographs are also useful for detecting the area of ILM peeling. Machida et al reported that the area of ILM peeling could be detected as hypofluorescence within diffuse hyperfluorescence in the posterior pole on postoperative indocyanine green autofluorescence fundus photographs. In this study, the limits of the area of ILM peeling were clearly visible in 30 eyes on indocyanine green autofluorescence fundus photographs.

Tadayoni et al reported that Goldmann VF testing was normal in 3 eyes with the DONFL appearance. Also in our cases, Humphrey VF testing was normal in 2 eyes with the DONFL appearance. Fortunately, the DONFL appearance may not be associated with any loss of VF. However, VF defects have been reported in cases of ILM peeling, and the possibility exists that damage to the RNFL by ILM peeling is in some way responsible for the field defects in these cases.

In conclusion, the present study indicates that the DONFL appearance might be related to ILM peeling and is not associated with the loss of optic nerve fibers. These results are consistent with the suggestion that the DONFL appearance is caused by cleavage of the optic nerve fiber bundles due to damage to the Müller cells, which are in close contact with the ILM and act to maintain the close proximity of the nerve fiber bundles. This hypothesis can be proved only after histopathologic study of the RNFL in a patient undergoing vitrectomy with ILM peeling. Therefore, further investigations, including histopathologic studies, are necessary to examine this hypothesis.
References
