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Restoration of Photoreceptor Outer Segments up to 24 Months after Pars Plana Vitrectomy in Patients with Diabetic Macular Edema

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Purpose: To evaluate the ellipsoid zone (EZ) and external limiting membrane (ELM) status on optical coherence tomography images in patients with diabetic macular edema (DME) before and after pars plana vitrectomy (PPV).

Design: Retrospective observational analysis.

Participants: Sixty-one eyes of 49 patients with DME.

Methods: We retrospectively reviewed the spectral-domain optical coherence tomography images of 61 eyes of 49 patients with DME who were treated with PPV and evaluated the percentage disruption of the EZ and ELM before and up to 24 months after PPV.

Main Outcome Measures: Longitudinal changes in visual acuity (VA), central retinal thickness (CRT), and EZ and ELM spectral-domain optical coherence tomography findings in patients with DME.

Results: The logarithm of the minimum angle of resolution VA was 0.477 before PPV and then improved to 0.372 and 0.344 at 12 and 24 months after PPV, respectively ($P < 0.005$ and $P < 0.001$, respectively). The CRT was 505.5 μm before PPV and then decreased gradually to 345.0 and 301.4 μm at 12 and 24 months, respectively ($P < 0.001$ for both). The percentage disruption of the EZ was 29.3% and ELM was 9.6% before PPV and then deteriorated to 41.6% ($P < 0.001$) and 15.1% ($P < 0.05$), respectively, 1 month after PPV. The disruption of the EZ and ELM decreased gradually. The percentage disruption of the ELM recovered but did not improve by 24 months, compared with baseline (11.6%; $P = 0.875$), whereas the percentage disruption of the EZ recovered to baseline by 6 months (29.4%; $P = 1.000$) and then decreased significantly at 24 months (21.3%; $P < 0.05$).

Conclusions: Both the EZ and ELM deteriorated after PPV. Whereas the ELM recovered but did not improve by 24 months when compared with baseline, the EZ and VA improved up to 24 months. *Ophthalmology Retina 2017;■:1–6* © *2017 by the American Academy of Ophthalmology*

Diabetic macular edema (DME) often causes significant acquired vision loss because the accumulation of fluid damages the retinal layer structures. Laser photocoagulation is beneficial in reducing the risk of visual loss caused by clinically significant DME and had previously been the standard therapy for DME.[1,2] It was recently reported that ranibizumab monotherapy or ranibizumab combined with laser therapy resulted in superior improvements in best-corrected visual acuity (VA) over laser treatment alone in patients with visual impairment resulting from DME.[3,4] Additionally, it has been reported that deferring focal/grid laser therapy may be associated with a greater chance of relatively larger improvements in VA through 5 years compared with adding focal/grid laser therapy when initiating intravitreal ranibizumab, although deferral of laser therapy may require more injections.[5] Anti–vascular endothelial growth factor (VEGF) agents have been the mainstay of treatment for DME, although frequent injections create a greater treatment burden for physicians and patients compared with that of treatment before the anti-VEGF era. Intravitreal and sub-Tenon's injection of triamcinolone acetonide (STTA) is a therapeutic option for DME,[6,7] but complications such as cataract progression and glaucoma develop over a longer period. Pars plana vitrectomy (PPV) is also considered a therapeutic option for DME with or without visible posterior hyaloidal traction[8–10] because longer-lasting effects can be expected with less frequent treatments and visits, decreasing the burden on the patient, although PPV also causes cataract in most patients, as well as other complications such as retinal detachment and vitreous hemorrhage. However, surgical complication rates other than cataract progression now fortunately are very low.

Spectral-domain optical coherence tomography (OCT) is currently used to detect morphological changes of the retina such as in the ellipsoid zone (EZ) and external limiting membrane (ELM). We previously reported that the ELM and EZ statuses appear to be closely related to visual outcomes.[11] Chronic retinal thickening may damage the outer layers of the retina and cause poor VA. Thus, treatment

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should be started early, before irreversible changes begin to develop in the outer layers. Sakamoto et al[12] reported that the postoperative photoreceptor status of the fovea is closely related to the final VA after resolution of DME by PPV; however, the association between the course of changes in the photoreceptor status by PPV and the resultant course of changes in VA is not well known. In this study, we investigated the EZ and ELM statuses on OCT images in patients with DME before and up to 24 months after PPV.

Patients and Methods

We retrospectively reviewed the medical records of 62 patients with diabetic retinopathy with clinically significant macular edema (n = 81 eyes) who were treated with PPV from April 2009 to May 2014 at Kobe City Medical Center General Hospital and were followed for ≥24 months postoperatively. Patients with any ocular diseases that could affect visual potential, such as macular degeneration, rhegmatogenous retinal detachment, glaucoma, cataract graded above grade III in the Emery−Little classification, and corneal pathologies, were not included in this study. Of the 81 eyes, we excluded 20 eyes. Among those eyes, 10 eyes were from patients who did not complete 24 months of follow-up, 8 eyes did not have adequate quality for the measurement of the outer layers on OCT imaging, 1 eye developed vitreous hemorrhage and neovascular glaucoma postoperatively, and 1 eye received an anti-VEGF agent and intravitreal triamcinolone acetonide within 24 months. Thirty-one eyes had received no treatment for DME before PPV, and 30 eyes had previous treatments (23 eyes with STTA, 7 eyes with anti-VEGF injection, and 4 eyes with focal laser). All procedures conformed to the Declaration of Helsinki for research involving human subjects, and institutional review board and ethics committee approval was obtained.

All of the patients had undergone standard three-port PPV with a 23- or 25-gauge system. The vitreous body was visualized with triamcinolone acetonide. A core vitrectomy was performed, with induction of a posterior vitreous detachment if a detachment was not already present. The internal limiting membrane (ILM) was peeled using 0.05% indocyanine green. The area of ILM peeling was 2 to 3 optic disc diameters around the fovea. Triamcinolone acetonide was injected into sub-Tenon's capsule at the end of the procedure. Thirty eyes (49.2%) were pseudophakic, and simultaneous lens extraction with intraocular lens implantation was performed for the remaining 31 eyes (50.8%). After PPV, additional STTA was administered at the investigator's discretion. Each patient underwent a complete ophthalmologic examination including best-corrected VA measurement, slit-lamp biomicroscopy, indirect fundus ophthalmoscopy, and OCT. These patients were examined with a spectral-domain OCT machine (Spectralis HRA+OCT; Heidelberg Engineering, Dossenheim, Germany). Spectral-domain OCT images were obtained with Spectralis (Spectralis Family Acquisition Module, version 4.0.2.0; Heidelberg Engineering GmbH, Heidelberg, Germany) and Heidelberg Eye Explorer (version 1.6.1.0; Heidelberg Engineering, Heidelberg, Germany) before PPV and 1, 3, 6, 12, and 24 months after PPV. Horizontal and vertical scans of the macula were recorded for each eye. The measurements were performed under pupillary dilation. The eye-tracking system of the device was used to ensure that the scans were in the correct position; the position of the fovea was manually detected during examination. On average, >40 B-scans were recorded and averaged per image for each eye. Images without appropriate eye tracking (an average of >40 images) were excluded from this study.

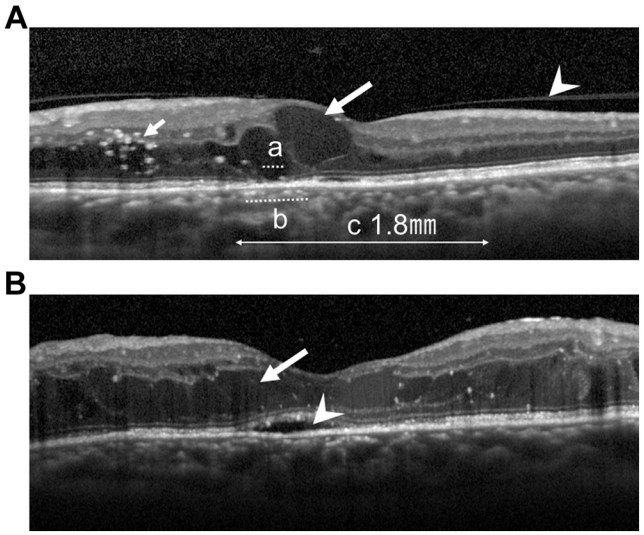

Figure 1. Spectral-domain optical coherence tomography images of a patient with diabetic macular edema. The assessment was performed for a foveal area with a 1.8-mm diameter. Parameters assessed in the present study were (**A**) hard exudate (small arrow), vitreous adhesion (arrowhead), and cystoid macular edema (large arrow); and (**B**) sponge-like retinal swelling (arrow) and serous retinal detachment (arrowhead). The percentage disruption of the ellipsoid zone and external limiting membrane is calculated as a/c × 100% and b/c × 100%, respectively.

We determined the presence or absence of cystoid macular edema (CME), serous retinal detachment (SRD), sponge-like retinal swelling (SLRS), hard exudates, and vitreous adhesion for each image (Fig 1). The foveal EZ and ELM on each image were reviewed, and the percentage disruption was averaged to generate a number from 0% to 100% (Fig 1A). This procedure was performed within a foveal area with a 1.8-mm diameter, which is considered to be the macula.[13] The central retinal thickness (CRT) was defined as the distance between the vitreoretinal border and the edge of the retinal pigment epithelial cells. Best-corrected VA was measured with a Landolt C chart and then converted to a logarithm of the minimal angle of resolution (logMAR) equivalent. The patients' clinical characteristics, including age, sex, duration of edema, and prior treatments (STTA, anti-VEGF agents, and focal laser), were also reviewed and analyzed.

The statistical program SPSS (version 11.0.1; SPSS Japan, Tokyo, Japan) was used to analyze the sample data. Descriptive analyses are reported as the mean ± standard deviation unless otherwise specified. Measurement values of the groups were compared using 1-way analysis of variance with the Tukey test to evaluate the difference between the baseline and postoperative (1−24 months) VA, CRT, EZ, and ELM. Bivariate relationships were examined using the Spearman correlation coefficient. Multivariable regression analysis was used to investigate which preoperative parameter is important for setting final VA as a dependent variable. A P value <0.05 was considered statistically significant.

Results

In total, 61 eyes of 49 patients (29 men and 20 women) with DME were included this study. The mean patient age was 65.6 ± 7.1 years, and the mean VA was 0.477 ± 0.248 logMAR (range, 0.10−1.15 logMAR) before PPV. Of the 61 eyes before PPV,