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Use of Scanning Laser Ophthalmoscope Microperimetry in Clinically Significant Macular Edema in Type 2 Diabetes Mellitus

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Purpose: We used scanning laser ophthalmoscope (SLO) microperimetry to evaluate scotomas in patients with clinically significant diabetic macular edema (CSME) in type 2 diabetes mellitus.

Methods: We studied 19 patients (mean age = 63 years; range, 45–78 years) (19 eyes). SLO microperimetry was performed in all eyes. We divided patients into three groups as follows: dense scotoma, relative scotoma, and no scotoma. The following variables were documented: age; duration of diabetes, hemoglobin A_{1c} levels; logarithm of the minimum angle of resolution (Log_{MAR}) visual acuity; refractive power; a history of panretinal photocoagulation; presence or absence of proliferative diabetic retinopathy, vitreomacular separation, and cystoid changes; the type of macular edema; and stability of fixation. All variables were compared in the three groups.

Results: We identified 4 eyes (21.1%) with dense scotoma, 10 (52.6%) with relative scotoma, and 5 (26.3%) with no scotoma. There were significant differences in log_{MAR} visual acuity among those with dense scotoma (1.4 ± 0.5), relative scotoma (0.6 ± 0.2), and no scotoma (0.2 ± 0.3) ($P < .05$), and in the prevalence of cystoid changes, diffuse edema, and unstable fixation among those with dense scotoma (75%, 75%, and 100%, respectively), relative scotoma (20%, 30% and 50%, respectively) and no scotoma (0%, 0% and 0%, respectively) ($P < .05$).

Conclusions: Macular scotoma was observed by SLO microperimetry in 74% of the patients in this study. A scotoma in CSME is related to the formation of cystoid changes and the type of macular edema. In eyes with CSME in type 2 diabetes mellitus, a scotoma in the macula causes visual acuity impairment and unstable fixation. **Jpn J Ophthalmol 2002;46:650–655** © 2002 Japanese Ophthalmological Society

Key Words: Diabetic macular edema, microperimetry, scanning laser ophthalmoscope, scotoma.

Introduction

Diabetic macular edema, which consists of fluid accumulation in the outer plexiform and inner nuclear retinal layers that causes retinal thickening, is one of the main causes of visual acuity impairment in patients with diabetes.[1,2] The important pathophysiology of diabetic macular edema is the loss of retinal capillary pericytes, resulting in increased vascular permeability.[3] However, the pathogenesis of diabetic macular edema is poorly understood. We reported that vitreomacular separation affects the natural history of diabetic macular edema and visual acuity changes.[4]

Microperimetry using the scanning laser ophthalmoscope (SLO) can detect a scotoma under direct fundus observation.[5–14] Because microperimetry using the SLO makes it possible to measure limited focal retinal sensitivity, its effectiveness has been reported in the evaluation of focal retinal sensitivity in

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eyes with several macular diseases.[6–9] Furthermore, the technique can measure not only the scotoma but also the fixation points.[10–14]

In the present study, we used SLO microperimetry to evaluate the scotoma in patients with clinically significant diabetic macular edema (CSME) in type 2 diabetes mellitus.

Materials and Methods

We studied 19 patients (19 eyes) with type 2 diabetes mellitus and CSME in the Department of Ophthalmology of Asahikawa Medical College Hospital, Asahikawa, Japan. All procedures adhered to the tenets of the Declaration of Helsinki, and informed consent was obtained in all cases.

The eyes were diagnosed based on the findings of best-corrected visual acuity, slit-lamp biomicroscopy, indirect ophthalmoscopy, fundus photography, and fluorescein angiography (FA). The ages of the 19 patients (11 women, 8 men) ranged from 45 to 78 years (mean ± SD = 63± 9 years). The duration of diabetes ranged from 3 to 23 years (mean ± SD = 13 ± 6 years). The hemoglobin A_{1c} ranged from 5.5 to 9.6% (mean ± SD = 6.9 ± 1.2%). The characteristics of the patients are summarized in Table 1.

Diabetic retinopathy was evaluated by fundus photography and FA and classified based on the presence or absence of proliferative diabetic retinopathy (PDR). The vitreoretinal relationship was examined using a preset lens with a slit-lamp microscope, which enabled us to observe the dynamics of the vitreoretinal relationship in the macular area with high magnification.[15,16] The vitreoretinal relationship was classified based on the presence or absence of vitreous attachment to the macula. The presence or absence of cystoid changes was evaluated by indirect ophthalmoscopy, fundus photography, and FA. The type of macular edema was classified during FA as diffuse; diffuse with leakage mainly from dilated capillaries and focal; intermediate with approximately equal leakage from microaneurysms and dilated capillaries. The best-corrected visual acuity was converted to the logarithm of the minimum angle of resolution (Log_{MAR}) for statistical analysis.

Table 1. Patient Characteristics

Variable	Mean	SD	Range
Age (y)	63	9	45–78
Duration (y)	13	6	3–23
Hemoglobin A_{1c} (%)	6.9	1.2	5.5–9.6
Log_{MAR} visual acuity*	0.7	0.5	−0.2–2.0
Refractive power (D)	−0.6	2.5	−7.0–3.8

*Log_{MAR} logarithm of the minimum angle of resolution.

Macular edema was described as clinically significant if at least one of the following characteristics was present[17]: retinal thickening at or within 500 μm from the center of the macula; hard exudates at or within 500 μm from the center of the macula is associated with thickening of the adjacent retina; or a zone or zones of retinal thickening 1 disc area or larger, any part of which is within 1 disc diameter from the center of the macula. Eyes with macular degeneration, preretinal macular fibrosis, central vein occlusion, and other macular abnormalities that complicated the assessment of macular edema were excluded from this study. Eyes with macular ischemia as determined by capillary nonperfusion on FA also were excluded from the study.

SLO (Rodenstock, Munich, Germany) microperimetry was performed in all eyes. An estimation of scotoma on the retina was performed using SLO microperimetry. Small flashing spots produced by a helium-neon red laser were used as visual stimuli for static microperimetry. With SLO microperimetry, the stimulus intensity can vary in 0.1-logarithmic steps from 0–31 dB; 0 dB (equivalent to the standard value of 6,200 candelas [cd]/m^2) represents the brightest luminance. We used 0 dB and 20 dB as the test stimuli. We defined a dense scotoma as one in which the stimulated area could not be detected with a 0-dB stimulus and a relative scotoma as one in which the stimulated area could be detected by a 0-dB stimulus but not by a 20-dB stimulus.[9] We defined the absence of a scotoma as one in which the stimulated area could be detected by 20 dB. We divided the scotoma into three groups: dense (Figure 1A), relative (Figure 1B), and no scotoma (Figure 1C). The other parameters were as follows: stimulation time, 100 milliseconds; stimulation spot size, 12 × 12 pixels squared (equivalent to 557.8 minutes of arc square, which corresponds to a Goldmann size III stimulus on the retina), with a resolution of 2 minutes of arc (10 μm); and retinal background illumination, 10 cd/m^2 of a helium-neon laser. We defined fixation as either stable, ie, stable fixation with a well-defined retinal locus, or unstable, ie, preferred but transient fixation detected.[13,14]

The following variables were documented for each patient: age; duration of diabetes; hemoglobin A_{1c} levels; log_{MAR} visual acuity; refractive power; a history of panretinal photocoagulation (PRP); the presence or absence of PDR, vitreomacular separation, and cystoid changes; the type of macular edema; and stability of fixation. All variables were compared in

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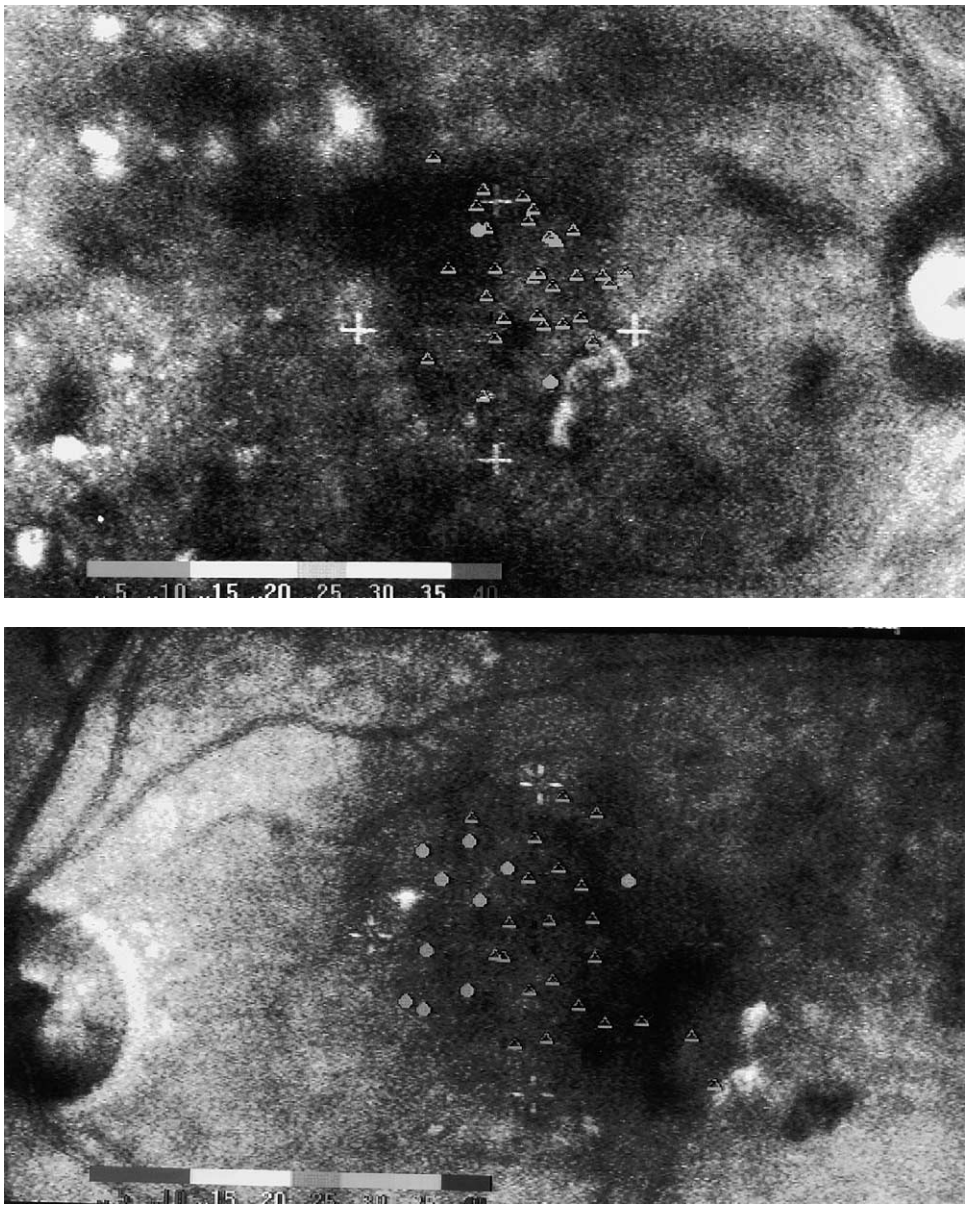

Figure 1. Microperimetry using the scanning laser ophthalmoscope (SLO). (A) Dense scotoma. The triangles indicate a dense scotoma and the circles indicate where the 0-dB test stimuli could be detected (68-year-old male patient, right eye). (B) Relative scotoma. The triangles indicate a relative scotoma and the circles indicate where the 20-dB test stimuli could be detected (63-year-old female patient, left eye). (C) No scotoma. The circles indicate where the 20-dB test stimuli could be detected (71-year-old female patient, left eye).

the three groups. Analysis of variance or chi-square test was used. A P value $<.05$ was considered statistically significant.

Results

The history of PRP and the presence or absence of PDR, vitremacular separation, and cystoid changes are shown in Table 2. Table 3 shows the presence of the variables in the three groups. Four eyes (21.1%) had a dense scotoma, 10 eyes (52.6%) had a relative scotoma, and 5 eyes (26.3%) had no scotoma in these 19 patients with diabetic macular edema. No significant differences were found in age, duration, hemoglobin A_{1c}, refractive power, history of PRP, and the presence or absence of PDR and vitremacular separation among the groups. There were significant differences in $\log_{MAR}$ visual acuity among the

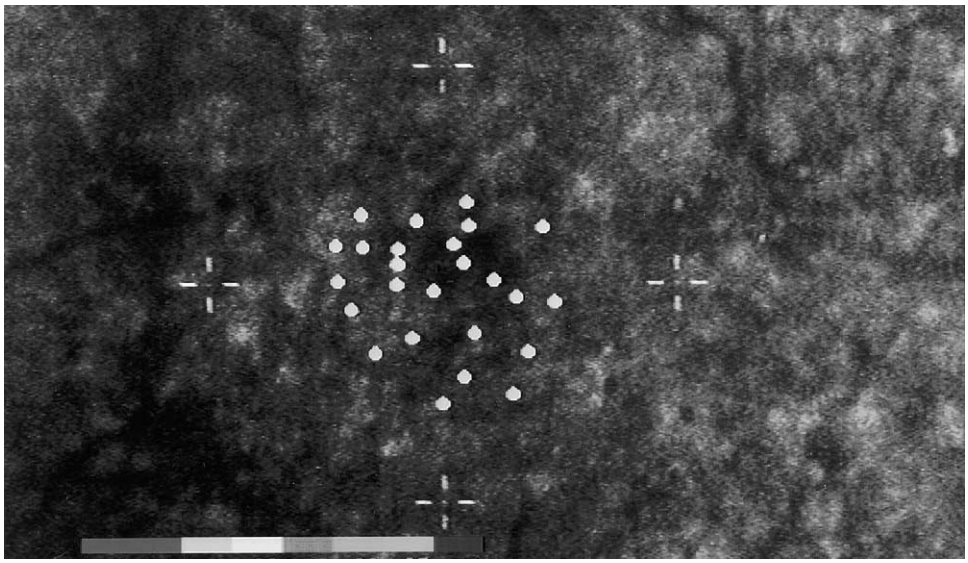

Figure 1. Continued.

patients with a dense scotoma (1.4 ± 0.5), relative scotoma (0.6 ± 0.2), and in the no scotoma group (0.2 ± 0.3) ($P < .05$). There were significant differences in the prevalence of cystoid changes, diffuse edema, and unstable fixation among those with a dense scotoma (75%, 75%, and 100%, respectively), relative scotoma (20%, 30%, and 50%, respectively), and no scotoma (0%, 0%, and 0%, respectively) ($P < .05$).

Discussion

In the present study, 74% of scotomas were identified in the patients with CSME in type 2 diabetes mellitus using SLO microperimetry. Our results indicate that there were significant differences in $\log_{MAR}$ visual acuity and the prevalence of unstable fixation in the three groups. In the eyes with CSME in type 2 diabetes mellitus, the scotoma in the macula caused impaired visual acuity and unstable fixation.

The formation of macular edema is thought to be promoted by systemic conditions such as poor glycemic control.[18] In the present study, there were no differences in age, duration of diabetes, and hemoglobin A_{1c} among the three groups. The glycemic control seemed to correlate with formation of macular edema but not with formation of scotoma in CSME. We reported that vitreomacular separation affects the natural history of diabetic macular edema and visual acuity changes.[4] However, there were no differences in the prevalence of vitreomacular separation among the three groups in the present study. Vitreomacular separation affects the natural history but is not related to the formation of scotoma in CSME.

The prevalence of cystoid changes and diffuse edema were significantly different among the groups. Cystoid changes within the retina are characteristic of diffuse macular edema. Cystoid changes may be

Table 2. Presence or Absence of Variables in Patients

	Present	Absent
	No. of Patients (%)	No. of Patients (%)
PRP*	15 (79)	4 (21)
PDR†	11 (58)	8 (42)
Vitreomacular separation	3 (16)	16 (84)
Cystoid changes	5 (26)	14 (74)

*PRP: panretinal photocoagulation.
†PDR: proliferative diabetic retinopathy.

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Table 3. Presence or Absence of Variables in Eyes with Scotoma

Variable	Dense Scotoma	Relative Scotoma	No Scotoma	*P* Value*
Number	4 (21.1%)	10 (52.6%)	5 (26.3%)	
Age (y)	70 ± 8	60 ± 6	64 ± 12	NS
Duration (y)	15 ± 7	12 ± 6	13 ± 7	NS
Hemoglobin A_{1c}	6.5 ± 0.4	7.0 ± 1.1	7.7 ± 2.7	NS
Log_{MAR} visual acuity†	1.4 ± 0.5	0.6 ± 0.2	0.2 ± 0.3	< 0.05
Refractive power (D)	−1.0 ± 2.9	−0.4 ± 2.0	−0.2 ± 2.4	NS
History PRP‡				
Yes	4	7	4	
No	0	3	1	
PDR§				NS
Yes	3	5	3	
No	1	5	2	
Vitreomacular separation				NS
Yes	1	1	1	
No	3	9	4	
Cystoid changes				< 0.05
Yes	3	2	0	
No	1	8	5	
Type of macular edema				< 0.05
Focal	1	7	5	
Diffuse	3	3	0	
Fixation				< 0.05
Stable	0	5	5	
Unstable	4	5	0	

*NS: not significant.
†Log_{MAR}: logarithm of the minimum angle of resolution.
‡PRP: panretinal photocoagulation.
§PDR: proliferative diabetic retinopathy.

visible clinically by ophthalmoscopy or slit-lamp examination, but are best seen in the late angiograms when fluorescein pools in the cystoid space.[19] Our results indicate that the formation of a scotoma in CSME is related to the the formation of cystoid changes and the type of macular edema.

Rohrschneider et al[20] reported the results of the use of SLO microperimetry before and after laser treatment in CSME. Those authors indicated that retinal sensitivity and stability of fixation in CSME were reduced compared with normal values. Based on our present results and their results, SLO microperimetry is a useful tool to evaluate visual function and visual acuity in eyes with CSME.

In conclusion, we evaluated the scotomas in the patients with CSME in type 2 diabetes mellitus using SLO microperimetry. Using SLO microperimetry, we found that 74% of the eyes with diabetic macular edema had a macular scotoma. The formation of a scotoma in CSME seems to be related to the formation of cystoid changes and the type of macular edema. In the eyes with CSME in type 2 diabetes mellitus, a scotoma in the macula causes visual acuity impairment and unstable fixation.

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