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Aniseikonia and Foveal Microstructure in Patients with Idiopathic Macular Hole

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Purpose: To quantify the severity of aniseikonia in patients undergoing vitrectomy for idiopathic macular hole (MH) and to examine any relationship between aniseikonia and the foveal microstructure.

Design: Prospective, consecutive, interventional case series.

Participants: We included 56 eyes of 56 patients who underwent vitrectomy to treat idiopathic MH.

Methods: We examined visual acuity, aniseikonia using the New Aniseikonia Test, and foveal structure using optical coherence tomography (OCT) before and 3, 6, and 12 months after surgery. Based on OCT images, minimum and base diameters of MH, height of MH, and defect lengths of the external limiting membrane (ELM), ellipsoid zone, and interdigitation zone were assessed.

Main Outcome Measures: Degree of aniseikonia before and after surgery.

Results: The mean aniseikonia was $-3.2\pm4.6\%$, ranging from -15.5% to +5.0%. Of the patients, 55% had micropsia, 7% had macropsia, and 38% had no aniseikonia. The mean absolute value of aniseikonia improved significantly from $3.8\pm4.1\%$ before surgery to $1.0\pm1.5\%$ at 12 months after surgery (P < 0.0001). The preoperative mean absolute value of aniseikonia showed a significant correlation with minimum diameters of MH (P < 0.01), base diameters of MH (P < 0.01), and the defect length of ELM (P < 0.05). In multivariate analysis, preoperative aniseikonia showed a significant correlation with the defect length of ELM (P < 0.05). In contrast, postoperative aniseikonia was not associated with any of the parameters.

Conclusions: Approximately half of MH patients had micropsia. Vitrectomy for MH improved aniseikonia. Preoperative aniseikonia was associated with MH size and the defect length of ELM. *Ophthalmology* 2016; \equiv :1-7 \otimes 2016 by the American Academy of Ophthalmology.

Idiopathic macular hole (MH) is a relatively common retinal disease that causes disturbance of visual functions such as reduced visual acuity and metamorphopsia. Recent advances in surgical techniques for MH have led to improvement of the anatomic success rate of surgery and MH-related disturbed visual acuity and metamorphopsia.^{1–8} However, previous studies have reported retinally induced aniseikonia in foveal diseases such as epiretinal membrane (ERM),^{9–15} retinal detachment (RD),^{15–20} macular edema,¹⁸ age-related macular degeneration,²¹ and central serous chorioretinopathy (CSC).²² Aniseikonia is a difference of perceived image sizes between 2 eyes, and the symptoms, such as headache, asthenopia, photophobia, reading difficulty, nausea, vertigo, and dizziness, and a sense of discomfort, differ depending on the individual.^{23,24} Thus, aniseikonia plays an important role in visual function and quality of life. It has been known that stretching or compression of the retina, resulting in a change of the perceived image size because of the alteration in spacing between the photoreceptors, may cause retinally induced aniseikonia.⁹ Because MH is caused by centrifugal movement of retinal photoreceptors,⁶ MH patients may demonstrate aniseikonia. However, no studies so far have assessed aniseikonia in patients with MH by a search using PubMed.

A couple of existing studies investigated the relationship between visual acuity and optical coherence tomography (OCT) findings in MH patients and found that visual acuity has a certain association with the defect lengths of the ellipsoid zone^{25–28} and the interdigitation zone.^{29,30} Kim et al³¹ reported that postoperative metamorphopsia was associated with asymmetric elongation of the foveal tissue after MH surgery. This study was aimed at quantifying aniseikonia of patients who underwent vitreoretinal surgery for the treatment of idiopathic MH and making an evaluation of the relationship between the aniseikonia and foveal microstructures.

Methods

We investigated 56 eyes of 56 patients with idiopathic MH who were followed up for 12 months after surgical treatment at the University of Tsukuba Hospital from October 2010 through April 2012. Twenty-two patients were men and 34 patients were women, averaging 65.3 ± 5.2 years of age (mean \pm standard deviation). We conducted this prospective, interventional, consecutive study in accordance with the Declaration of Helsinki and received approval from the institutional review committees of University of Tsukuba Hospital. Signed informed consent was obtained from all study subjects. Exclusion criteria comprised traumatic MH, MH

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Figure 1. Optical coherence tomography parameters of macular hole (MH): (a) minimum diameters of MH, (b) base diameters of MH, (c) height of MH, (d) defect lengths of external limiting membrane, (e) defect lengths of ellipsoid zone, and (f) defect lengths of interdigitation zone.

secondary to proliferative diabetic retinopathy or uveitis, ophthalmic disorders except mild refractive errors and cataract, and a history of vitrectomy. Patients with more than 2.0 diopters (D) of anisometropia before or 12 months after surgery, or both, also were excluded from the study.

The examinations comprised measurements of the bestcorrected visual acuity, the severity of aniseikonia as assessed by the New Aniseikonia Test (NAT; Handaya, Tokyo, Japan), fundus examinations, and examination of the retinal microstructure by spectral-domain OCT (Cirrus high-definition OCT; Carl Zeiss, Dublin, CA). All ophthalmologic examinations were performed before and 3, 6, and 12 months after surgery. Instead of bestcorrected visual acuity, the corresponding logarithm of the minimum angle of resolution (logMAR) was used for statistics and is presented throughout this article.

The NAT, introduced in 1988 by Katsumi et al,³² is a simple method to quantify the amount of aniseikonia. The test consists of matched pairs of red and green semicircles with a target size of 4 cm and allows for measurement from 1% to 24% of aniseikonia. Two semicircles with different sizes in each pair are placed in a consecutive manner, with a difference in 1% increments. A subject who wears red and green spectacles views the plates so that the right eye can see either of the semicircles in every pair and the left eye can see the other one. The subject is asked to indicate the pair in which 2 semicircles seem to be the same size. The actual ratio of the size of the half-moons in the corresponding pair represents the percentage of the subject's aniseikonia. Measurements were repeated 3 times at a distance of approximately 40 cm in vertical as well as horizontal meridians, and the obtained mean values also were used during data analysis. The examiners administrating the NAT tests were professional orthoptists and were masked to the fundus findings of the patients. Aniseikonia of 2% or more was deemed macropsia, whereas that of -2% or less was considered micropsia. Patients with visual acuity more than 1.0 logMAR were excluded because it was difficult for them to perceive the half-moon.³² However, patients with visual acuity more than 1.0 logMAR were included if they were able to undergo the tests correctly. If they could not perceive the half-moon sufficiently, they were excluded.

In spectral-domain OCT examination, we performed 5-line Raster scans of each eye using a commercially available analytic software package (Cirrus analysis software, version 3.0; Carl Zeiss) with signal strength of more than 7/10. Based on an array of obtained OCT images, we quantified the following parameters before

surgery: minimum and base diameters of MH, height of MH, and the defect lengths of external limiting membrane (ELM), ellipsoid zone, and interdigitation zone (Fig 1). Using images obtained with 5-line Raster scans, we measured the parameters by a free imageprocessing software (ImageJ, developed by Wayne Rasband; National Institutes of Health, Bethesda, MD; available at http:// rsbweb.nih.gov/ij/index.html). The defect length of each line was determined by agreement between 2 masked, well-trained observers (Y.S., Y.M.), and the mean was used for analysis.

Surgery, consisting of 25-gauge transconjunctival sutureless vitrectomy under sub-Tenon local anesthesia, was performed by 3 vitreoretinal surgeons (F.O., Y.O., Y.S.). When a clinically significant cataract was observed, we simultaneously performed surgery for cataract with intraocular lens implantation. After inducing posterior vitreous detachment and performing core vitrectomy, we injected 0.2 ml of 0.025% brilliant blue G solution gently over the macula for 15 seconds and washed it out with irrigation solution. Internal limiting membrane peeling and fluid—gas exchange were performed in all cases. For the subsequent 1 to 5 days, the patients maintained a face-down position.

The mean scores were compared and standard deviation values were calculated for each parameter of visual function (best-corrected visual acuity and aniseikonia) and OCT measurements. The Wilcoxon signed-rank test was performed to compare preoperative and postoperative as well as vertical and horizontal aniseikonia. The Friedman test was used to clarify changes in visual function. Upon detecting a significant difference, we conducted the Dunnett post hoc test for multiple comparisons to reveal the time point that demonstrated a significant difference from the baseline value. The relationship between visual function and OCT parameters was analyzed with the Spearman rank correlation coefficient. Multivariate analysis with stepwise regression was adopted to evaluate the relationship between visual function and OCT parameters. Any difference was considered statistically significant at P < 0.05. All of the statistical analyses were performed with StatView software (version 5.0; SAS, Inc., Cary, NC).

Results

Clinical Features of Aniseikonia in Patients with Macular Hole

The patient characteristics are summarized in Table 1. The severity of mean aniseikonia ranged from -15.5% to +5.0% (Fig 2). Of 56

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