Central Retinal Function Assessment Using Microperimetry in Patients with Idiopathic Epiretinal Membrane

İdyopatik Epiretinal Membranlı Hastalarda Santral Retina Fonksiyonunun Mikroperimetri ile Değerlendirilmesi

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ABSTRACT

Purpose: To examine the relations between visual acuity, optical coherence tomography, and microperimetry measurements in an attempt to explore the potential role of microperimetry in the evaluation of patients with ERM.

Materials and Methods: Thirty-four eyes of 27 ERM patients were included. In addition to visual acuity measurements, all patients underwent OCT and microperimetry examinations.

Results: LogMAR best corrected visual acuity values were positively correlated with central macular thickness (r=0.564, p=0.001), indicating an inverse relation between visual acuity and macular thickness. A weak correlation was found between LogMAR visual acuity and central mean sensitivity (r=-0.473, p=0.005). Retinal thickness was inversely correlated with retinal sensitivity in the central fovea (r=-0.755, p<0.001).

Conclusions: Assessment of retinal sensitivity with fundus microperimetry is a rapid, safe, non-invasive diagnostic procedure that might be utilized as a complementary tool to assess changes in central macular function in patients with ERM.

Key Words: Idiopathic epiretinal membrane, microperimetry, optical coherence tomography.

ÖZ

Amaç: Bu çalışmada epiretinal membranı (ERM) bulunan hastaların değerlendirilmesinde mikroperimetrenin potansiyel rolünü araştırmak için görme keskinliği, optik koherens tomografi (OKT) ve mikroperimetre ölçümleri arasındaki ilişki incelenmiştir.

Gereç ve Yöntem: Çalışmaya 27 ERM'li hastanın 34 gözü dahil edildi. Görme keskinliğine ilave olarak, tüm olguların OKT ve mikroperimetri incelemeleri yapıldı.

Bulgular: En iyi düzeltilmiş LogMAR görme keskinliği değerlerinin santral makula kalınlığı ile pozitif korelasyon göstermesi görme keskinliği ve makula kalınlığı arasındaki ters bağıntıyı belirtmekteydi (r=0.564, p=0.001). LogMAR görme keskinliği ve santral makula hassasiyeti arasında zayıf korelasyon bulundu (r=-0.473, p=0.005). Retina kalınlığı ve santral foveadaki retina hassasiyeti arasında ters korelasyon mevcuttu (r=-0.755, p<0.001).

Sonuç: Retina hassasiyetinin fundus mikroperimetresi ile değerlendirilmesi hızlı, güvenilir ve invaziv olmayan bir tanısal yöntem olup ERM'li olguların santral makula fonksiyonlarındaki değişikliklerin tespitinde tamamlayıcı olarak kullanılabilir.

Anahtar Kelimeler: İdyopatik epiretinal membran, mikroperimetri, optik koherens tomografi.

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INTRODUCTION

Epiretinal membrane (ERM) is characterized by the formation of a membranous tissue over the macula,[1,2] and may be classified as idiopathic or secondary. ERMs are referred to as idiopathic when there is no antecedent ocular condition or surgical procedure other than posterior vitreous detachment. Secondary ERMs may be associated with many ocular conditions including previous ocular surgery, retinal detachment, retinal vascular diseases or other retinal pathologies.[3] Although exact pathogenesis of idiopathic epiretinal membrane is still unknown, it is thought to result from the glial proliferation through the defects in the internal limiting membrane, after posterior vitreous detachment.[4]

The ophthalmoscopic features of ERMs are quite variable from a cellophane-like translucent membrane to a thick opaque one with retinal folds.[2] Increased permeability and retinal edema may be present due to the contraction of these membranes resulting in traction on the adjacent retinal vessels.

ERM is diagnosed by funduscopic examination, and currently BCVA (best corrected visual acuity) and OCT (optical coherence tomography) are routinely used for the follow-up of patients with ERM, and these examinations aid in treatment decision. Visual acuity reflects foveal function only; and OCT is useful to identify the ERM with accompanying morphological changes including the increase in macular thickness, but it does not provide direct information on macular function. Microperimetry (MP) is able to quantify the relationship between anatomical and functional changes in macular disorders. Fundus-related microperimeter, MP1 (Nidek Technologies, Padova, Italy), is a novel automatic fundus perimeter that has been shown to evaluate the macular function efficiently in several macular pathologies such as age-related macular degeneration, diabetic macular edema, central serous chorioretinopathy, cystoid macular edema, and idiopathic juxtafoveal retinal telangiectasia.[5-10]

In this study, we aimed to investigate the potential role of microperimetry in the evaluation of patients with ERM by examining the relations between visual acuity, macular thickness and macular function.

MATERIAL AND METHODS

Patients

Thirty-four eyes of 27 consecutive patients who were diagnosed with idiopathic ERM during years 2007 and 2009 at Yeditepe University Department of Ophthalmology were included in this study. Signed informed consent was obtained from all patients and study procedures were carried out in accordance with the principles of Declaration of Helsinki.

Eyes with significant media opacity, cataract, glaucoma, previous laser treatment, and paramacular ERM were excluded. In addition, patients with secondary ERM due to cataract surgery, retinal detachment, retinal vascular diseases or other retinal pathologies were excluded in order to avoid interference with other retinal pathologies that may influence retinal functions. Complete ophthalmic examination followed by optical coherence tomography was performed in all subjects. Ophthalmic examination involved the determination of best corrected visual acuity (logMAR), anterior segment evaluation, intraocular pressure detection by applanation tonometry, and a detailed fundus examination.

Optical Coherence Tomography Examination

OCT was performed using the Humphrey model 3000 device (Zeiss-Humphrey Instruments, San Leandro, CA). Fast Macular Thickness Map protocol was used for the study, which consists of six 6 mm long radial line scans at equally spaced angular orientations simultaneously centered on the fovea in a radial spoke pattern. Using Retinal Thickness Mapping Software, retinal thickness measured in the central disc with a diameter of 1000 μm at the center of the macula was used as central foveal

Table: Mean values of visual acuity, central macular thickness and central macular sensitivity for fixation subgroups.

	Mean BCVA	Mean Central OCT	Mean Central MS
Stability of fixation			
Stable	0.17±0.25	305.93±68.62	15.65±4.39
Relatively unstable	0.19±0.19	304. 23±87.60	15.69±3.55
Unstable	0.66±0.42	465.67±175.11*	10.23±5.04†
Localization of fixation			
Predominantly central	0.13±0.17	297.89±61.62	16.55±2.88
Poor Central	0.31±0.32	342.30±98.24	13.50±4.91
Predominanty eccentric	0.67±0.44‡	451.00±217.70	10.16±6.04#

*p=0.005, vs. stable; †p=0.012, vs. stable; ‡p=0.002, vs. predominantly central; #p=0.015, vs. predominantly central. Bonferroni correction was used for pair-wise comparisons. Data are expressed as mean±standard deviation.

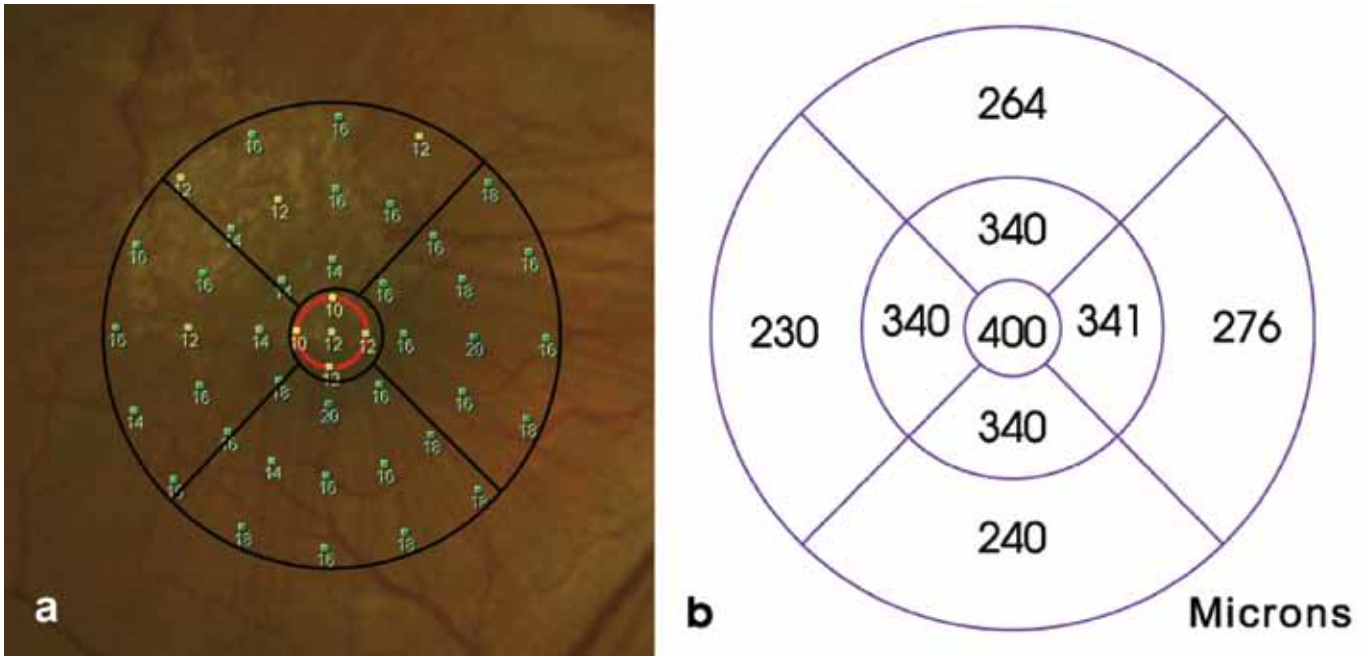

Figure 1: (a) Retinal sensitivity map of MP-1 microperimetry. **(b)** OCT thickness map showing the central area of 6 mm diameter. Central 1 mm and the inner 1-3 mm areas of the OCT map were used for comparisons and retinal sensitivity map was divided into corresponding quadrants.

thickness. In addition, the four quadrants of the area between 1 and 3 mm diameter rings of the OCT thickness map were used for analysis. Since microperimetric map encompasses only a certain proportion of the macula, the area between 3 and 6 mm diameter rings in the OCT thickness map was not included in the study.

Microperimetry Examination

Macular function of the eyes with idiopathic ERM was assessed by an automatic fundus-related perimeter (MP1 Microperimeter, Nidek Technologies, Italy) as previously describes elsewhere.[11]

A red circle target of 1° diameter, a white monochromatic background at 4 asb, a Goldmann III size of stimulus with 200 ms projection time, and a customized radial grid of 45 stimuli covering central 12° that was centered onto the fovea were the parameters used for microperimetry examination of a 4-2 double-staircase strategy. At the end of each examination, a color fundus photograph was obtained, which was then aligned with the infrared image, so that the results were automatically overlapped onto the color fundus image.

Mean sensitivity (MS) was estimated to evaluate the foveal and parafoveal functions, and the results were reported in decibels. In addition to macular function, fixation patterns and loci were also assessed by microperimetry. A circular, standard, central fixation area 2° in diameter (approximately 700 μm) centered on the fovea was labeled. This standard 2° circle was positioned on the centre of foveal avascular zone. Eyes with more than 50% of the preferred fixation points located within the central fixation area were classified as having predominantly central fixation. Eyes with more than 25% but less than 50% of the preferred fixation points within central area were classified as having poor central fixation. Eyes with less than 25% of the preferred fixation points within central area were classified as having eccentric fixation. Fixation was regarded as stable if more than 75% of the fixation points were inside the 2° diameter circle, as relatively unstable if less than 75% were inside the 2° diameter circle but more than 75% were inside the 4° diameter circle, and as unstable if less than 75% of the fixation points were inside the 4° diameter circle.

Microperimetry data were collected for central area and following four quadrants: superior quadrant from 10.30 to 1.30, nasal quadrant from 1.30 to 4.30, inferior quadrant from 4.30 to 7.30, and temporal quadrant from 7.30 to 10.30. In other words, this division of microperimetric sensitivity map was similar to that of the central 3 mm OCT thickness map. A sample image for OCT and microperimetry examination of an eye is shown in Figure 1.

Analysis of the Data

SPSS version 15.0 was used for statistical analyses. The correlations between microperimetry measurements, BCVA, and OCT results were examined by Spearman correlation analysis. Correlations between OCT and microperimetry measurements were examined for central 1 mm and 1 to 3 mm superior, nasal, inferior, temporal quadrants. The differences between fixation and stability groups were examined using Kruskal-Wallis test, and Mann Whitney U test was used for pair-wise comparisons with Bonferroni correction. A p value <0.05 indicated statistical significance.

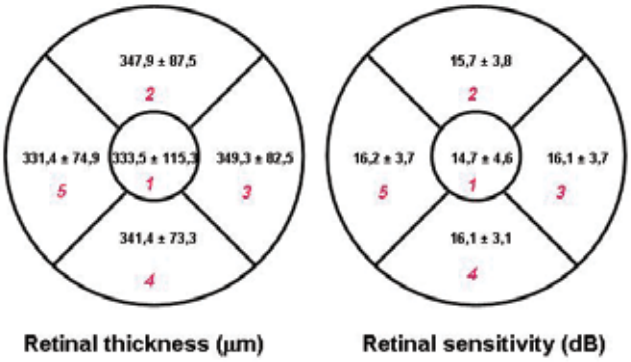

Figure 2: Schematic representation of the macular area corresponding to 5 OCT fields numbered as 1 (central 1 mm), 2 (superior 1-3 mm), 3 (nasal 1-3 mm), 4 (inferior 1-3 mm), and 5 (temporal 1-3 mm). (a) and (b) shows the mean values for retinal thickness and mean sensitivity of 34 eyes, respectively. Values for measured by OCT and the mean sensitivity estimated by MP-1, respectively.

RESULTS

Patients

Thirty-four eyes of 27 patients (13 female, 14 male) with a mean age of 69.2±7.5 y (range: 49-86 y) were included in the study. Mean BCVA (logMAR) was 0.26±0.32 (median: 0.18). In all eyes, OCT revealed a highly reflective layer on the inner retinal surface of the central macula. Macular thickness and mean sensitivity measurements from central fovea and 1-3 mm macular quadrants of the eyes are given in Figure 2.

Relations Between Visual Acuity, OCT and Microperimetry Measurements

LogMAR best corrected visual acuity values were positively correlated with central macular thickness (r=0.564, p=0.001) indicating an inverse relation between visual acuity and central macular thickness. On the other hand, a weak correlation was found between LogMAR best corrected visual acuity and central MS (r=-0.473, p=0.005). There was a statistically significant and inverse correlation between mean macular thickness and MS for central fovea and each of 4 peripheral quadrants: central fovea, -0.755, p<0.001; superior 1-3 mm, -0.543, p=0.001; nasal 1-3 mm, -0.559, p=0.001; inferior 1-3 mm, -0.354, p=0.040; temporal 1-3 mm, -0.478, p=0.004. The correlation was strong for central fovea and moderate for superior and nasal quadrants, whereas only a weak correlation was present for inferior and temporal quadrants.

Fixation was stable in 15 eyes (44.1%), relatively unstable in 13 eyes (38.2%), and unstable in 6 eyes (17.6%). Fixation loci were predominantly central in 19 eyes (55.9%), poor central in 10 eyes (29.4%), and predominantly eccentric in 5 eyes (14.7%). Mean values of visual acuity, central macular thickness and central macular sensitivity for fixation subgroups are given in Table. Although the numerically better visual acuity among the eyes with stable fixation could not reach statistical significance, eyes with central fixation had significantly better visual acuity compared to the eyes with eccentric fixation (p=0.002).

There was a tendency for a high central macular thickness with eccentric fixation but the differences were not significant. On the other hand, eyes with unstable fixation had significantly higher central macular thickness compared to the eyes with stable fixation (p=0.005). Central macular sensitivity was significantly higher among the eyes with stable fixation versus unstable fixation (p=0.012) and among the eyes with central fixation versus eccentric fixation (p=0.015).

DISCUSSION

In this study, macular sensitivity was found to be correlated with macular thickness and BCVA. The association between macular sensitivity and macular thickness was evident both for the foveal and parafoveal areas.

Despite inconclusive results that have been reported for the relationship between visual acuity and macular thickness in patients with ERM, the majority of the studies have suggested the existence of such a relationship.[12-14] Similar to previous findings, we also found a significant inverse correlation between central macular thickness and visual acuity.

Visual acuity is the most frequently used parameter to evaluate foveal function in retinal disease. Currently, OCT is routinely used for the assessment of macular diseases and allows in vivo assessment of morphological and thickness changes of retina. Although important in the evaluation of foveal function, visual acuity is not able to assess the complete retinal area affected by the disease and may not distinguish between central and eccentric fixation. Therefore, visual acuity alone may not completely reflect the visual performance. Other methods used to assess macular function include static perimetry, focal or multifocal electroretinography, and microperimetry.

Conventional central visual field testing is not a preferred method in cases with maculopathy, since unstable or extrafoveal fixation may frequently cause inaccurate results. Fundus perimetry, known as microperimetry, allows quantitative evaluation of the macular function, in addition to its ability to determine the location and stability of the retinal fixation.[15] Scanning laser ophthalmoscope (SLO) microperimetry was the first commercially available microperimeter, which allowed to analyze retinal sensitivity and fixation characteristics.[16]

The recently developed MP1 microperimeter performs automatic full-threshold perimetry independent of fixation characteristics and allows functional mapping of the macula,[15-16] and it has been shown that MP1 provides

perimetric results comparable to the results obtained with the well-established SLO.[16] Its major advantage compared to the SLO is the automatic eye tracking, which allows real-time compensation for eye movements and therefore presentation of any stimulus exactly at the predefined retinal location.[17] In addition, MP1 perimeter allows to obtain an overlay of the perimetric results onto a real colored fundus image and provides information on the relation between the retinal pathology and functional alteration representing another advantage in clinical use.[16-17]

Recently in a study by Karacorlu et al. retinal sensitivity in the central macular area determined by MP-1 microperimetry was found to be significantly correlated with BCVA and with foveal thickness in patients with idiopathic ERM.[18] Similar to their results, in our study involving patients with idiopathic ERM, retinal sensitivity was inversely correlated with macular thickness whereas a positive correlation was found between central retinal sensitivity and visual acuity. The strength of the relation between macular thickness and macular sensitivity showed variation across central and different parafoveal areas, which may be attributed to the individual differences of membrane topography and variations of membrane thickness across regions.

Several studies have examined macular function in patients with ERM using electrophysiological methods. For instance, Tanikawa et al.[19] studied the functional status of retina in idiopathic ERM patients using focal macular electroretinography and found significant reduction in electroretinography responses of the eyes with ERM. Moschos et al.[20] found a decrease in retinal function recorded by multifocal electroretinogram both in the foveal and parafoveal retina. Suzuki et al.[12] evaluated the relationship between retinal thickness and retinal function determined by focal macular electroretinogram in eyes with ERM and macular pseudohole; and they found a strong correlation between retinal thickness and retinal function for parafoveal retina. In this study, we also found a statistically significant and inverse correlation between retinal thickness and retinal sensitivity of the parafoveal area.

Besides providing retinal sensitivity maps of the macula, microperimetry is also useful for more accurate evaluation of the shift in the loci of fixation. Fixation characteristics are known to play an important role in reading, writing, symbol recognition, and some other daily tasks. Decreased fixation stability and the loss of central fixation are typical for the deterioration in central visual function in macular pathologies such as the age-related neovascular macular degeneration associated with eccentric and unstable fixation, which indicate the preference for an extrafoveal retinal locus as the maculopathy progresses.[5] In two recent studies, fixation characteristics in diabetic macular edema were examined and both studies found a significant association between the site and stability of fixation, and visual acuity.[21-22] The present study examined the relation between fixation characteristics (i.e. localization or stability) and visual acuity, central macular thickness, or central retinal sensitivity. Eyes with unstable fixation had lower visual acuity and central macular sensitivity, and higher central macular thickness; however, statistical significance could be achieved only for macular sensitivity and macular thickness. Similarly, eyes with eccentric fixation had lower visual acuity and central macular sensitivity, and higher central macular thickness, with statistical significance of the relation with visual acuity and macular sensitivity. Duration of the disease and macular edema, and the resulting photoreceptor cell injury may have role in the differences of fixation localization and stability. Due to the relatively small sample size of subgroups, it would not be wise to draw definite conclusions based on the present results. Studies with larger sample size and focused on fixation characteristics of patients with epiretinal membrane would shed further light on this issue.

Determination of the fixation locus in patients with ERM may prove to be valuable in the preoperative evaluation of these patients, since peeling of epiretinal membrane requires extra attention to avoid damaging new loci of fixation.[23] Another potential benefit of microperimetric evaluation in patients with ERM is its ability to record the changes in visual performance and fixation characteristics after macular surgery.[9,24,25]

MP1 microperimetry is an effective method for evaluating the changes in retinal function associated with the changes in retinal thickness in patients with ERM, allowing follow-up examinations on identical points previously tested and assessment of the location and stability of retinal fixation. Evaluation of retinal sensitivity with fundus microperimeter is a rapid, safe and non-invasive diagnostic procedure, and MP1 might be utilized as a complementary technique in addition to OCT and visual acuity measurements to assess the changes in central macular function in patients with ERM.

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