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ORIGINAL PAPER

MP-3 measurement of retinal sensitivity in macular hole area and its predictive value on visual prognosis

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Abstract

Purpose To explore a measuring method for retinal sensitivity in macular hole area by Microperimeter-3 (MP-3) and evaluate its predictive value on visual prognosis.

Methods This was a case series study including 44 eyes of 44 patients with idiopathic macular hole. Retinal sensitivity inside and 0.5 degree outside the macular hole margin was measured, and its mean value was defined as macular hole sensitivity (MHS). Best-corrected visual acuity (BCVA), minimum diameter of macular hole (MD), IS/OS defect diameter, retinal sensitivity in 8 degrees and 2 degrees were also recorded preoperatively and 4 months after operation.

Results All macular holes were closed after surgery. BCVA was significantly improved from 1.06 ± 0.39 at baseline to 0.31 ± 0.24 at 4 months postoperatively ($P < 0.001$). Meanwhile, MHS was also significantly improved from 12.02 ± 3.74 dB at baseline to 20.72 ± 4.00 dB at 4 months postoperatively ($P < 0.001$). MD, preoperative IS/OS defect diameter, preoperative BCVA, preoperative retinal sensitivity in 8 degrees and 2 degrees, and preoperative MHS were all correlated with postoperative BCVA at 4 months, but only preoperative MHS showed liner relationships to postoperative BCVA at 4 months by multivariate stepwise linear analysis.

Conclusions Macular hole sensitivity by MP-3 could reflect the change of central retinal function after

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successful macular hole surgery. Compared to preoperative retinal sensitivity in 8 degrees and 2 degrees, preoperative macular hole sensitivity is a better predictor for visual prognosis.

Keywords Idiopathic macular hole · The MP-3 microperimetry · Visual prognosis · Vitrectomy

Introduction

Idiopathic macular hole (IMH) is an ocular disease often affect females from middle-aged to senile [1, 2]. Central vision impairment is one of its major symptoms described by most patients [2]. Vitrectomy combined with inner limiting membrane (ILM) peeling is an effective surgical procedure to close the hole [3], which could restore patients' best-corrected visual acuity (BCVA) to varying degrees [4–7]. Since BCVA represents basic visual function [7], many ophthalmic tests were used to predict postoperative BCVA, such as minimum diameter of macular hole (MD) and IS/OS defect diameter in spectral-domain optical coherence tomography (SD-OCT) [8], first harmonic amplitude in focal electroretinogram recording (fERG) [9], and, applied in this research, retinal sensitivity in Microperimetry [10, 11]. Microperimeter-1 (MP-1) and its next generation product Microperimeter-3 (MP-3) could provide two major measurements for macular function assessment, retinal sensitivity, and fixation [12, 13]. At the same time, they both could evaluate subregional retinal sensitivity automatically or manually to assess retinal function in specific area. Sun et al. [7] measured retinal sensitivity in 8 degrees with MP-1 and found it could predict visual prognosis after surgery. Bonnabel et al. [14] measured retinal sensitivity in 8 degrees and 2 degrees with MP-1 and found postoperative visual acuity was correlated with each of them. But apparently, 8 degrees is an absolutely oversized range for measuring macular hole area. In Bonnabel's study, MD was from 274 to 711 μm, which didn't match 2 degrees theoretically. In a word, neither 8 degrees nor 2 degrees could reflect authentic lesion region caused by macular hole. It is unreasonable to measure retinal sensitivity by those ranges, but a range of retinal sensitivity measurement should be set by the size of macular hole.

The purpose of this study was to explore a precisely measuring method to evaluate retinal sensitivity according to minimum diameter of macular hole in macular hole area and its predicting value on visual prognosis was discussed, we hypothesized that preoperative retinal sensitivity in macular hole area has a predictive effect on visual prognosis.

Methods

Study population

In this case series study, forty-four eyes in 44 patients experienced IMH surgery in Beijing Tongren Hospital from September 2016 to December 2017. All the patients were diagnosed as IMH by medical history, indirect ophthalmoscopy and OCT (Cirrus HD-OCT, Carl Zeiss, Dublin, CA, USA), and the surgeon observed and identified the macular hole during the surgery. The exclusion criteria were: glaucoma, severe cataract, myopia > -6.00D, history of intraocular procedure, and cases in which MH wasn't closed after the primary surgery. The Medical Ethics Committee of Beijing Tongren Hospital approved the study protocol, and all participants gave their informed consent. All patients had a standard ophthalmologic examination before and 1, 4 months after surgery.

Other examinations included: best-corrected visual acuity (BCVA), non-contact intraocular pressure measurement, slit-lamp biomicroscope, color fundus photography, Microperimeter-3 (NIDEK, Gamagori, Japan). Macular hole stages were confirmed by Gass classification system, and MD, IS/OS defects were measured manually using the caliper function in HD-OCT. The BCVA was measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) regimen and was converted to logarithm of minimum angle of resolution (LogMAR) units.

MP-3 examinations

Microperimetry assessment was conducted in a dark room with the fellow eye patched. The examination was operated by two experienced operators. Microperimeter-3 (MP-3) would take high-definition color images of fundus to observe structures of macular hole. The customized pattern of macular hole consists of 45 stimulus test locations in 8° around the

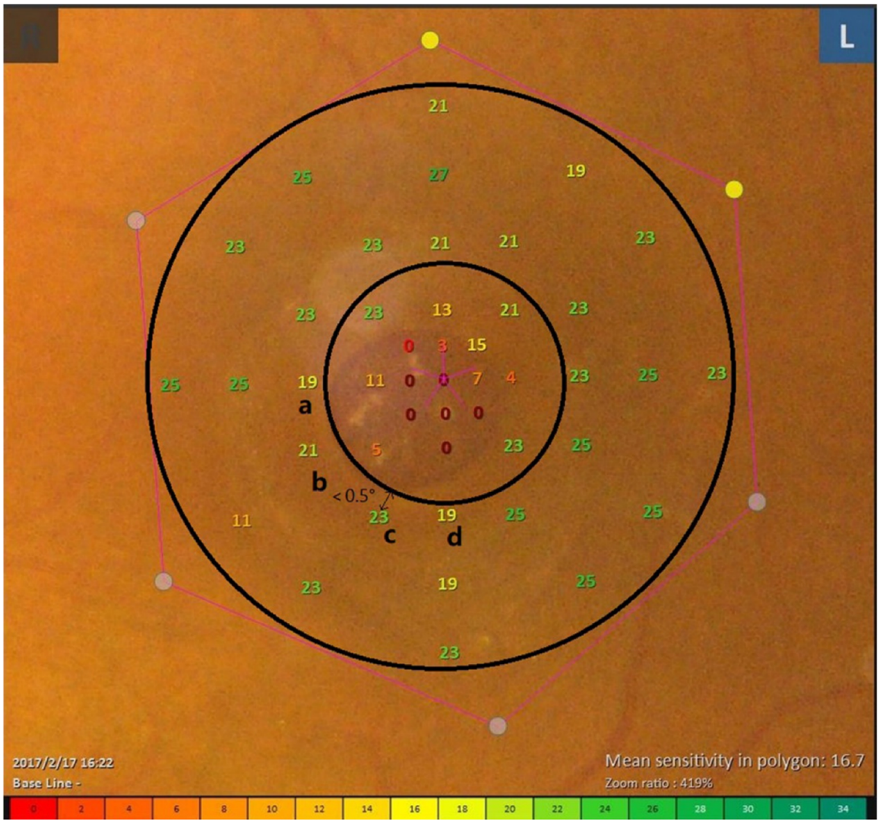

Fig. 1 A Microperimeter-3 image of a 58-year-old male patient whose MD is 628 µm. Spot a(19 dB), b(21 dB), c(23 dB), and d(19 dB) were all excluded because their distance to macular hole margin was less than 0.5 degree

fovea, the fixation target was shown as the 1° red circle, and center of the pattern was moved to center of macular hole as near as possible. The MP-3 measurement is carried out by a 4-2-1 staircase strategy with the Goldmann III stimulus size. Maximum luminance of MP-3 was 10,000 asb, and the stimulus dynamic range is between 0 and 34 dB. The automatic fundus eye tracking system enables accurate projection of stimulus in order to ensure the same points on retina during the follow-ups.

Following Chen's [8] study, retinal sensitivity in 8 degrees was named as mean macular hole sensitivity (MMS), retinal sensitivity in 2 degrees was named as central macular sensitivity (CMS). Both of them were evaluated for analysis in our study, and we defined macular hole sensitivity (MHS) as the mean value of spots inside and 0.5 degree outside macular hole margin (Fig. 1).

Surgical procedure

A 23-gauge transscleral sutureless vitrectomy system was used for pars plana vitrectomy. All the vitrectomies and, if it is necessary, phacoemulsification and intraocular lens implantation were performed by the same surgeon (W.L.). The internal limiting membrane (ILM) was peeled with forceps for 2 optic disk diameters around the macular hole without any staining. Clean air tamponade was used in all cases and patients were asked to take a strict face-down position for one week. Tobramycin, Tropicamide, Prednisolone Acetate, and Diclofenac sodium eye drops were used after surgery following doctor's advice. 1-month and 4-month follow-up were requested for the patients.

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS for Windows, version 22.0, Chicago, IL, USA). The parameters were presented as

Table 1 Characteristics of patients

Age (years)	54–79; median 65
Gender	Female: 34; Male: 10
Minimum diameter of macular hole (μm)	534.02 ± 162.67
Laterality	OD:21 OS:23
Stage II IMH	9 eyes
Stage III IMH	24 eyes
Stage IV IMH	11 eyes
Pars plana vitrectomy (PPV)	9 eyes
PPV + Phaco + IOL	35 eyes

mean ± standard deviations. Comparisons of these data were analyzed with paired-samplest test. Spearman correlation analysis was performed for correlation analysis. Multivariate stepwise linear regression analysis was performed to investigate the relationship between postoperative BCVA and preoperative parameters. A P value of less than 0.05 was considered statistically significant.

Results

General characteristics

Characteristics of patients are shown in Table 1. Thirty-four females (34 eyes, 77.27%) and ten males (10 eyes, 22.73%) were included. IMH was occurred in left eyes in 21 patients and right eyes in 23. The median age was 65 years. Nine eyes were in stage 2, 24 eyes in stage 3, and 11 eyes in stage 4 by Gass classification.

Anatomical and functional changes after macular hole surgery

All macular holes in these patients were closed with one operation. No postoperative complications were observed during follow-up. During 4 months follow-up, BCVA (logMAR), IS/OS defect diameter, MMS(dB), CMS(dB), and MMS (dB) were significantly improved from baseline to 1 month and 4 months postoperatively ($P < 0.001$).However, from 1 month to 4 months postoperatively, MMS and CMS didn't show significant improvement ($P > 0.05$) while MHS did ($P < 0.05$) (Fig. 2). The number of selected spots for MHS was 15.73 ± 3.52 (10–25). No patients showed decrease in BCVA, MMS, and MHS at

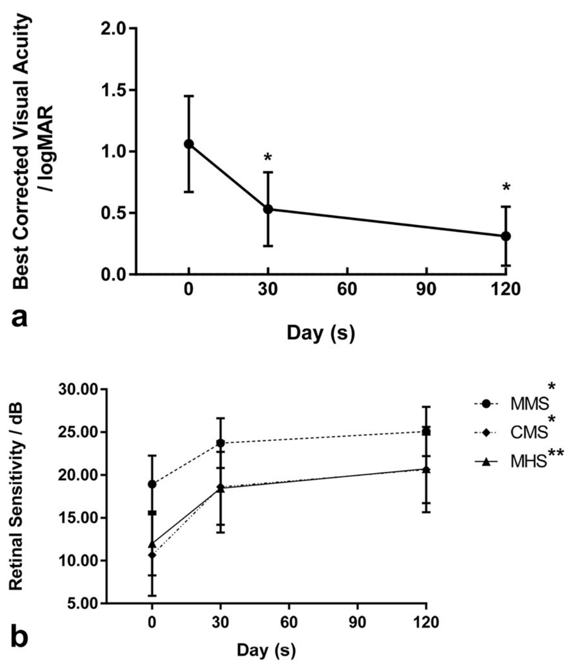

Fig. 2 Graphs showing functional before and after successful macular hole surgery. **a** Changes in best-corrected visual acuity (BCVA) after MH surgery. *Significantly improvement was shown at 1 and 4 months after surgery. **b** Changes in retinal sensitivity of MMS, CMS, and MHS after MH surgery. Significantly improvement was shown at 1 and 4 months after surgery ($P < 0.01$).*no significantly improvement in MMS ($P = 0.053$) and CMS ($P = 0.093$) from 1 month to 4 months postoperatively. **MHS showed significantly improvement ($P = 0.039$) from 1 month and 4 months postoperatively. (Mann–Whitney U test). *MMS* mean macular sensitivity, *CMS* central macular sensitivity, *MHS* macular hole sensitivity

4 months postoperatively. Patients with a preserve IS/OS line postoperatively gain a better MMS and MHS. On the basis of age and stages of cataract, phacoemulsification and IOL implantation were performed in 35 eyes. No difference on improvement

between patients with phacoemulsification and patients without ($P > 0.05$).

Correlations of MD and IS/OS defect diameter with MP-3 results and BCVA

Preoperative MMS($r = -0.474$), CMS($r = -0.443$), and MHS($r = -0.743$) were all significantly correlated with MD ($P < 0.05$), and significant correlations were also showed between postoperative MMS($r = -0.543$), CMS($r = -0.341$), MHS($r = -0.588$), and MD ($P < 0.05$). Meanwhile, preoperative BCVA ($r = 0.344$) and postoperative BCVA ($r = 0.582$) were significant correlations with MD ($P < 0.05$). However, preoperative IS/OS defect diameter showed no relationships with BCVA, MMS, CMS, or MHS at 4 months postoperatively. ($P > 0.05$).

Correlations of preoperative BCVA and MP-3 results with postoperative BCVA and roles of MP-3 results in predicting visual prognosis

Preoperative BCVA was significantly correlated with postoperative BCVA at 4 months ($r = 0.512$, $P < 0.001$). Preoperative MMS ($r = -0.504$), CMS ($r = -0.555$), and MHS ($r = -0.611$) were all significantly correlated with postoperative BCVA at 4 months postoperatively ($P < 0.001$). Moreover, preoperative macular hole sensitivity had linear relationship with BCVA at 4 months postoperatively ($r = 0.583$, $P < 0.001$; multiple stepwise linear regression analysis, Fig. 3). It meant every 1 dB augment in preoperative MHS, postoperative BCVA at 4 months would increase 0.0368 LogMAR units.

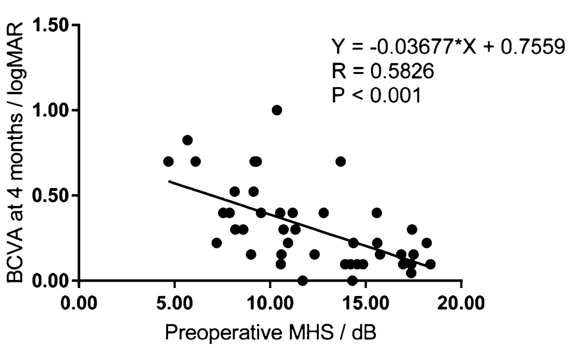

Fig. 3 Correlation of preoperative MHS with postoperative BCVA at 4 months. Linear regression analysis showed that visual prognosis at 4 months was related to preoperative MHS ($r = 0.5826$, $P < 0.001$) (Mann–Whitney U tests. BCVA: best-corrected visual acuity; MHS: macular hole sensitivity)

Discussion

As BCVA reflects basic visual function for fixation point [15], and fixation point may change by pathological changes in IMH [16], exploration predictors for visual prognosis are essential not merely for presurgical evaluation but functional recovery prediction after surgery by doctors. Microperimetry had been applied in many ophthalmic disorders [17–20], especially in macular disease like macular hole [21–23]. It could provide retinal sensitivity and fixation for retinal function assessment, and it could give detailed and precise information for function change before and after surgery. In previous studies, basic detection range for mean macular sensitivity (MMS) was from 8 degrees [24] to 12 degrees [7, 14] owing to different types of equipment, and 1 degree converts to 250 µm in length according to fundus structure. Thus, it was certain that the range was much larger than the area actually damaged by IMH, and, undoubtedly, relatively normal retina was included and caused overestimation. Scholars consequently narrowed the detection range to 2 degrees, which equals 500 µm, aiming to exclude the confounders, and the mean value of retinal sensitivity in 2 degrees was called central macular sensitivity (CMS) or fovea sensitivity (FS). Nonetheless, an unaltered range couldn't match diverse MD. For example, MD ranged from 148 to 726 µm in a study by Ooto et al. [25], 274 µm to 711 µm in Bonnabel's [14] study, and preoperative IS/OS defect diameter ranged 130 µm to 3000 µm in Chen's study [8]. Theoretically, as 2 degrees equals 500 µm by anatomical structure, relatively normal retina would still be included in smaller macular hole and partial dysfunctional retina would be excluded in larger macular hole. In current study, center of MP-3 pattern was moved to the center of macular hole, and then stimulus spots inside and 0.5 degrees outside macular hole margin were collected and the mean value of these spots was calculated and named as macular hole sensitivity (MHS). The reason for the range determination was that retinal function reflected by BCVA was moved gradually from macular hole margin to macular fovea after successful macular hole surgery [8, 16, 26, 27], the morphological structure of macular hole and image resolution of MP-3 were also considered. To proof the accuracy of MHS, correlations of MHS with MD were explored and we found MHS was the most relevant parameter with MD than MMS and CMS. Previous studies hardly mentioned the correlations between preoperative microperimetric results with MD, Sun et al. found preoperative MMS had a weak association with macular hole diameters [7]. The most correlation between MHS and MD showed the accordance between them and testify the accuracy of MHS.

MHS was more sensitive to reflect function recovery before and after macular hole surgery. We found significant improvement in BCVA, MMS, CMS, and MHS at 1 month and 4 months postoperatively, but neither MMS nor CMS showed a significantly improvement from 1 month to 4 months postoperatively while both BCVA and MHS did. The results suggested that recovery in MHS was more sensitive than MMS and CMS, and MHS had closer relationships with BCVA. Our results are partly similar to other research in the respect of improvement during the follow-up [7, 12, 14, 24]. However, discrepancies among BCVA, MMS, CMS, and MHS appeared. Chen et al. found CMS had a closer relationship with photoreceptor restoration [8], for CMS reflected the function over the area of macular hole. As previously mentioned, CMS reflects mean value of retinal sensitivity in 2 degrees, which couldn't match diverse size of macular hole. On the contrary, MHS showed reasonably significant correlations between MD, and MHS should be a more appropriate and sensitive parameter to evaluate the function improvement over the area of macular hole.

Previous researches reported MD and preoperative BCVA was correlated with postoperative BCVA [28, 29], which coincide with our study. Specialists also investigated probable predictors for visual prognosis. MD [29], preoperative IS/OS defect diameter or area [8], BCVA, mean macular sensitivity [14] were all considered as the predict factors for visual prognosis. In the current study, MD, preoperative BCVA, MMS, CMS, and MHS were all showed significant correlations with postoperative BCVA at 4 months postoperatively. At the same time, we found preoperative MHS has linear relationship with postoperative BCVA, which means preoperative MHS might be a probable predictor for visual prognosis. Sun et al. [7] found preoperative mean macular sensitivity and fixation percent in 2 degrees could predict visual prognosis, but the detective range in their study was 12 degrees, which was much larger than area of dysfunction retina caused by macular hole. Previous studies showed preoperative IS/OS defect diameter might be a predictor or indicator for visual prognosis [8, 28]. We also calculated the relationship between preoperative IS/OS defect area with postoperative BCVA at 4 month, while no linear correlations showed. However, five patients showed preserve IS/OS line at 4 months after surgery, and their MMS ($P = 0.023$) and MHS ($P = 0.021$) were significant better than patients whose IS/OS line were still inconsecutive. In Bonnabel's study [14], they found patients with a postoperative preserved IS/OS line had better preoperative MMS and CMS and lower preoperative MH size, which resembles the current study. However, CMS and MH size showed no differences between two groups. Discordance in facilities and measuring method for IS/OS defect diameter and Microperimetry might differ the result. The relationship between IS/OS defect diameter and macular sensitivity needs to investigate.

It is generally acknowledged that cataract formation and nuclear sclerosis would influence postoperative BCVA after macular hole surgery. In our study, we found no distinction between patients who underwent phacoemulsification and intraocular lens implantation and patients who didn't. It means cataract formation might not influence the improvement of BCVA and Microperimeter-3 results. All patients' inner limiting membrane was peeled off without any staining, so as to avoid the negative influence caused by toxicity of stains, which reported by previous literatures [9, 30].

Fixation is another critical functional parameter in Microperimeter-3. In previous study, patients in IMH showed paracentral fixation, which is always at the edge of macular hole, and a part of them showed central fixation after surgery [16, 26]. In our study, all patients showed paracentral fixation preoperatively, and 27 patients moved back to the fovea 4 months after surgery. However, no relationships were shown between fixation recovery and MHS, BCVA, or MD before and after surgery.

The limitation in our study is relatively short follow-ups and lack of fixation in MP-3. However, this study showed macular hole sensitivity, which was confirmed by the size of macular hole, could be a critical functional parameter to assess function damages caused by macular hole and function recovery in macular hole area after success surgery. A comprehensive assessment of fixation, parameters of macular hole (basal diameter, macular hole index, etc.), and vitreoretinal traction to visual prognosis need further study.

In conclusion, Microperimeter-3 is a useful equipment to evaluate retinal function in idiopathic macular hole. Compared with retinal sensitivity in 8 degrees and 2 degrees, macular hole sensitivity could evaluate retina function in macular hole area more precisely, sensitively, and objectively. Correlations between preoperative macular hole sensitivity and MD showed accuracy and sensitibility of macular hole sensitivity. Preoperative macular hole sensitivity might be an ideal, reliable, and sensitive predictor factor for visual prognosis after successful surgery.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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