EJO
ISSN 1120-6721

Eur J Ophthalmol 2017; 27 (6): 781-785
DOI: 10.5301/ejo.5000953

ORIGINAL RESEARCH ARTICLE

Open Access

Correlation between postoperative area of high autofluorescence in macula and visual acuity after macular hole closure

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ABSTRACT

Purpose: To determine the correlation between the preoperative basal diameter of macular hole, the postoperative area of high autofluorescence (AF) in macula, and visual acuity in full-thickness macular hole.

Methods: Forty-nine patients with full-thickness macular hole who underwent vitrectomy and C_3F_8 filling were reviewed. The preoperative diameter of macular hole, the 6 months postoperative area of high AF in macula if it existed, the length of inner segment/outer segment (IS/OS) defect, and visual acuity were obtained. The correlation between them was determined.

Results: At postoperative 6 months, the rate of high AF in macula was 63.3%. There were statistical differences between with and without high AF groups in postoperative best-corrected visual acuity (BCVA) (t = -2.751, p = 0.008), preoperative basal diameter of macular hole (t = -4.946, p = 0.00001), and postoperative length of IS/OS defect (t = -8.351, p<0.00001). Simple linear regression analysis showed high positive correlations between preoperative basal diameter of macular hole and area of high AF (p<0.00001, r = 0.893), postoperative length of IS/OS defect and area of high fundus AF (FAF) (p<0.00001, r = 0.779), and negative correlations between area of high AF and postoperative BCVA (p = 0.037, r = 0.375). There was low correlation between diameter of macular hole and postoperative BCVA (p = 0.112).

Conclusions: The preoperative basal diameter of macular hole and postoperative length of IS/OS defect decides the postoperative area of high AF in macula to some degree, and the postoperative area of high AF in macula can be an evaluating indicator for poor macular function recovery.

Keywords: Autofluorescence, Macular hole, Visual acuity

Introduction

A macular hole is an anatomic opening in the retina that develops at the fovea. It results in a defect from the inner limiting membrane to the photoreceptor layer. If full-thickness macular hole is untreated, the prognosis is poor, because spontaneous closure is rare (1). Pars plana vitrectomy has been used for more than a decade to treat full-thickness macular hole. With improvements in surgical methods, the closure rate of macular hole has increased, but some patients still cannot obtain functional success after surgery. There is a great deal of literature regarding predictors of visual results following macular hole surgery (2-5). Advanced stage of macular hole and longer duration of symptoms predict a worse visual outcome. As optical coherence tomography (OCT) can produce high-resolution retinal images, OCT has become an essential tool for assessment of macular hole. Some parameters obtained from OCT have been studied. Some parameters were associated with better postoperative visual acuity, such as a smaller minimum diameter, shorter preoperative inner segment/outer segment (IS/OS) defect length, smaller preoperative central subfield retinal thickness, the presence of an intact ellipsoid layer in the early postoperative period, the integrity of the external limiting membrane layer, larger HFF (the quotient of the summation of the left and right arm lengths divided by the basal hole diameter), MHI (the ratio of the hole height to the basal hole diameter) value ≥0.5, and THI (the ratio of the hole height to the minimum diameter) value >1.41. It is important to counsel patients appropriately. Therefore, prediction and assessment of visual outcome is increasingly important. We explored a convenient technique to evaluate macular function recovery after macular hole closure.

Natural fluorescence in the eye may change if diseases affect the retina. Imaging methods based on confocal scanning

Accepted: February 25, 2017
Published online: March 21, 2017

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laser ophthalmoscopy (cSLO) can detect this fundus autofluorescence (FAF) by illuminating the retina using an excitation wavelength light. Confocal scanning laser ophthalmoscopy can provide high-resolution fundus images of different wavelengths, and it is helpful to observe the different layers of the retina (6). Fundus autofluorescence (AF) imaging could assist the diagnosis or monitoring of retinal conditions. Following successful macular hole surgery, FAF in macula decreased markedly. The amount of remaining FAF is related to macular sensitivity as measured by microperimetry after successful macular hole surgery (7). There is no study explaining the correlation between FAF and visual acuity.

We observed postvitrectomy FAF changes and the correlation between FAF, basal diameter of macular hole, length of IS/OS defect, and visual acuity in patients with full-thickness macular hole. We emphasized blue light FAF. This study could provide a basis for clinical prognosis evaluation.

Methods

Patients diagnosed with idiopathic full-thickness macular hole in the Department of Ophthalmology in Second Hospital of Hebei Medical University were observed. All included patients were operated with pars plana vitrectomy, internal limiting membrane peeling, gas filling in vitreous, and strict face-down position. The study was conducted in accordance with the recommendations of the Declaration of Helsinki. A signed informed consent was obtained from all patients before surgery and examinations following detailed explanation of the purpose of the study and the procedures to be used.

The inclusion criteria were as follows: idiopathic full-thickness macular hole; operated with pars plana vitrectomy, internal limiting membrane peeling, gas filling in vitreous, and strict face-down position; optical coherence tomography confirmed macular hole closure in postoperative 2 weeks; no other fundus operation or treatments, such as reoperation or laser coagulation; and follow-up time longer than 6 months.

The exclusion criteria were as follows: other ocular diseases, such as age-related macular degeneration, retinal detachment, macular edema, or glaucoma; systemic diseases that could affect the eyes, such as diabetes or autoimmune disease; refracting media and images not clear during the follow-up period; macular hole caused by trauma and high myopia.

A 23-G vitrectomy was performed under peribulbar anesthesia. The surgical technique consisted of a standard 3-port pars plana vitrectomy with removal of the posterior cortical vitreous and creation of posterior hyaloidal detachment when necessary. Peeling of internal limiting membrane (ILM) was performed in all included patients. The diameter of ILM peeling was determined by the size of the macular hole. Following fluid-air exchange, the vitreous cavity was filled with gas. Patients were instructed to maintain strict face-down position for 7 days.

Outcomes recorded included demographics, basal diameter of macular hole, preoperative best-corrected visual acuity (BCVA), postoperative area of AF in macula, postoperative BCVA, and postoperative length of IS/OS defect at 6 months. Spectral-domain OCT was used to obtain tomographic images of the macular area. The preoperative basal diameter of the

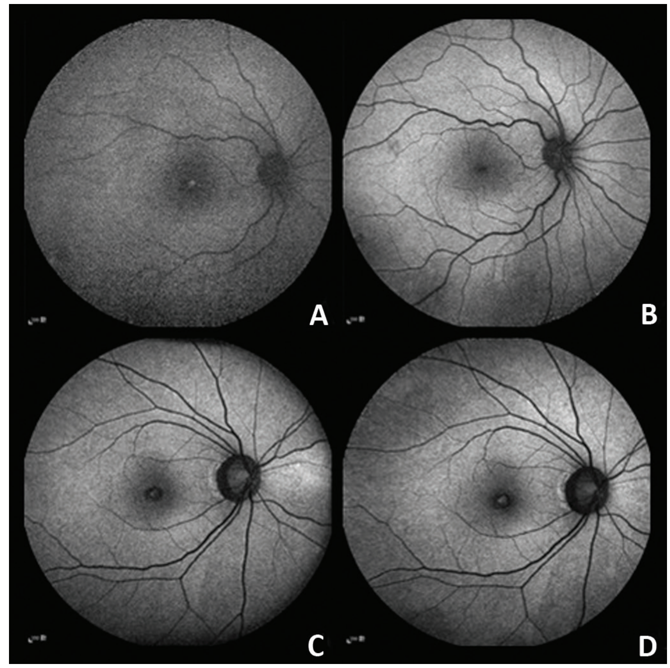

Fig. 1 - Preoperative and postoperative fundus autofluorescence (FAF) images of 2 patients with full-thickness macular hole. (**A**) A 67-year-old woman with full-thickness macular hole. The macular hole diameter is 412 µm. Fundus autofluorescence (AF) shows hyperautofluorescence in the macula before surgery. (**B**) Fundus AF 6 months postoperation shows that hyperautofluorescence in the macula is absent. (**C**) A 58-year-old man with full-thickness macular hole. The macular hole diameter is 836 µm. Fundus AF shows hyperautofluorescence in the macula with distinct boundary before surgery. (**D**) Fundus AF 6 months postoperation shows that hyperautofluorescence in the macula is still present, although the macular hole is closed, confirmed by optical coherence tomography.

macular hole was measured at the level of the retinal pigment epithelium. Mean values of the distance in the vertical and horizontal images at the fovea were taken. The area of high AF in macula was circled manually and the ratio to optic disc area calculated. The FAF images of 2 patients are displayed in Figure 1.

Statistical analysis was performed using SPSS software. Best-corrected visual acuity was converted to a logarithm of the minimal angle of resolution (logMAR) for statistical analysis. *T* test was used to compare statistics in different groups. Simple linear regression analysis were used to evaluate relationships between factors. A p value of 0.05 was considered significant. Values are shown as mean and standard deviation (SD).

Results

Forty-nine patients were reviewed. The demographic and clinical features of included patients are listed in Table I.

At 6 months postoperatively, there were 31 patients with abnormal FAF in the macula. The rate of high FAF in the macula was 63.3%. The mean area of high FAF in the macula was 0.16 DA (SD 0.05 DA). The mean basal diameter of the macular hole in the high FAF group and the normal FAF group were 790.32 µm (SD 185.38) and 533.5 µm

TABLE I - Preoperative demographic and clinical features

	Values
No. of eyes (patients)	49
Age, y, mean ± SD	64.7 ± 5.6
Female/male	25/24
Eye, right/left	30/19
Preoperative best-corrected visual acuity, logMAR, mean ± SD	1.1 ± 0.2
Preoperative basal diameter of macular hole, µm, mean ± SD	695.9 ± 213.8

(SD 155.66), respectively. The mean postoperative length of IS/OS defect in the normal FAF group and the high FAF group were 337.06 µm (SD 23.79) and 635.94 µm (SD 23.48), respectively. The mean logMAR BCVA in the high FAF group and the normal FAF group was 0.76 (SD 0.03) and 0.6 (SD 0.04). There were statistically significant differences between the 2 groups in preoperative basal diameter of the macular hole (t = -4.946, p = 0.00001) (Fig. 2A), postoperative BCVA (t = -2.751, p = 0.008) (Fig. 2B), and postoperative length of the IS/OS defect (t = -8.351, p<0.00001) (Fig. 2C). Simple linear regression analysis showed high positive correlations between preoperative basal diameter of macular hole and area of high FAF (p<0.00001, r = 0.893) (Fig. 3A), negative correlation between area of high FAF and postoperative BCVA (p = 0.037, r = 0.375) (Fig. 3B), positive correlation between postoperative length of IS/OS defect and area of high FAF (p<0.00001, r = 0.779) (Fig. 3C). There was low correlation between basal diameter of macular hole and postoperative BCVA (p = 0.112).

Discussion

Full-thickness macular hole is a full-thickness defect of retinal tissue involving the anatomical fovea. Vitrectomy is a surgical technique involving removal of the vitreous, relieving traction caused by the vitreous or epiretinal membranes to the macula, inducing glial tissue to bridge and close the hole (8). A review in 2015 showed that vitrectomy was effective in improving visual acuity, resulting in moderate visual gain, and in achieving hole closure in people with macular hole (1). Although the postoperative closure rate of macular hole was greatly improved, the recovery of macular function was not satisfactory (9, 10). The factors influencing and predicting macular function in postoperative patients are controversial. There is a great deal of literature regarding the predictors of visual results following macular hole surgery (2-5). Advanced stage of macular hole and longer duration of symptoms predict a worse visual outcome. Some parameters obtained from OCT were studied. Some parameters were associated with better postoperative visual acuity, such as a smaller minimum diameter, shorter preoperative IS/OS defect length, smaller preoperative central subfield retinal thickness, the presence of an intact ellipsoid layer in the early postoperative period, the integrity of the external limiting membrane layer, larger HFF, MHI value ≥0.5, and THI value >1.41. It is important to

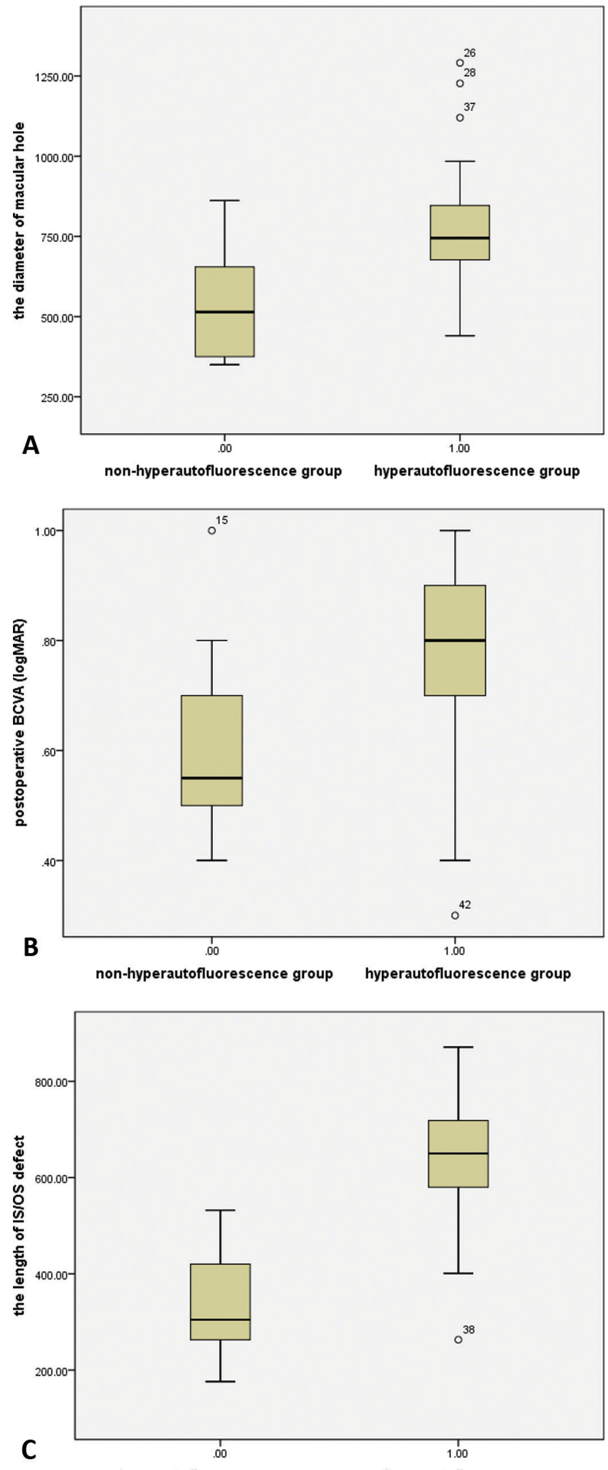

Fig. 2 - Box plots show comparisons of diameter of macular hole, postoperative best-corrected visual acuity (BCVA) and postoperative length of IS/OS defect between the non-hyperautofluorescence group and the hyperautofluorescence group. (**A**) Box plots show the diameter of the macular hole in the non-hyperautofluorescence group and the hyperautofluorescence group. (**B**) Box plots show 6-month postoperative BCVA in the nonhyperautofluorescence group and the hyperautofluorescence group. (**C**) Box plots show 6-month postoperative length of inner segment/outer segment defect in the non-hyperautofluorescence group and the hyperautofluorescence group.

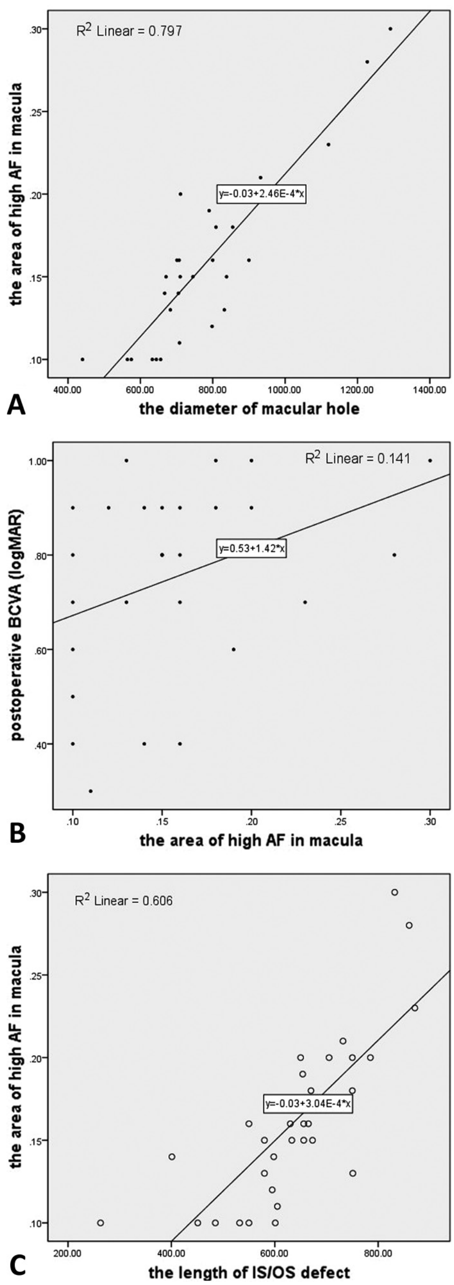

Fig. 3 - Correlations between the diameter of the macular hole and the area of high autofluorescence (AF) in the macula, the area of high AF in the macula and 6-month postoperative best-corrected visual acuity (BCVA),and the area of high AF in the macula and postoperative length of inner segment/outer segment (IS/OS) defect. (**A**) Correlation between the diameter of the macular hole and the area of high AF in the macula determined by simple linear regression analysis. There is significant correlation between the area of high AF in the macula and the diameter of macular hole (F = 114.18, SPRC = 0.893, p<0.00001). (**B**) Correlation between the area of high AF in the macula and 6-month postoperative BCVA determined by simple linear regression analysis. There is significant correlation between the area of high AF in the macula and 6-month postoperative BCVA (F = 4.755, SPRC = 0.375, p = 0.037). (**C**) Correlation between the area of high AF in the macula and postoperative length of IS/OS defect determined by simple linear regression analysis. There is significant correlation between the area of high AF in the macula and postoperative length of IS/OS defect (F = 44.632, SPRC = 0.779, p<0.00001).

counsel patients appropriately. Precise prediction and assessment of visual outcome is increasingly important.

Fundus AF imaged using a cSLO derives from the lipofuscin-laden retinal pigment epithelium (RPE). Normally, AF of the RPE underlying the fovea is decreased because the overlying macular yellow pigments absorb the exciting light. If the overlying absorptive pigments disappear, a high-AF window defect is visible. Thus, this change in visible AF can be used as an indication of a full-thickness macular hole or of failure of surgical repair. Studies showed that after successful surgical repair of macular hole, high AF would be absent, suggesting that RPE was again covered by retinal and/or glial tissue (11, 12). Our clinical observation found that there were some patients with high fluorescence after successful macular hole closure confirmed by OCT. A study showed that the amount of remaining FAF is related to macular sensitivity as measured by microperimetry after successful surgery (7). There is no study explaining the correlation between FAF and visual acuity.

At postoperative 6 months, 63.3% of patients had abnormal FAF in macula. Postoperative BCVA in the normal AF group was better than that in the high AF group. The postoperative presence of high AF in the macula indicated poor macular functional recovery. In addition, the basal diameter of the macular hole and the postoperative length of the IS/OS defect in the high AF group was larger than that in the normal AF group. Thus basal diameter of macular hole and postoperative length of IS/OS defect correlates with postoperative high AF in macula to some degree. Our investigation also explored whether AF in macula can predict and assess the recovery of macular function.

Statistical analysis showed highly positive correlations between preoperative basal diameter of macular hole and area of high FAF. Lipofuscin and fluorescent substance complex are the main materials that induce AF. The RPE constitutes a polygonal monolayer between the neurosensory retina and the vascular choroid. Lipofuscin is the final metabolite after RPE cells swallow the outer segment of photoreceptor. Autofluorescence in the RPE is dependent upon outer segment renewal and potentially is affected by a balance between accumulation and clearance (6). If the neurosensory layer covering the RPE is defective, high AF will appear in the corresponding defective region (13). A study by Itoh et al (14) showed that normal retina may be replaced by glial cells postoperatively. Although macular holes are closed with a neurosensory retina, reduced uptake of macular carotenoids in RPE results in lower macular pigments, such as lutein and zeaxanthin. Lutein and zeaxanthin are closely arranged on the axon of cone cells in normal macula. Lutein and zeaxanthin can shelter AF from RPE (15). Postoperative IS/OS defects affect the distribution of lutein in the macular area. This may explain the highly positive correlations between the postoperative length of IS/OS defect and area of high FAF.

Our study found a highly negative correlation between areas of high AF in macula and BCVA. A study by Villate et al (16) showed that outer retinal features appear to be more important in determining postoperative visual function. In addition, a study by Sano et al (17) demonstrated that visual outcomes were significantly better in eyes with a continuous IS/OS line than in those with a disrupted IS/OS line. The ability of the photoreceptors to capture and stabilize lutein and zeaxanthin following successful macular hole surgery would indicate a good degree of physiologic recovery and may reflect successful recovery of function (7). All the above studies were consistent with the highly negative correlation between area of high AF in macula and BCVA that we found. Fundus AF can provide a view of the entire macula instead of cross-sections from OCT. Moreover, it can provide more information about macular function than the simple macular structure from OCT. Fundus AF is a convenient means to assess visual outcome after macular hole surgery.

In this study, we did not find a statistical correlation between preoperative diameter of macular hole and postoperative BCVA. A study by Haritoglou et al (18) demonstrated that a negative correlation was seen between final visual acuity and preoperative base diameter of the hole. A study by Ullrich et al (19) showed that preoperative measurement of macular hole size with OCT can provide a prognostic factor for postoperative visual outcome, especially base and minimum diameters. However, in the study by Yip et al (20), OCT measurement of apical and not the basal diameter of macular hole correlated with postoperative visual acuity. Determining whether preoperative basal diameter of a macular hole is a predictive factor for postoperative BCVA may need a larger sample and multicenter study or meta-analysis. Based on our results, the postoperative area of high AF in macula was a more sensitive indicator for visual acuity outcome.

In conclusion, the preoperative basal diameter of the macular hole and postoperative length of IS/OS defect decides the postoperative area of high AF in macula to some degree, and the postoperative area of high AF in the macula can be an evaluating indicator of macular function recovery.

Acknowledgments

Qingli Shang conducted the conception and design of the study, acquisition and interpretation of data, and final approval of the version to be published. Peng Zhang conducted acquisition and interpretation of data, analysis and interpretation of data, writing and revising the article, and final approval of the version to be published. Jingxue Ma, Yuhua Hao, and Cunxi Ye conducted acquisition of data and final approval of the version to be published.

Disclosures

Financial support: No financial support was received for this submission.
Conflict of interest: None of the authors has conflict of interest with this submission.

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