The macular microstructure repair and predictive factors of surgical outcomes after vitrectomy for idiopathic macular hole

Jing-Ling Zou, Jun Zeng

Department of Ophthalmology, the Second Xiangya Hospital, Central South University, Changsha 410011, Hunan Province, China

Correspondence to: Jun Zeng. Department of Ophthalmology, the Second Xiangya Hospital, Central South University, Changsha 410011, Hunan Province, China. zengjun001@csu.edu.cn

Received: 2019-01-27        Accepted: 2019-03-07

Abstract
• To evaluate the macular microstructure repair and explore the factors related to those changes and visual improvement after vitrectomy for idiopathic macular hole (IMH). Totally 19 eyes of 18 IMH patients who underwent macular hole (MH) surgery were evaluated with best-corrected visual acuity (BCVA) and spectral-domain optical coherence tomography (SD-OCT) images. All 19 eyes closed at 6mo postoperatively. BCVA was observed gradually improved \((P<0.001)\), with subretinal fluid (SRF) gradually absorbed \((P=0.021)\) and the rate of external limiting membrane (ELM) defects gradually decreased \((P=0.011)\) with follow-up time. Poorer postoperative logMAR BCVA correlated with larger MH minimum diameter \((P<0.001)\), larger MH basal diameter \((P=0.008)\), longer symptom duration \((P=0.002)\) and poorer preoperative logMAR BCVA \((P=0.010)\). More improvement in BCVA correlated only with poorer preoperative logMAR BCVA \((P=0.002)\). The earlier reconstruction of ELM was associated with smaller MH basal diameter \((P=0.022)\) and shorter symptom duration \((P=0.008)\). In conclusion, smaller basal diameter of MH and shorter symptom duration were key factors in earlier reconstruction of ELM.

• KEYWORDS: idiopathic macular hole; macular microstructure; predictive factors

DOI:10.18240/ijo.2019.05.25

INTRODUCTION
After Kelly and Wendel[1] first reported successful vitreous surgery for the macular hole (MH), Park et al[2] reported internal limiting membrane (ILM) peeling technology and then Michalewska et al[3] proposed inverted ILM flap technique. Liggett et al[4] first used autologous serum as an adjuvant to increase the MH closure rate, and serum was deeded that contains numerous growth factors, which can induce fibrocellular migration, adhesion, and proliferation[5]. Gas, usually C₃F₈ or SF₆, as tamponade materials were widely used in MH surgery. Recently, several studies found that air filling is equivalent to long-effect air tamponade in MH surgery[6-8]. With the rapid development of MH surgery technique, the closure rate of MH surgery already reached more than 90%[9-10]. Since spectral-domain optical coherence tomography (SD-OCT) has been used to observe the macular microstructure, the fine changes in the process of MH reconstruction are being detected. Grewal et al[11] found the size of foveal lucency correlated with visual recovery and preoperative basal hole diameter was related to foveal lucency. Liu et al[12] reported that macular hole closure index (MHCI) was a new predictive method for anatomical outcomes after IMH surgery. Shpak et al[13] suggested preoperative central subfield retinal thickness could predict postoperative anatomical results of IMH. Kitao et al[14] have reported that the time until external limiting membrane (ELM) bridge and the glial cell disappearance were associated with postoperative best-corrected visual acuity (BCVA) at 3y, which indicates that ELM maybe a crucial early predictive factor to visual improvement. However, the predictive factors of visual improvement are still controversial and the relevant elements to the macular microstructure repair process are still unclear. The purpose of this study was to explore the macular microstructure changes after vitrectomy for idiopathic macular hole (IMH) and investigate the correlative predictive factors to visual improvement and macular microstructure repair for MH surgery.

SUBJECTS AND METHODS

Ethical Approval  This was a retrospective study. The study was approved by the Second Xiangya Hospital Ethics Committee and conducted in accordance with the Declaration of Helsinki. All patients were informed about the risks and benefits of the surgery, and written informed consent was obtained in accordance with the guidelines for the Second Xiangya Hospital of Central South University.
The medical records of 19 eyes of 18 patients with an IMH who underwent surgery in the Second Xiangya Hospital between October 2016 and April 2018 were reviewed. All patients included had been diagnosed with a stage 2, 3 or 4 IMH according to the Gass classification[15]. We excluded eyes with retinal detachment, glaucoma, diabetic retinopathy, high myopia, follow-up length less than 6mo postoperatively or any other secondary MHs. All patients had a standard ophthalmological examination before and 1wk, 1, 3, 6mo after surgery. Examinations included BCVA, binocular indirect ophthalmoscopy, slit-lamp bio-microscopy and SD-OCT. One surgeon (Zeng J) operated on all eyes under local anesthesia. Standard 23-gauge pars plana vitrectomy was performed for all MHs. Before surgery, two to three milliliters blood from patients of MH were collected in a syringe and kept it in a vertical and static position for more than 30min. Triamcinolone acetonide (TA) was used to clarify the vitreous gel. Eighteen of 19 patients of MH underwent phacoemulsification. After core vitrectomy, posterior vitreous detachment was performed. Indocyanine green (ICGI; 0.125%) was used for ILM staining. The ILM was peeled around vascular arch. Peeling cases then give gas-fluid exchange and intraocular lens implantation directly. For inverted ILM flap cases, the ILM around macular about one to two papillary diameter (PD) was inverted into MH so that it completely covered and filled the MHs. Next, serum was extracted gently from the post-static stratified blood and has been intravitreal injection about 0.05 mL. Gas-fluid change was given slightly to prevent the flapped ILM shifting. Intraocular lens implantation was performed. All the patients were instructed to remain face-down position for 3 to 5d postoperatively. SD-OCT was used to confirm whether the MH closed and detect the macular microstructure changes. The glial proliferation was defined as the presence of a foveal hyporreflective lesion on SD-OCT based on the previous reports of histopathologic studies of autopsy eyes and OCT images of surgically closed MHs[16-17].

For statistical analysis, logMAR BCVA and central retinal thickness (CRT) were analyzed using a one-way analysis of variance (ANOVA) when quantitative parameters were compared among baseline, postoperative 1wk, 1, 3 and 6mo. If the parameter was not normally distributed, the non-parametric Kruskal-Wallis one-way ANOVA on ranks was applied. Fisher’s exact test was performed to test the existent subretinal fluid (SRF), ELM defects, retinal never fiber layer (RNFL) defects, internal plexiform layer (IPL) defects and the closure of MH at postoperative 1wk, 1, 3 and 6mo. Correlations between preoperative parameters and postoperative visual acuity were analyzed with Spearman’s ranked correlation. Independent-samples t-test was used to analysis the influential factors between the continuous ELM and ELM defects. All analyses were conducted using SPSS (Version 19.0, USA), and P<0.05 was deemed to indicate statistical significance.

RESULTS

The retrospective study was comprised of 19 eyes of 18 patients. Totally 19 of 19 the MHs closed successfully at postoperative 6mo. The 19 cases consisted of 17 (89%) women and 2 (11%) men ranging in age from 49 to 74y with an average age of 64.0±5.4y. The operated eye was the right eye in 11 patients (58%) and left eye in 8 patients (42%). All patients were phakic eyes before surgery, and 18 (95%) of them underwent phacoemulsification and foldable lens implantation during surgery. Preoperative mean logMAR BCVA was 1.3±0.48. The MHs were classified as stage 2 in 8 eyes (42%), stage 3 in 9 eyes (47%) and stage 4 in 2 eyes (11%) preoperatively. The mean axial length was 23±0.65 mm (range, 22.06-24.61 mm). Mean preoperative minimum diameter of the holes was 430±169 μm (range, 177-780 μm). Mean preoperative basal diameter of the holes was 763±228 μm (range, 304-1165 μm). Symptom duration was 6.0±7.1mo (range, 0.5-24).

Changes in logMAR BCVA are shown in Table 1, which suggested that postoperative BCVA continuously increased over 6mo (P<0.001). Totally 19 operated eyes (100%) observed were anatomically closed detected by OCT at postoperative 1mo. It was observed that ELM reconstructed earlier compared to the reconstruction of the ellipsoid zone (EZ) and cone interdigitation zone (CIZ; Figure 1). At 1wk, 1, 3, 6mo postoperatively, ELM defects were seen in 18 eyes (95%), 15 eyes (79%), 13 eyes (68%), 9 eyes (47%), respectively (P=0.011). EZ defects, CIZ defects were observed in all the eyes during all the follow-up period. During this process, the ELM was concomitantly reconstructed with the length of EZ defects and CIZ defects shorten showed in Figure 1. The area of the RNFL defects were observed in 11 eyes (63%) at 1wk, 15 eyes (84%) at 1mo, 18 eyes (95%) at 3mo and 18 eyes (95%) at 6mo postoperatively. The IPL defects were observed earliest at 1mo with 2 eyes (11%), and then 6 eyes (32%) at 3mo, 7 eyes (37%) at 6mo postoperatively. Poorer postoperative logMAR BCVA correlated with larger MH minimum diameter (P<0.001), larger MH basal diameter (P=0.008), longer symptom duration (P=0.002) and poorer preoperative logMAR BCVA (P=0.010). More improvement in BCVA correlated only with poorer preoperative in logMAR BCVA (P=0.002). But improvement in BCVA has no correlation with symptom duration, MH minimum diameter and basal diameter. As for the change in age, it has no correlation with both postoperative logMAR BCVA and improvement in logMAR BCVA (Table 2).

In addition, it was found that cases with continued ELM at 6mo postoperatively had smaller MH basal diameter (P=0.022).
and shorten symptom duration ($P=0.008$). But there were not differences in age, MH minimum diameter, preoperative in logMAR BCVA, postoperative logMAR BCVA and change in logMAR BCVA (Table 3).

**DISCUSSION**

In this study, we aimed to investigated OCT-measured microstructure characteristics in fovea post MH surgery and relevant predictive factors to visual improvement and macular microstructure features.

SRF was a common appearance after successful MH surgery\textsuperscript{[18]}. But the exact effects of SRF on surgical outcomes of MH were still controversial. Zambarakji et al\textsuperscript{[19]} had reported that cases with SRF had bad effects on visual or IS/OS outcomes after successful MH surgery. On the contrary, Tranos et al\textsuperscript{[18]} observed that the presence of SRF was not related to worse outcomes. In our study, we found that postoperative SRF absorbed with the follow-up time. It should be noted that our study observed that the main SRF disappearance period was in the first 3mo after surgery. The closure of MHs was observed on OCT within postoperative 1wk in most successful cases. In present study, CRT was 200±74 μm at postoperative 1wk. Then it has a decreasing period and a gentle increase, and

---

**Table 1** Postoperative time-dependent changes in logMAR BCVA and foveal microstructure

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1wk</th>
<th>1mo</th>
<th>3mo</th>
<th>6mo</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>logMAR BCVA, (mean±SD)</td>
<td>0.96±0.34</td>
<td>0.81±0.26</td>
<td>0.65±0.25</td>
<td>0.54±0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRT, μm (mean±SD)</td>
<td>200±74</td>
<td>183±74</td>
<td>177±70</td>
<td>186±61</td>
<td>0.781</td>
</tr>
<tr>
<td>Presence of SRF</td>
<td>9 (47)</td>
<td>4 (21)</td>
<td>3 (16)</td>
<td>1 (5)</td>
<td>0.019</td>
</tr>
<tr>
<td>ELM defects</td>
<td>18 (95)</td>
<td>15 (79)</td>
<td>13 (68)</td>
<td>9 (47)</td>
<td>0.010</td>
</tr>
<tr>
<td>EZ defects</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>1.0</td>
</tr>
<tr>
<td>Glial proliferation</td>
<td>16 (84)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>1.0</td>
</tr>
<tr>
<td>Inner retinal defects</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RNF defects</td>
<td>11 (63)</td>
<td>15 (84)</td>
<td>18 (95)</td>
<td>19 (100)</td>
<td>0.002</td>
</tr>
<tr>
<td>IPL defects</td>
<td>0</td>
<td>2 (11)</td>
<td>6 (32)</td>
<td>7 (37)</td>
<td>0.006</td>
</tr>
<tr>
<td>Closure</td>
<td>17 (89)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>19 (100)</td>
<td>0.240</td>
</tr>
</tbody>
</table>

logMAR BCVA: Logarithm of the minimum angle of resolution best-corrected visual acuity; CRT: Central retinal thickness; SRF: Subretinal fluid; ELM: External limiting membrane; EZ: Ellipsoid zone; CIZ: Cone interdigitation zone; RNFL: Retinal never fiber layer; IPL: Internal plexiform layer.

---

**Table 2** Correlation between preoperative parameters and logMAR BCVA

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean±SD (range)</th>
<th>Postoperative logMAR BCVA at 6mo Correlation</th>
<th>$P$</th>
<th>Change in logMAR BCVA Correlation</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>MH size (minimum diameter)</td>
<td>430±169 (177-780)</td>
<td>0.721</td>
<td>&lt;0.001*</td>
<td>0.104</td>
<td>0.672</td>
</tr>
<tr>
<td>MH size (basal diameter)</td>
<td>763±228 (304-1165)</td>
<td>0.590</td>
<td>0.008a</td>
<td>0.144</td>
<td>0.556</td>
</tr>
<tr>
<td>Preoperative logMAR BCVA</td>
<td>1.3±0.48 (0.7-2.4)</td>
<td>0.574</td>
<td>0.010a</td>
<td>0.655</td>
<td>0.002*</td>
</tr>
<tr>
<td>Symptom duration, mo</td>
<td>6.0±7.1 (0.5-24)</td>
<td>0.655</td>
<td>0.002a</td>
<td>-0.207</td>
<td>0.396</td>
</tr>
<tr>
<td>Age, y</td>
<td>64.0±5.4 (49-74)</td>
<td>-0.082</td>
<td>0.739</td>
<td>-0.098</td>
<td>0.690</td>
</tr>
</tbody>
</table>

logMAR BCVA: Logarithm of the minimum angle of resolution best-corrected visual acuity; MH: Macular hole. *Statistically significant correlation ($P<0.05$); aIndependent-samples $t$-test.

---

**Table 3** BCVA (logMAR) and ELM reconstruction at 6mo after surgery

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes, n (%)</td>
<td>10 (53)</td>
</tr>
<tr>
<td>Postoperative logMAR BCVA at 6mo</td>
<td>0.45±1.86</td>
</tr>
<tr>
<td>Preoperative logMAR BCVA</td>
<td>1.01±0.35</td>
</tr>
<tr>
<td>Mean difference in logMAR BCVA</td>
<td>0.57±0.31</td>
</tr>
<tr>
<td>MH size (minimum diameter)</td>
<td>383.19±125.89</td>
</tr>
<tr>
<td>MH size (basal diameter)</td>
<td>650.80±216.37</td>
</tr>
<tr>
<td>Symptom duration, mo</td>
<td>2.05±1.64</td>
</tr>
<tr>
<td>Age, y</td>
<td>62.60±6.19</td>
</tr>
</tbody>
</table>

logMAR BCVA: Logarithm of the minimum angle of resolution best-corrected visual acuity; ELM: External limiting membrane; MH: Macular hole; *Statistically significant correlation ($P<0.05$); aIndependent-samples $t$-test.

---

And shorten symptom duration ($P=0.008$). But there were not differences in age, MH minimum diameter, preoperative in logMAR BCVA, postoperative logMAR BCVA and change in logMAR BCVA (Table 3). **DISCUSSION**

In this study, we aimed to investigated OCT-measured microstructure characteristics in fovea post MH surgery and relevant predictive factors to visual improvement and macular microstructure features.

SRF was a common appearance after successful MH surgery\textsuperscript{[18]}. But the exact effects of SRF on surgical outcomes of MH were still controversial. Zambarakji et al\textsuperscript{[19]} had reported that cases with SRF had bad effects on visual or IS/OS outcomes after successful MH surgery. On the contrary, Tranos et al\textsuperscript{[18]} observed that the presence of SRF was not related to worse outcomes. In our study, we found that postoperative SRF absorbed with the follow-up time. It should be noted that our study observed that the main SRF disappearance period was in the first 3mo after surgery. The closure of MHs was observed on OCT within postoperative 1wk in most successful cases. In present study, CRT was 200±74 μm at postoperative 1wk. Then it has a decreasing period and a gentle increase, and
develop into 186±61 μm at postoperative 6mo. Takamura et al\textsuperscript{[20]} suggested that postoperative CRT was associated with visual outcomes. But it is difficult to ensure the precise measurement to CRT considering all those values were measured manually. The reconstruction of ELM, EZ and CIZ represents the integrity of the photoreceptor layer. In our study, ELM reconstruction completed earliest compared to EZ and CIZ and the reconstruction of EZ and CIZ have not completed at postoperative 6mo but with the length of EZ defects and CIZ defects shortened (Figure 1). It suggested that macular microstructure repair was step by step and mostly more than 6mo. After MH surgery, there were some arcuate striae observed in the field of ILM peeling, which was named dissociated optic nerve fiber layer (DONFL)\textsuperscript{[21]}. The DONFL appearance was found correlate with RNFL defects and IPL defects, which maybe caused by the irreversible damage to the part of the Müller cell during the process of peeling ILM\textsuperscript{[21]}. It was deemed that macular microstructure repair was step by step and mostly more than 6mo. After MH surgery, there were some arcuate striae observed in the field of ILM peeling, which was named dissociated optic nerve fiber layer (DONFL)\textsuperscript{[21]}. The DONFL appearance was found correlate with RNFL defects and IPL defects, which maybe caused by the irreversible damage to the part of the Müller cell during the process of peeling ILM\textsuperscript{[21]}. It was deemed that macular microstructure repair was step by step and mostly more than 6mo. After MH surgery, there were some arcuate striae observed in the field of ILM peeling, which was named dissociated optic nerve fiber layer (DONFL)\textsuperscript{[21]}. The DONFL appearance was found correlate with RNFL defects and IPL defects, which maybe caused by the irreversible damage to the part of the Müller cell during the process of peeling ILM\textsuperscript{[21]}. It was deemed that macular microstructure repair was step by step and mostly more than 6mo.

As for the study of the predictive factors, there were still controversial. Goker et al\textsuperscript{[25]} reported that duration of hole symptom, Gass stage and preoperative BCV A did not find to affect visual outcome. Kim et al\textsuperscript{[26]} found that choroidal thickness and MH basal diameter were significant predictors of visual improvement, but there were not significant differences between final visual acuity and preoperative visual acuity, hole size, sex or age. Table 2 showed correlations between preoperative parameters and logMAR BCV A. In present study, it suggested that postoperative logMAR BCV A at 6mo had significantly positive correlation with MH minimum diameter ($P<0.001$) and symptom duration ($P=0.002$). Also, there were positive correlations between postoperative logMAR BCV A and preoperative logMAR BCV A ($P=0.01$), postoperative logMAR BCV A and basal diameter ($P=0.008$). Contrary to Kim et al\textsuperscript{[26]} study, there was a positive correlation between postoperative logMAR BCV A and MH minimum diameter. In former studies, Kazmierczak et al\textsuperscript{[27]} reported that IS/OS junction defects correlated with the diameter of the MH and the presence of ELM defects were the reason of inferior BCV A. In our study, we found that cases with continued ELM at 6mo postoperatively had smaller MH basal diameter ($P=0.022$) and shorten symptom duration ($P=0.008$; Table 3, Figure 2). As we all known, the integrity of outer retina is key to visual outcomes. ELM restored earliest than IS/OS, that means that only after ELM completed its reconstruction, can IS/OS become continuous. As for MH basal diameter, it is the base of the disruption of hole, also the beginning of outer retina
restoration. Kitao et al\(^{14}\) had reported that there was significant correlation between the time until ELM reconstruction and postoperative BCV A at 3y. Thus, it suggested that basal diameter of MH maybe a crucial factor to final visual acuity. Apart from that, it was also found that cases with continued ELM at 6mo postoperatively had shorten symptom duration. It indicated that symptom duration played an important role in visual outcome. Anatomically, shorten symptom duration was benefit to the early restoration of macular microstructure, which also contributed to visual improvement.

One of the limitations of the present study was small number of patients. Further studies are needed to confirm our results. In addition, we only applied one examination to detect the repair of MHs. It needs more examinations including microperimetry, electroretinogram or OCT angiography to has a more comprehensive exploration about the repair process and predictive factors of MHs.

In conclusion, ELM reconstruction completed earliest compared to EZ and CIZ in the process of macular microstructure repair after successful MH surgery. Preoperative BCVA, symptom duration, minimum diameter and basal diameter of MH were important predictive factors for visual improvement. The MH basal diameter and symptom duration were key factors in early reconstruction of ELM.

ACKNOWLEDGEMENTS

Conflicts of Interest: Zou JL, None; Zeng J, None.

REFERENCES


