Influence of Foveal Avascular Zone on Postoperative Visual Acuity in Macular Hole Surgery

Hongbang An
Weifang Medical University

Shu’na Wang
Weifang Medical University

Wenxuan Yu
Weifang Medical University

Meng Gao
Weifang Medical University

Lihua Li
Weifang Medical University

Fengqin Hao
Weifang Medical University

Bing Liang
Weifang Medical University

Cao Yongliang (caoyongliang1965@163.com)
Weifang Medical University

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Abstract

**Background:** To investigate the correlation between the pre- and post-operative foveal avascular zone (FAZ) area and visual acuity in patients with idiopathic macular hole (IMH).

**Methods:** Optical coherence tomography angiography (OCTA) was used to measure the values of the pre- and post-operative FAZ in IMH patients, and all patients were followed up for at least 3 months with changes in visual acuity recorded.

**Results:** A total of 30 IMH patients were included, 13 males and 17 females. All patients showed varying degrees of improvement in visual acuity after surgery. The correlation analysis results showed that the preoperative superficial, deep, and full-thickness FAZ were closely related to the best-corrected visual acuity at 3 months after surgery (r=0.521, 0.605, and 0.704, P <0.05, 0.01, and 0.01), with the deep and full-thickness FAZ showing a more significant correlation than the superficial FAZ. At 1 week after surgery, the superficial, deep, and full-thickness FAZ showed significant differences compared to the preoperative values (t=4.8, P <0.01, t=7.1, P <0.01, and t=4.4, P <0.01). At 1 month after surgery, the superficial, deep, and full-thickness FAZ showed significant differences compared to each layer's FAZ at 1 week after surgery (t=-2.1, P=0.046, t=-2.9, P <0.01, and t=-4.1, P <0.01).

**Conclusion:** There is a correlation between preoperative FAZ and postoperative visual acuity in IMH patients, with smaller preoperative FAZ associated with better postoperative visual acuity recovery.

**Background**

The macular fovea is the most sensitive region of the retina for visual perception. It contains only two layers of cells, the pigmented epithelium and the cones, and is nourished solely by the choroid. The fovea is surrounded by the parafovea, which contains capillary loops and a foveal avascular zone (FAZ) of approximately several hundred micrometers in size. Macular hole (MH) is an organic lesion of the fovea that not only impairs the anatomical integrity of the macula, but also affects its function. Okumichi et al.\(^1\) found that the size of the deep FAZ is related to best-corrected visual acuity (BCVA), and Kim et al.\(^2\) reported that BCVA is significantly correlated with the areas of both the superficial and deep FAZ at 6 months after MH surgery. Kotaro Tsuboi et al.\(^3\) found that the FAZ area decreases temporarily after MH closure and then gradually returns to normal values, and that changes in FAZ size after surgery are related to visual recovery. Linderman et al.\(^4\) discovered a negative correlation between FAZ area measured by OCTA and axial length, but this trend can be eliminated by correcting for differences. While many studies have shown that the FAZ of patients with MH is larger than that of healthy individuals, the impact of FAZ enlargement on visual acuity after MH surgery is unclear. With the widespread application of OCT angiography (OCTA), it is possible to obtain clear images and analyses of the retinal capillary network without invasive procedures, making OCTA a valuable tool for examining FAZ. To predict visual outcomes in patients with MH, we conducted a study on idiopathic MH to minimize the influence of other factors on postoperative visual acuity.
Methods

General information: This is a prospective study that collected 30 patients diagnosed with idiopathic macular hole (IMH) and who underwent vitrectomy surgery at the Ophthalmology Center of Weifang Medical College from June 2021 to November 2021. The study was approved by the Weifang Medical College Ethics Committee. Inclusion criteria included being diagnosed with IMH, having undergone vitrectomy surgery, and being between 55 and 65 years old, with a follow-up time of at least 3 months. Exclusion criteria included poor quality scan images, axial length less than 22 mm or greater than 26 mm, the presence of other retinal diseases, age less than 55 or greater than 65, loss to follow-up, and patients who did not undergo phacoemulsification combined with intraocular lens implantation during vitrectomy surgery. The study followed the Helsinki Declaration.

Examination methods: All patients underwent a comprehensive ophthalmic examination before and after surgery. This included slit lamp and fundus examinations, obtaining clear OCTA images using Avanti RTVue XR (Optovue Inc, Fremont, CA, USA), measuring axial length using Nidek (Japan, Gamagori), measuring intraocular pressure, and collecting patient-related information. At the 3-month follow-up, the patient's best-corrected visual acuity was obtained.

Optical coherence tomography angiography (OCTA) A 3×3 mm OCTA scan of the macular area was performed before surgery using a central wavelength of 840 nm and a frequency of 70 kHz. The AngioVue software (version 2017.1.0.131; Optovue) was used to analyze the FAZ area. The superficial and full-layer FAZ were automatically calculated, and the deep-layer FAZ was calculated using Image J (as shown in Fig. 1). If the FAZ detection was inaccurate, it was manually corrected by a professional technician.

IMH surgical method: The surgical method was a 25G vitrectomy combined with internal limiting membrane (ILM) peeling. Phacoemulsification combined with intraocular lens implantation was performed in all cases with a crystalline lens. After creating or confirming the posterior vitreous detachment (PVD), the vitrectomy probe was used for core vitrectomy. Triamcinolone acetonide (Tokyo and Hakko Kirin Co., Ltd., Japan) was injected into the vitreous cortex if necessary. In all cases, ILM peeling was performed using indocyanine green within the central 3 mm (2 disk diameters). Gas-fluid exchange was performed, and if necessary, inert gas (6% perfluoropropane) was injected into the vitreous cavity.

Statistical methods: SPSS 25.0 was used to analyze all data. The data was represented as mean ± standard deviation (SD) and appropriate range. BCVA was measured using a Landolt C visual acuity chart and statistically analyzed by converting decimal BCVA to log minimum resolution angle. Spearman rank correlation coefficient was used to analyze the correlation between the data. The Wilcoxon signed-rank test was used to analyze the preoperative and postoperative differences. The statistical significance level was set at P < 0.05.
Results

The study included a total of 30 local Han Chinese patients, 13 males and 17 females, with an average age of 64.13 ± 5.029 years and an average axial length of 23.195 ± 0.714. The preoperative average visual acuity was 0.114 ± 0.089, and the postoperative visual acuity improved to an average value of 0.254 ± 0.159, with an average visual acuity recovery value of 0.14 ± 0.094. The preoperative and postoperative superficial, deep, and full-thickness FAZ, logMAR, and visual acuity recovery value for patients with disease onset time less than 4 months and those with onset time greater than 4 months showed no significant difference. The preoperative average superficial, deep, and full-thickness FAZ area was 0.587 ± 0.143, 0.523 ± 0.154, and 0.389 ± 0.123 mm², respectively. The preoperative and postoperative FAZ area, visual acuity, and logMAR showed no significant difference between males and females. The axial length showed no significant correlation with preoperative superficial, deep, and full-thickness FAZ. Preoperative superficial, deep, and full-thickness FAZ showed a significant correlation with postoperative visual acuity, and deep and full-thickness FAZ showed a stronger correlation than the superficial FAZ. LogMAR and logmar were also correlated with preoperative superficial, deep, and full-thickness FAZ (Table 1, Table 2).

The difference between postoperative and preoperative visual acuity was defined as the visual recovery value, and the logarithm of the visual recovery value was taken as the logmar.

Linear regression was used to describe the relationship between logMAR (logarithm of the minimum angle of resolution) and logmar (logarithm of the difference in visual acuity before and after surgery) with each layer of FAZ (foveal avascular zone).

The linear regression analysis indicated that the full layer of FAZ showed the best fit with logmar (logarithm of the difference in visual acuity before and after surgery) (Table 3). The equation for the relationship between logmar and FAZ was Y = 0.104 + 2.238X, with an F value of 42.185 and a P value less than 0.001. This suggests that there is a linear relationship between the preoperative FAZ and the logarithm of the visual acuity recovery value. In other words, preoperative FAZ can predict the improvement of postoperative visual acuity.

Out of the 30 patients, 23 were selected who had clear FAZ images at 1 week, 1 month, and 3 months after surgery, and their changing trends are shown in Fig. 3:

As shown in Table 4, there was a statistically significant difference in the comparison of superficial layer, deep layer, and full layer FAZ between postoperative 1 week and preoperative. Additionally, there was a statistically significant difference in the comparison of superficial layer, deep layer, and full layer FAZ between postoperative 1 month and each layer FAZ at postoperative 1 week.

Discussion
A macular hole (MH) refers to an anatomical opening in the center of the macula, which is a complete defect in the neurosensory retina of the macular area from the internal limiting membrane (ILM) to the outer layer of photoreceptors. MH can be classified as either idiopathic (IMH) or secondary, with IMH occurring spontaneously and being unrelated to any underlying ocular disease. Secondary MH is often caused by ocular trauma, high myopia, or cystoid macular edema. Clinical manifestations of IMH include decreased visual acuity, visual distortion caused by displacement of photoreceptors, and a central scotoma caused by the macular hole. Fundus photography shows a clear, circular or elliptical, dark red hole in the macular area, with varying diameters, and a yellowish deposit resembling a vitreous membrane nodule at the base of the hole. The retina neuroepithelium can be seen to be detached around the hole. Epidemiological investigations and clinical reports suggest that the incidence of IMH is higher in women than in men, with a male-to-female ratio of 1:6, which may be related to the later occurrence of posterior vitreous detachment (PVD) in women. MH can greatly reduce a patient's quality of life related to visual health. Currently, vitrectomy with internal limiting membrane peeling, intraocular filling, and postoperative prone positioning is the preferred and gold standard treatment for IMH. The initial closure rate after surgery can reach up to 90%\textsuperscript{[5–6]}.

Although there have been significant improvements in the anatomical closure rate of macular holes with the continuous exploration and improvement of surgical techniques, postoperative visual function remains unpredictable. Numerous studies have shown that while a patient's best-corrected visual acuity after surgery may be improved compared to preoperative levels, it does not fully recover to pre-disease levels.

The foveal avascular zone (FAZ) is an avascular area in the central macular region surrounded by a continuous network of capillaries. The retinal capillary plexus is composed of the superficial vascular plexus located in the nerve fiber layer and ganglion cell layer, and the deep vascular plexus located in the inner nuclear layer. In the superficial vascular plexus, the vessels are radially distributed, while in the deep vascular plexus, the vessels are distributed around the fovea with vertical connections. Under physiological conditions, the FAZ of the normal eye is circular or elliptical with a diameter of about 500–600µm. The reported measurements of the superficial and deep FAZ of the normal eye vary among different studies, with the superficial FAZ ranging from 0.17 to 0.573mm\textsuperscript{2} and the deep FAZ ranging from 0.3 to 0.659mm\textsuperscript{2}\textsuperscript{[7]}. Most studies have reported significant differences between the superficial and deep FAZ. Enlargement of the FAZ in the macular region is a pathological change reflecting foveal ischemia, which is related to visual function and prognosis in retinal vascular diseases\textsuperscript{[8]}.

Our research found that IMH patients who had a greater improvement in postoperative vision had a relatively smaller preoperative FAZ (Fig. 2). We speculate that there are several mechanisms at play. Tornambe\textsuperscript{[9]} proposed the hydration theory after observing OCT images of a large number of IMH patients, which suggests that the liquefied vitreous hydrates the surface of the macular region after retinal defects caused by posterior vitreous detachment. In a normal physiological state, the integrity of the retinal pigment epithelial layer ensures retinal homeostasis. Once small defects occur in the retinal pigment epithelium, the integrity and stability of the retinal pigment epithelium are disrupted, and the unique structure of the macular region causes it to accumulate fluids in an unbalanced state and become
exposed to vitreous fluid, resulting in thickening and outward displacement of the edges of the macular hole. We speculate that when fluid accumulates in the macular region, the choroid underneath the macula plays the main role in fluid outflow, while the capillary network in the macular area also contributes to some degree due to the macular hole. Patients with a larger FAZ may have insufficient capillary network outflow, which may make them more prone to macular ischemia and edema caused by DCP ischemia, as reported by Scarinci et al.\textsuperscript{[10]}, which can lead to damage to the outer retina, including the outer nuclear layer and photoreceptors, and impair vision. Therefore, a larger FAZ corresponds to a lower visual acuity. Another mechanism is that when a macular hole appears in patients, visual function decreases, and the energy needed by photoreceptors and related cells decreases, leading to a corresponding decrease in blood flow. As the choroidal blood flow in the macular area decreases, the avascular zone of the macular fovea will also expand to a certain extent along with the decrease in visual function. As shown in Kotaro Tsuboi et al.'s\textsuperscript{[3]} research, this expansion is reversible, and if the macular hole is closed, the avascular zone of the macular fovea will gradually return to normal. Yoshiyuki Kita et al.\textsuperscript{[11]} reported that after MH closure, FAZ will significantly decrease, and the size of the FAZ in the affected eye will be symmetric with that in the contralateral eye. The size of the postoperative FAZ is affected by the postoperative thickness of the macular fovea and is unrelated to the size of the MH. However, Miao Zeng et al.\textsuperscript{[12]} reported that the superficial and deep FAZ gradually increased before and after surgery at 1, 3, 6, and 12 months. Due to the difficulty in follow-up caused by the epidemic situation in China, this study did not complete the follow-up work for 6 months after surgery. Many studies have now confirmed that after the successful closure of the macular hole, retinal tissue undergoes centripetal movement\textsuperscript{[13]} as seen in fundus photographs, OCT, and OCTA. In our study, we also found a corresponding decrease in FAZ after surgery (Fig. 3). Due to the inflammatory response caused by the surgery and the influence of the vitreous cavity filling material, visual acuity does not improve significantly in the short term after surgery. Generally, from 1 month to 3 months after surgery, as the intraocular environment gradually stabilizes, visual acuity gradually improves to its peak. At this time, the FAZ of each layer tends to be stable, and a smaller preoperative FAZ corresponds to a stronger macular function, a smaller diameter of the macular hole, more blood vessels in the macular.

Lafe et al.\textsuperscript{[14]} reported that the vessel density of the superficial capillary plexus (SCP) and deep capillary plexus (DCP) of the retina decreases with age, while the foveal avascular zone (FAZ) area increases with age. Patients within 10 years of age were selected to control for the impact of age on FAZ. Among the 23 patients with clear postoperative FAZ imaging selected in this study, significant reductions in FAZ size were observed in all layers one week after surgery, followed by a significant increase in size in all layers one month after surgery. Akahori et al.\textsuperscript{[15]} reported that after macular hole surgery, the retina in the foveal area moves toward the nasal side, which may be due to the contraction of the retina after removal of the internal limiting membrane during surgery, or the buoyancy generated by gas filling and the centripetal contraction during closure causing the retina to rotate downwards. Due to the closure of the macular hole and the centripetal displacement of the retina, the FAZ will shrink rapidly one week after surgery, but this shrinkage is artificially induced. As time passes and the ocular blood flow stabilizes, the avascular zone in the center of the macula gradually increases as blood flow decreases. This result is consistent with
many domestic and foreign studies. However, there was no statistically significant difference in the FAZ size among the layers one month and three months after surgery, which may be due to the inclusion of patients with unhealed macular holes in this study. For these patients, tissue repair is limited, and the demand for blood flow is reduced, which may lead to stabilization of blood flow one month after surgery. It is also possible that tissue repair in the eyes of patients with macular holes slows down after one month postoperatively, and although FAZ size increases in all layers, the rate of increase is not statistically significant.

Many scholars have used OCT to study preoperative morphology of macular holes (MH) and to identify predictive factors for postoperative visual outcomes. Ogasawara et al.\cite{16} reported a positive correlation between superficial foveal avascular zone (FAZ) and best-corrected visual acuity (BCVA) after treatment for macular branch retinal vein occlusion (BRVO), while all other FAZ layers were not related to microstructural parameters of photoreceptors. D.H. Steel et al.\cite{17} prospectively studied 1483 patients using the BEAVRS database to investigate pre- and postoperative MH size and BCVA, and found that patients with higher preoperative BCVA, smaller hole diameter, shorter symptom duration, and no age-related macular degeneration (AMD) had better postoperative BCVA. They also found that maximizing the time from symptom onset to surgery could greatly improve postoperative BCVA, especially for patients within 4 months of symptom onset. However, our study did not show such results, possibly due to the small sample size and the fact that most patients in this study had a short duration of illness, which may not be representative of patients with symptom onset of more than 4 months. Gupta and Meng\cite{18,19} reported that the final BCVA of patients with closed macular holes was influenced by preoperative BCVA. Many researchers, such as Dan Cheng\cite{20}, have found that the deep FAZ is more representative than the entire FAZ, but this study only showed that the superficial FAZ was less representative than the deep and entire FAZ, possibly due to the use of manually drawn deep FAZ in this experiment.

This study made efforts to minimize the influence of axial length, age, and race on preoperative FAZ, and included patients who underwent a unified surgical procedure. Since all patients received cataract surgery and had no other ocular diseases, the closure of the macular hole was the most important factor influencing postoperative visual acuity. The aim of this study was to provide reference for the prognosis of patients with idiopathic macular holes based on preoperative examination results.

As this study was a prospective study with a small sample size and lacked a control group, there were certain limitations. The results of this study need to be further validated by expanding the sample size and conducting multicenter controlled studies.

**Abbreviations**

Declarations

Acknowledgement

Not applicable.

Authors’ contributions

Yongliang Cao made contribution to supervision and final approval, made critical revision of the manuscript and fund application. Hongbang An, Wenxuan Yu, Bing Liang and Fengqin Hao collected, analyzed and interpreted data, wrote the manuscript. Shu’na Wang and Meng Gao collected data and made critical revision of the manuscript. Lihua Li provided expert technical assistance with the measurement and made contribution to the design of the experiment. Shu’na Wang and Fengqin Hao provided the instrument used in the experiment and made contribution to the design of the work. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Affiliated Hospital of Weifang Medical College and followed the principles of the Declaration of Helsinki. We obtained written informed consent from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

1 Weifang Medical University, Weifang City, Shandong Province, 261000
References


Tables

Table 1: Correlation between logMAR (logarithm of the minimum angle of resolution) and FAZ in each layer.

<table>
<thead>
<tr>
<th>Pearson correlation</th>
<th>Significance (two-tailed)</th>
<th>number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial FAZ</td>
<td>0.521</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Deep FAZ</td>
<td>0.605</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Full-thickness FAZ</td>
<td>0.704</td>
<td>&lt;0.01</td>
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</table>

Table 2: Correlation between logmar (logarithm of the difference between postoperative and preoperative best-corrected visual acuity) and deepFAZ.
### Table 3: Coefficient of determination (R²) values for each group.

<table>
<thead>
<tr>
<th></th>
<th>Pearson correlation</th>
<th>Significance (two-tailed)</th>
<th>number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superficial FAZ</strong></td>
<td>0.658</td>
<td>&lt;0.01</td>
<td>30</td>
</tr>
<tr>
<td><strong>Deep FAZ</strong></td>
<td>0.665</td>
<td>&lt;0.01</td>
<td>30</td>
</tr>
<tr>
<td><strong>Full-thickness FAZ</strong></td>
<td>0.775</td>
<td>&lt;0.01</td>
<td>30</td>
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</table>

### Table 4: Differences in Each Layer of FAZ (foveal avascular zone) Between Adjacent Timepoints

<table>
<thead>
<tr>
<th></th>
<th>logMAR</th>
<th>logmar</th>
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<tr>
<td><strong>Superficial FAZ</strong></td>
<td>0.271</td>
<td>0.432</td>
</tr>
<tr>
<td><strong>Deep FAZ</strong></td>
<td>0.366</td>
<td>0.438</td>
</tr>
<tr>
<td><strong>Full-thickness FAZ</strong></td>
<td>0.495</td>
<td>0.601</td>
</tr>
</tbody>
</table>

Table 3: Coefficient of determination (R²) values for each group.

Table 4: Differences in Each Layer of FAZ (foveal avascular zone) Between Adjacent Timepoints
<table>
<thead>
<tr>
<th>Comparison</th>
<th>t</th>
<th>P</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial preoperative FAZ - Superficial FAZ 1 Week after surgery</td>
<td>4.8</td>
<td>0.01</td>
<td>0.075~0.188</td>
</tr>
<tr>
<td>Deep preoperative FAZ - Deep FAZ 1 Week after surgery</td>
<td>7.1</td>
<td>0.01</td>
<td>0.1601~0.294</td>
</tr>
<tr>
<td>Full-thickness preoperative FAZ - Full-thickness FAZ 1 Week after surgery</td>
<td>4.4</td>
<td>0.01</td>
<td>0.060~0.166</td>
</tr>
<tr>
<td>Superficial FAZ 1 Week after surgery - Superficial FAZ 1 month after surgery</td>
<td>-2.1</td>
<td>0.046</td>
<td>-0.048~0.001</td>
</tr>
<tr>
<td>Deep FAZ 1 Week after surgery - Deep FAZ 1 month after surgery</td>
<td>-2.9</td>
<td>0.01</td>
<td>-0.117~0.020</td>
</tr>
<tr>
<td>Full-thickness FAZ 1 Week after surgery - Full-thickness 1 month after surgery</td>
<td>-4.1</td>
<td>0.01</td>
<td>-0.070~0.023</td>
</tr>
<tr>
<td>Superficial FAZ 1 month after surgery - Superficial FAZ 3 months after surgery</td>
<td>-0.9</td>
<td>0.363</td>
<td>-0.045~0.017</td>
</tr>
<tr>
<td>Deep FAZ 1 month after surgery - Deep FAZ 3 months after surgery</td>
<td>-0.1</td>
<td>0.894</td>
<td>-0.064~0.056</td>
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<tr>
<td>Full-thickness 1 month after surgery - Full-thickness 3 months after surgery</td>
<td>-1.4</td>
<td>0.175</td>
<td>-0.050~0.009</td>
</tr>
</tbody>
</table>

Figures
Figure 1

Illustrations of the various layers of FAZ.
Figure 2

Scatter plots of logMAR (logarithm of the minimum angle of resolution of the best-corrected visual acuity) and logmar (logarithm of the difference between postoperative and preoperative visual acuity) against each layer’s FAZ prior to surgery.
Figure 3

Trend of Changes in Each Layer of FAZ (foveal avascular zone) Before and After Surgery, at 1 Week, 1 Month, and 3 Months.