· Clinical Research ·

Prediction of visual recovery after idiopathic macular hole surgery: a triad of tractional mechanics, subfoveal anatomy, and preoperative function

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Abstract

● **AIM:** To establish and validate a multidimensional predictive model of postoperative visual recovery after idiopathic macular hole (IMH) surgery.

● **METHODS:** Retrospective cohort study. Examinations within a three-month period, both pre- and postoperative, included assessments of best corrected visual acuity (BCVA), intraocular pressure (IOP), and morphological parameters of IMH with optical coherence tomography (OCT). Then, a series of indices were derived, including the IMH index (MHI), diameter hole index (DHI), macular hole closure index (MHCI), hole form factor (HFF), and tractional hole index (THI). Subfoveal anatomical damage (macular hole inferior volume, Vi) was calculated based on the basal diameter (BD), minimum diameter (MD), and height at the narrowest point (H_{MD}) of IMH. Pearson correlation analysis was utilized to discern significant correlations between postoperative BCVA and the multiple indices examined. A subsequent linear correlation analysis was performed.

● **RESULTS:** The study involved 51 eyes from 51 patients (mean age 66.90±6.07y) diagnosed with IMH. Preoperative BCVA was 1.22±0.76 logMAR and improved to 0.88±0.38 logMAR after surgery (P<0.001). The correlation analysis results showed significant correlations between postoperative BCVA and preoperative BCVA (P<0.001), BD (P=0.042), MD (P=0.001), MHI (P=0.047), THI (P=0.004), and Vi (P=0.007). The multidimensional model integrating THI, Vi, and preoperative BCVA significantly outperformed traditional predictors (MD, BD, and height) in terms of postoperative visual recovery prediction. THI, reflecting posterior vitreous traction mechanics, independently predicted anatomical reset potential (β=-0.06, P=0.022), while Vi, quantifying subfoveal photoreceptor disruption, was correlated with structural-functional recovery (β=0.01, P=0.046). Preoperative visual acuity served as a critical surrogate for retinal functional reserve (β=0.15, P=0.020). Redundant morphometric parameters (MHI, DHI, MHCI, HFF) were excluded, as their predictive contributions were subsumed by THI/Vi or mediated by preoperative vision.

● **CONCLUSION:** The combination of biomechanical traction (THI), subfoveal anatomical damage (Vi), and preoperative BCVA represents a clinically applicable framework for predicting postoperative visual recovery after IMH surgery. This model can be used as a practical tool to guide surgical planning, facilitating the identification of high-risk patients who may benefit from additional techniques (such as an internal limiting membrane flap) while optimizing resource allocation for standard cases.

● **KEYWORDS:** macular hole surgery; visual acuity; biomechanical traction; optical coherence tomography; prediction

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INTRODUCTION

Macular hole (MH) is a macular lesion that can cause severe visual impairment. The most prevalent type of MH is idiopathic macular hole (IMH), with an incidence rate of approximately 0.3% in individuals ≥55y[1]. In recent years, technological advancements and a deeper understanding of pathological anatomy[2] have significantly improved surgical techniques and prognostic evaluation methods[3-5]. Predicting postoperative visual improvement is a critical issue in MH surgery studies. Several factors affect the visual prognosis after MH surgery, including the macula's structural characteristics before surgery, the extent of internal limiting membrane (ILM) detachment during surgery, and the displacement of the macular area after surgery[6-9].

Considerable research has been conducted to enhance the accuracy and reliability of predictive methods in this regard. The utilization of optical coherence tomography (OCT) and other imaging techniques has significantly improved the ability to accurately predict postoperative visual recovery, as shown in numerous studies[10-12].

Various parameters have been defined to delineate the morphology of the MH, including the macular hole index (MHI), traction hole index (THI)[5], hole form factor (HFF), MH healing index (MHCI)[13], basal diameter (BD), and minimum diameter (MD). Research has indicated positive correlation between visual acuity and HFF, MHI, and THI, while BD and MD have demonstrated negative correlations with visual acuity[12]. Some studies have introduced models based on the external limiting membrane (ELM) and ellipsoid zone (EZ) to predict postoperative defect size and best corrected visual acuity (BCVA)[14].

This study expands the typical two-dimensional parameters to consider three-dimensional volumes as potential indicators, thereby offering additional visual parameters for clinical prognostic use. Through a retrospective analysis of clinical data, we aim to establish a comprehensive reference framework to optimally time and strategize regarding surgery, ultimately improving patients' postoperative vision.

PARTICIPANTS AND METHODS

Ethical Approval All study procedures adhered to the guidelines of the Helsinki Declaration of 2024 and its subsequent revisions and received approval from the Ethics Committee of Xi'an First Hospital with the assigned ethics number 2024-012. Written informed consent was obtained from all patients.

Participants We enrolled patients diagnosed with IMH who underwent surgery at Xi'an First Hospital between October 2021 and December 2023. Previous studies have indicated that within 1 to 3mo post-vitrectomy, there is a significant improvement in both BCVA and retinal sensitivity in patients with IMH[4]. Consequently, our follow-up period was set within this three-month window. The detailed patient selection and exclusion flowchart is presented in Figure 1.

Inclusion criteria: 1) age ≥50y; 2) patients exhibiting levels 2–3 of healing post-MH-surgery according to the International Vitreomacular Traction Study (IVTS) Group, as evident from OCT images showing the complete closure of the retinal tissue at the hole's edge, without any gap[15]; 3) patients having completed at least one full follow-up visit within 1 to 3mo post-surgery.

Exclusion criteria: 1) IMH combined with other eye diseases, such as corneal diseases, uveitis, glaucoma, high myopia (axial length >26 mm), macular epiretinal membrane, diabetic retinopathy, optic neuropathy, or other retinal diseases; 2) patients who did not undergo cataract surgery; 3) the presence of an unclosed MH post-surgery; 4) incomplete preoperative or postoperative visual acuity and OCT data; 5) unclear preoperative or postoperative OCT images.

Surgical Methods All patients underwent cataract extraction *via* phacoemulsification and subsequent intraocular lens implantation. The primary corneal incision measured 2.8 mm, with target refractive error being set between -0.3 and -0.5 D. Vitrectomy procedures were performed using either 23 gauge (G) or 25G glass cutting heads. The ILM was stained with indocyanine green dye, followed by a circular dissection around the MH, with diameters ranging from 2 disc diameters (DDs) to 4 DDs. Three senior doctors, each with considerable surgical expertise conducted all the surgeries. Post-operatively, patients' vitreous cavities were injected with 0.7 mL of perfluoropropane (C_3F_8) gas, and patients were advised to maintain a prone position for 2wk to facilitate MH closure.

Measure Parameters The preoperative data include each patient's age, gender, preoperative and postoperative BCVA, non-contact tonometry images (CT-80, Topcon Medical Systems, Oakland, US), and OCT images (Spectralis OCT, Heideberg Engineering GmbH, Germany). The postoperative evaluation was conducted 1 to 3mo after the surgery. OCT images intersecting horizontal tangents of the MH center were selected. All images underwent denoising and contrast enhancement processing with the Visual Paradigm Online Image Denoising Tool (Visual Paradigm Corporation, Hong Kong, China).

All OCT images utilized in this study were horizontally oriented, bisecting the central MH. Height of IMH was the distance between the retinal pigment epithelium (RPE) layer and vitreoretinal interface at its maximum, measured perpendicular to the RPE line. H_{MD} represents the measurement from a line approximately perpendicular to the RPE at the most narrow point of neuroepithelial defect. BD was the largest BD of MH parallel to the RPE. MD was measured by drawing a line parallel to the RPE at the narrowest point and determining the width. THI was the ratio of crack height to MD. It signifies the relative tensile forces in the anteroposterior direction of the vitreous body compared to the tangential direction. MH inferior volume can be approximated as a cone where the base area is the ground and MD of the crack is the top surface. By

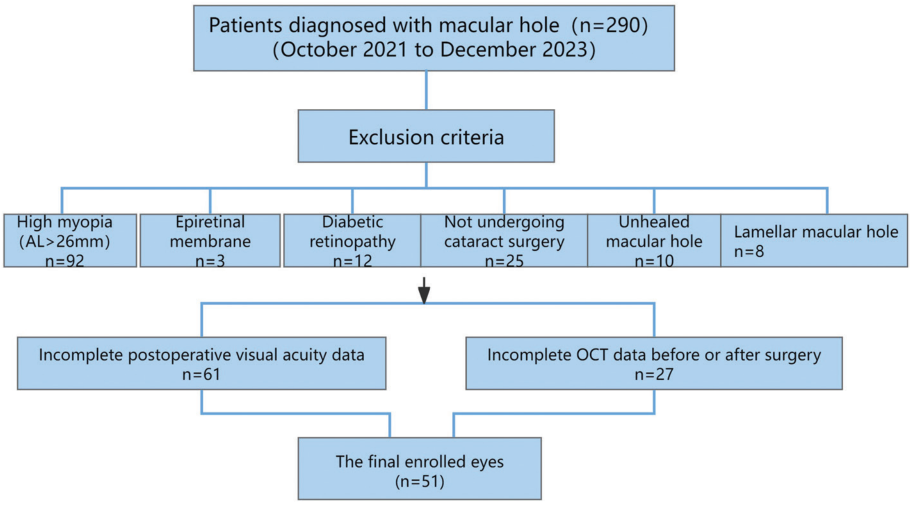

Figure 1 Patient flowchart AL: Axial length; OCT: Optical coherence tomography.

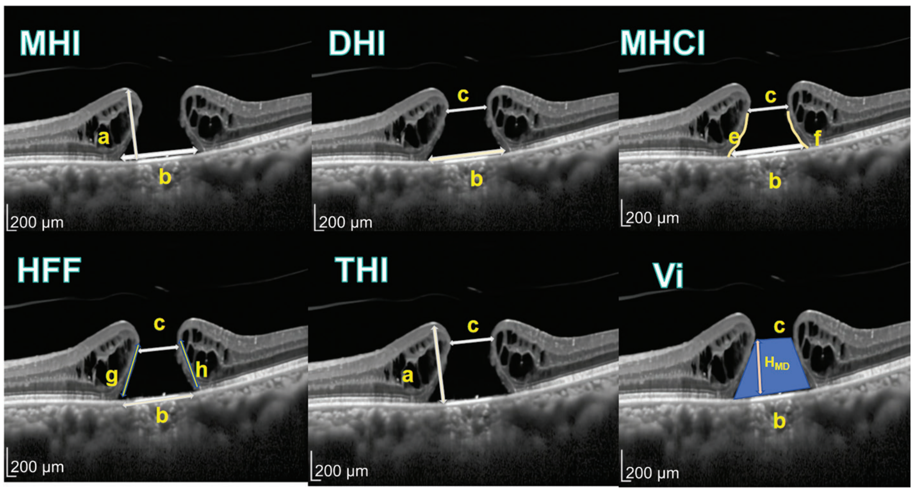

Figure 2 Several measurements are defined with respect to features of the MH a: The height of the MH's vertex, measured perpendicularly to the RPE layer; b: The BD, gauged parallel to the RPE layer at the base of the hole; c: The MD, determined parallel to the RPE layer at the narrowest section; e, f: This likely represents a specific point of measurement related to the photoreceptor branch. It is described as beginning at the junction with the RPE layer and ending at the site of photoreceptor cell rupture, which is also deemed the rupture endpoint of the ELM; g, h: The distance between the two ends of the hole diameter and the two ends of their respective bottom diameters measured diagonally (left and right); H_{MD}: The height at the narrowest point of the MH. Macular hole index (MHI)=a/b; Diameter hole index (DHI)=c/b; Macular hole closure index (MHCI)=(e+f)/b; Hole form factor (HFF)=(g+h)/b; Tractional hole index (THI)=a/c. R1=BD/2, R2=MD/2, h=H_{MD}, Vi=1/3πh($R1^2$+$R2^2$+R1R2). MH: Macular hole; BD: Basal diameter; MD: Minimum diameter; RPE: Retinal pigment epithelium; ELM: External limiting membrane.

designating half of BD as R1 and half of MD as R2, the height of H_{MD} as h, the definitive equation for Vi becomes $1/3\pi h(R1^2+R2^2+R1R2)$. The method of parameter annotation was shown in Figure 2.

All line lengths are quantified and analyzed using Image J software (National Institutes of Health, Bethesda, MD, USA), in accordance with the ruler measurement, and subsequently incorporated into the relevant formulae for calculating MH-associated parameters. This equation is further computed using WPS Excel (Kingsoft Office Software, Beijing, China).

Statistical Analysis For statistical analysis, the preoperative and postoperative BCVA were converted to logarithm of the minimum angle of resolution (logMAR)-equivalent values. A statistical description of the patient population was provided. Correlations between postoperative BCVA and various measured parameters were assessed using either Pearson's or Spearman's correlation methods. These parameters encompassed preoperative BCVA, age, gender, preoperative BD, MD, H_{MD}, MHI, DHI, MHCI, HFF, THI, and Vi. A multivariable linear regression analysis was conducted with postoperative BCVA as the dependent parameter, employing the enter procedure. Independent parameters that yielded a P-value of <0.05 in the single factor analysis were incorporated into the multivariate model. All analyses were two tailed, with statistical significance set at a P-value of <0.05. The results of the two-sided tests were deemed significant if $P<0.05$. Data processing and analysis were performed using R Version 4.3.3 (R Foundation for Statistical Computing, Vienna, Austria), Zstats 1.0 (Hangzhou Yunxiang Statistics Technology Company, Ltd, China; www.zstats.net), and Statistical Package for the Social Sciences (SPSS) 25.0 software (International Business Machines Corporation, Armonk, New York, USA).

RESULTS

The 51 enrolled patients had an average age of 66.90±6.07y (range: 53–81). Preoperatively, their mean BCVA was 1.22±0.76 logMAR (range: 0.53–5.0), which improved to 0.88±0.38 logMAR postoperatively (range: 0.22–1.69). The demographic characteristics of the patients are shown in Table 1.

The correlation analysis demonstrated that the postoperative BCVA in IMH patients was primarily associated with BD, MD, MHI, THI, and Vi (Table 2). Given that MHI, DHI, MHCI, and HFF were combined measures of BD, MD, and H_{MD} and that linear regression necessitates non-collinearity among indicators, the dependent variable for the linear regression was postoperative BCVA, and the independent variables were preoperative BCVA, DHI, THI, Vi, and age. Univariate and multivariate analysis of pre-operative factors associated with post-BCVA showed better postoperative BCVA was correlated with superior preoperative BCVA (P=0.02), higher THI (P=0.022), and reduced Vi (P=0.046). However, the linear regression forest plot showed that final postoperative visual acuity was predominantly influenced by the combined effects of preoperative BCVA and longitudinal tensile force in the macular area (Figure 3).

Table 1 Basic demographic characteristics mean±SD or *n* (%)

Characteristics	Total (n=51)
Age (y)	66.90±6.07
Sex	
Male	13 (25.49)
Female	38 (74.51)
Stage	
1	5 (9.80)
2	9 (17.65)
3	11 (21.57)
4	26 (50.98)
Pre-BCVA (logMAR)	1.22±0.76
Post-BCVA (logMAR)	0.88±0.38
MD (μm)	191.47±73.85
BD (μm)	371.08±134.84
MHI	1.39±1.24
MHCI	2.39±3.47
DHI	0.67±0.97
HFF	2.12±2.17
THI	2.65±1.86
EZ distance (μm)	259.34±103.71
Vi (μm^3)	$(2.11\pm1.49)\times10^7$

Pre-BCVA: Preoperative best corrected visual acuity; Post-BCVA: Postoperative best corrected visual acuity; MD: Minimum diameter; BD: Basal diameter; MHI: Macular hole index; MHCI: Macular hole closure index; DHI: Diameter hole index; HFF: Hole form factor; THI: Tractional hole index; EZ: Ellipsoid zone; Vi: Inferior volumes of the macular hole; SD: Standard deviation.

Table 2 The *r* and *P* values of bivariate correlations analyzed between post-BCVA and all MH parameters

Parameters	r	P	95%CI
Pre-BCVA	0.607	<0.001[b]	0.384 to 0.771
BD	0.285	0.042[a]	0.041 to 0.521
MD	0.468	0.001[b]	0.175 to 0.714
MHI	-0.279	0.047[a]	-0.538 to 0.041
DHI	0.283	0.093	-0.073 to 0.517
MHCI	-0.224	0.114	-0.482 to 0.066
HFF	0.245	0.083	0.072 to 0.528
THI	-0.400	0.004[b]	-0.665 to -0.074
Vi	0.374	0.007[b]	0.067 to 0.412

Pre-BCVA: Preoperative best corrected visual acuity; post-BCVA: Postoperative best corrected visual acuity; MH: Macular hole; BD: Basal diameter; MD: Minimum diameter; MHI: Macular hole index; DHI: Diameter hole index; MHCI: Macular hole closure index; HFF: Hole form factor; THI: Tractional hole index; Vi: Inferior volumes of the MH; CI: Confidence interval. [a]$P<0.05$, [b]$P<0.01$.

DISCUSSION

Full-thickness defects in the fovea, characterized by MH, result in central vision impairment and decreased quality of life for patients. Surgical treatments, primarily vitrectomy and ILM peeling, have demonstrated variable degrees of success in visual recovery and anatomical closure in cases of these defects[16]. In this retrospective cohort study, the results suggest that preoperative visual acuity, THI, and Vi are strongly associated with postoperative visual outcomes.

Research into preoperative visual acuity and OCT features prediction remains a central area of MH study. Pre-surgical visual acuity can provide some indication of MH stage and the extent of the damage to the photoreceptor cells in the outer layer of the retina[17]. Accordingly, the preoperative BCVA exhibits a strong predictive relationship with the postoperative BCVA. A retrospective continuous case series study indicated that the BD at 6mo, preoperative BCVA and BD at 12mo, as well as a smaller ELM-ganglion cell layer (GCL) distance at the final visit, were utilized as predictors of postoperative BCVA[18]. In a study conducted by Zou and Zeng[19] on 19 patients with IMH, it was found that postoperative visual impairment was significantly associated with several factors: the MD, BD, duration of symptoms, and preoperative BCVA. Conversely, improvement in vision was exclusively linked to

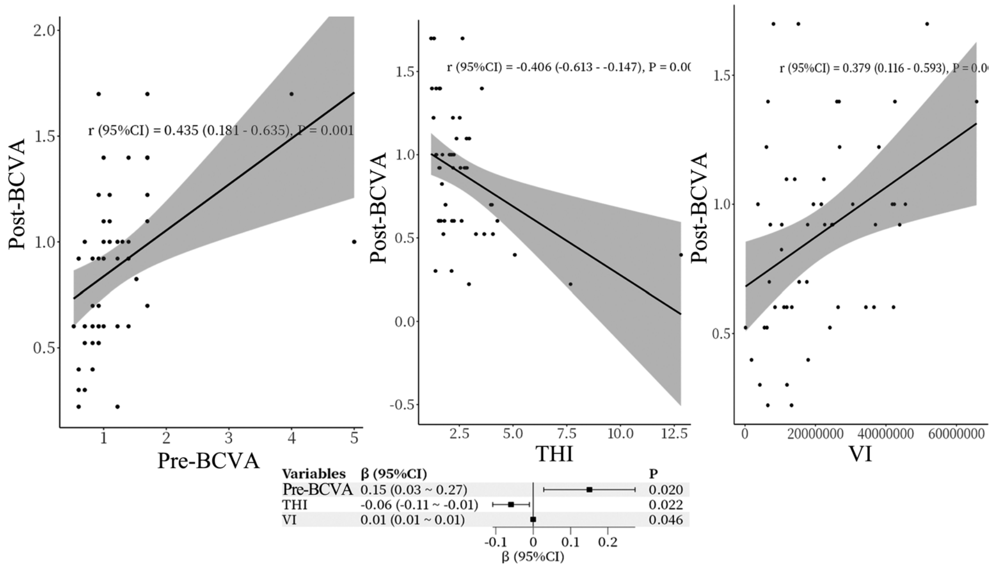

Figure 3 The linear regression scatter plot and forest plot showed the final post-BCVA was influenced by pre-BCVA, THI, and Vi Pre-BCVA: Preoperative best corrected visual acuity; Post-BCVA: Postoperative best corrected visual acuity; THI: Tractional hole index; Vi: Inferior volumes of the macular hole; CI: Confidence interval.

preoperative BCVA, a finding that aligns with our multiple regression analysis results. Among these related indicators, preoperative vision was the most significant factor. These results show that preoperative BCVA is a comprehensive reflection of residual retinal function. Better preoperative visual acuity may indicate a higher rate of photoreceptor survival.

In terms of OCT features, one study has shown that the shape of the macula significantly affects the detection of IMH at various stages, particularly stages 2 and 4[20]. Previous research has proposed numerous parameters as predictors of visual acuity following MH surgery, including the calculated pore shape factors, such as HFF[21], MHI[22], and THI[23]. Similarly, our research focuses on the crucial parameter of THI which reflects the balance between vertical and horizontal tensile forces, and is directly related to the mechanical state of the vitreoretinal interface. A high THI may be indicative of a vertical-traction-dominant fissure, with an especially potential for closure following the surgical release of traction.

Furthermore, our study primarily concentrated on a novel parameter, Vi, derived from two-dimensional parameters. Nevertheless, statistical analyses revealed that Vi possesses independence distinct from the other two-dimensional parameters, suggesting that it is utilized to forecast postoperative BCVA. Past research has also conducted quantitative analyses based on three-dimensional structural parameters. Geng *et al*[6] discovered that the area ratio factor (ARF) of the MH, compared to the MHI and HFF, can effectively capture the three-dimensional characteristics of an MH, providing superior sensitivity and specificity. Consequently, ARF may be the most effective parameter for use in predicting the visual outcomes of MH surgery. Recent studies have revealed a stronger correlation between automated MH volume and 1-year postoperative visual acuity changes than with the traditional minimum linear diameter[24]. Our approach diverges from conventional methods, we integrated BD, MD, and H_{MD} into volume parameters to enhance the prediction of postoperative visual acuity. A notable advantage of this method is its independence from sophisticated software, making it more accessible for widespread adoption. In alignment with these findings, our study also demonstrated a robust linear correlation between Vi of MH and postoperative visual prognosis. However, there is a limitation in this regard due to potential errors in volume calculation, which may influence this measure's predictive accuracy.

In addition, several other confounding factors may influence BCVA following MH surgery. These include the extent of peeling in ILM, the surgical technique selected, the cross-sectional area of the interlayer vesicles within the MH.

1) Some studies found no significant difference in the complete closure rate after ILM dissection between <2 DDs and >2 DDs, but more extensive ILM stripping might be more beneficial for larger MH[25-26]. Based on our research findings, we also identified a correlation between postoperative BCVA and the diameter of the excised ILM; however, the effect was relatively insignificant. This could be attributed to our selection of patients within the 2–4 DDs spectrum for the ILM removal procedure to mitigate its potential impact on visual health.

2) In recent years, the surgical approach to large full-thickness MH has advanced beyond the standard peeling of the ILM to include techniques such as the inverted ILM flap[27], pedicle transposition flap, inverted flap, free flap[28], and the preservation of the macular fovea[29]. To eliminate confounding

factors associated with surgical techniques, we only included patients who underwent standard ILM surgery peeling in our analysis.

3) In the research conducted by Ozturk *et al*[30], cystic change area (CA) represented the cross-sectional area of the interlayer vesicles within the MH, whereas MH area depicted the cross-sectional area of the MH itself. This paper introduces a new parameter, Vi, which primarily quantifies the Vi of the MH. Distinct from CA, we posit that the cross-sectional area of vesicles in the horizontal section of the macula exhibits a degree of variability. However, this may also serve as an indicator of the tensile force exerted by the MH. It is important to note that our study did not incorporate the cystic space. Future research is warranted to explore the potential benefits of including this cystic space to enhance both predictive and clinical relevance.

Upon examining the abovementioned factors and the prediction model, we have reached the following conclusions: 1) elevated preoperative BCVA may indicate a higher survival rate on the part of photoreceptors and enhanced compensatory capacity on the part of the patient's retina; 2) a higher THI for the hole (dominated by vertical traction) indicates that following vitrectomy to relieve traction, there is greater potential for anatomical reduction; 3) the Vi of MH corresponds more accurately to the core area of macular structure. The higher the value, the more severe the loss of photoreceptor cells, and the greater the difficulty of repairing the outer retinal structure (EZ distance) after surgery. The correlation between these three indicators is low [variance inflation factor (VIF)<2.0], contributing predictive information from three independent dimensions (function, mechanics and anatomy), thereby avoiding model overfitting caused by multicollinearity.

Their interaction enhances the ability to predict results and make decisions, such as high THI and low Vi indicating good anatomical reduction after tension release, mild photoreceptor damage, and great potential for visual recovery. However, the impact of HFF, DHI, and MHI may have been diminished by THI (height/diameter) and Vi (volume distribution), resulting in insignificant contributions on their part. The indicators used in this study, which are without additional three dimensional reconstruction software, make them more suitable for adoption in primary hospitals. The next step is to use a nomogram or online calculator to input THI, Vi, and preoperative visual acuity and directly output the postoperative visual acuity probability for clinical translation.

In recent years, machine learning has emerged as a power tool that can be trained to utilize statistically significant explanatory variables to predict subjective variables and analyze intricate relationships between multiple variables. Specifically, in terms of visual prognosis following MH surgery, the incorporation of deep learning technology has significantly enhanced predictive accuracy regarding visual improvement. One notable study developed automated framework-leveraging deep learning to forecast visual acuity post-MH surgery using SD-OCT images, yielding high-precision outcomes[31]. By quantifying the macular area's microstructure and employing automated quantitative analysis tools, the sustained impacts of surgery can be evaluated with increased precision[3,32-34]. In the context of these developments, our study was intended to offer parameters for the application of deep learning analysis to MH, with the goal of enhancing the comprehensibility of the findings.

Our study had some limitations. The first limitation was the small sample size, and the second was the lack of multicenter data. Furthermore, its retrospective design may have influenced the outcomes, thereby affecting the generalizability of the conclusions. A notable limitation of this study was the absence of external validation for the current model. It did not utilize internal validation procedures like cross-validation, and also did not use external datasets for testing purposes. Therefore, further prospective studies are warranted to confirm our findings in larger, ethnically diverse populations with extended follow-up periods. Long-term follow-up studies are necessary to ascertain the enduring effects of preoperative factors on postoperative visual acuity. Future research should endeavor to further validate the findings of this study through practical application.

In summary, our study has identified significant predictors of postoperative visual acuity in patients who underwent surgery for IMH. This study emphasizes the significance of the preoperative evaluation of these factors to improve visual outcomes. These findings suggest that the quality of patient management and clinical decision-making can be improved by paying attention to the relevant factors identified in this study. Further research is required to overcome the limitations of this study by validating the results in a larger population with more heterogeneity. Such efforts would contribute to the more profound comprehension of the outcomes associated with MH.

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Data Availability: All data pertinent to the study are either included within the article or provided as supplementary information. The datasets generated and/or analyzed during the current study are not publicly accessible, but are available from the corresponding author upon reasonable request.

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