Health Leadership and Quality of Life. 2025; 4:820
doi: 10.56294/hl2025820

ORIGINAL

Effect of Vitreoretinal Surgery Combined with Platelet-Rich Plasma on the Quality of Life of Patients with Macular Hole

Efecto de la cirugía vitreorretiniana combinada con plasma rico en plaquetas en la calidad de vida de pacientes con agujero macular

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Cite as: Kyrykbayev D. Effect of Vitreoretinal Surgery Combined with Platelet-Rich Plasma on the Quality of Life of Patients with Macular Hole. Health Leadership and Quality of Life. 2025; 4:820. https://doi.org/10.56294/hl2025820

Submitted: 01-10-2024 **Revised:** 20-02-2025 **Accepted:** 28-08-2025 **Published:** 29-08-2025

Editor: PhD. Neela Satheesh

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ABSTRACT

Introduction: this study evaluates the impact of pars plana vitrectomy (PPV) combined with internal limiting membrane (ILM) peeling and platelet-rich plasma (PRP) application on anatomical, functional, and quality-of-life (QoL) outcomes in patients with macular holes.
Method: prospective cohort study. Tertiary eye care center, January 2021 to December 2023. A total of 155 patients underwent PPV with ILM peeling and PRP. Visual acuity (logMAR), macular hole closure, and QoL were assessed pre- and postoperatively. QoL evaluation used a localized adaptation of the NEI VFQ-25 questionnaire. Anatomical outcomes were measured by Optical Coherence Tomography (OCT).
Results: the mean age was 65,90 ± 8,84 years; 38 % were female. The closure rate was 94 %. Visual acuity improved significantly, with average logMAR improving from 0,7 to 0,3 ($p < 0,001$). QoL scores improved across all domains: visual functioning increased from 55,3 to 85,7, daily activities from 48,2 to 80,4, and psychological well-being from 50,1 to 82,9. Patients reported greater independence and improved ability in activities like reading, recognizing faces, and participating in sports.
Conclusion: PPV with ILM peeling and PRP is highly effective for macular holes, yielding strong anatomical and functional outcomes alongside significant QoL enhancements.

Keywords: Macular Hole; Pars Plana Vitrectomy; Internal Limiting Membrane Peel; Platelet-Rich Plasma, Quality of Life, Ophthalmic Surgery.

RESUMEN

Introducción: este estudio evalúa el impacto de la vitrectomía pars plana (VPP) combinada con el pelado de la membrana limitante interna (MLI) y la aplicación de plasma rico en plaquetas (PRP) sobre los resultados anatómicos, funcionales y la calidad de vida (CdV) en pacientes con agujero macular (AM).
Método: se llevó a cabo un estudio prospectivo de cohortes en un centro oftalmológico terciario entre enero de 2021 y diciembre de 2023. Un total de 155 pacientes con diagnóstico de AM fueron intervenidos mediante VPP con pelado de la MLI y aplicación intraocular de PRP. Se evaluaron la agudeza visual (logMAR), la tasa de cierre del AM mediante tomografía de coherencia óptica (OCT) y la CdV antes y después de la cirugía. La CdV se midió utilizando una adaptación regional del cuestionario NEI VFQ-25, centrada en la funcionalidad visual, autonomía y bienestar psicológico.
Resultados: la edad media de los pacientes fue de 65,9 ± 8,8 años, con un 38 % de mujeres. Se logró una tasa de cierre anatómico del 94 %. La agudeza visual mejoró significativamente, de un logMAR medio de 0,7 a 0,3 ($p < 0,001$). Las puntuaciones de CdV aumentaron en todas las dimensiones, reflejando mejoras en lectura, reconocimiento facial, movilidad y práctica deportiva.

Conclusión: La VPP combinada con pelado de la MLI y PRP representa una estrategia eficaz para el tratamiento del AM, proporcionando resultados anatómicos y funcionales favorables, y una mejora significativa en la calidad de vida visual y general del paciente.

Palabras clave: Agujero Macular; Vitrectomía Pars Plana; Pelado de la Membrana Limitante Interna; Plasma Rico en Plaquetas; Calidad de Vida; Cirugía Oftálmica.

INTRODUCTION

The emergence of contemporary ocular microsurgery has transformed the treatment of macular holes.[1] Innovations like internal limiting membrane (ILM) staining agents, high-frequency vitrectomy cutters, pars plana vitrectomy (PPV) and adjuvant treatments such as platelet-rich plasma (PRP) have improved surgical accuracy and results.[2,3] Anatomical success rates, characterized by macular hole closure, currently surpass 90 % in several trials; nonetheless, the relationship between closure and functional recovery remains intricate.[4] Preoperative macular hole size, symptom duration, and postoperative retinal remodeling greatly affect visual prognosis.[5] Moreover, in addition to visual acuity, quality of life (QoL) outcomes are widely acknowledged as essential indicators for assessing surgical effectiveness.[6] Nevertheless, few studies have thoroughly evaluated the psychological and functional aspects of quality-of-life post-macular hole surgery, underscoring a significant deficiency in literature.

Macular holes are a major contributor to visual impairment and blindness, especially in older persons, impacting daily functioning and QoL.[7] Full-thick abnormalities in the central retina compromise the anatomical and functional integrity of the macula, resulting in a progressive and sometimes permanent decline in visual acuity if untreated. The pathophysiology of macular holes is complex, with the primary cause being vitreomacular traction pressures due to partial posterior vitreous detachment. With the passage of time, these pressures induce retinal damage, resulting in a macular hole. Notwithstanding their clinical importance, macular holes are often underdiagnosed in the first phases, sometimes advancing to significant vision impairment prior to patients pursuing medical treatment.[8,9]

In recent decades, the care of macular holes has significantly evolved, mostly because of breakthroughs in ocular surgical procedures.[10] Historically, macular holes were deemed untreatable, resulting in individuals enduring irreversible visual impairment. The advent of pars plana vitrectomy (PPV) in the 1980s transformed the discipline, providing an effective surgical remedy for macular hole repair.[11] This procedure, entailing the excision of the vitreous gel to alleviate traction stresses, has subsequently established itself as the gold standard for macular hole healing.[12] Subsequent enhancements, such as ILM peeling, have significantly improved surgical results, attaining closure rates of 90 % in the majority of instances.[13,14] These advancements have redirected research and therapeutic practice from only attaining anatomical success to enhancing functional recovery and patient satisfaction.

The evolution of ocular microsurgery has revolutionized macular hole treatment, with innovations like ILM staining, advanced vitrectomy cutters, and PRP, improving surgical precision and outcomes. Despite anatomical success rates exceeding 90 %, functional recovery and QoL outcomes remain underexplored, highlighting a gap in current research. Macular holes, primarily caused by vitreomacular traction, significantly impair vision and daily functioning, particularly in older adults, but advancements such as PPV and ILM peeling have transformed care, shifting focus from anatomical repair to patient-centric recovery.

The Role of Pars Plana Vitrectomy in Macular Hole Repair

PPV has developed into a refined surgical technique using high-precision devices and methodologies to enhance both anatomical and functional results.[15] ILM peeling, often performed during the PPV technique, has shown efficacy in promoting macular hole closure.[13] The ILM, a delicate foundation membrane on the retinal surface, is carefully excised to eradicate residual traction pressures and facilitate retinal glial growth, hence assisting in the closure of macular holes. This method has several obstacles. ILM peeling requires extraordinary surgical expertise, since inadequate management may lead to retinal injury or incomplete excision, hence jeopardising surgical results. Technological advancements, including the creation of ILM staining agents like trypan blue, have reduced these hazards by improving the surgeon's capacity to see and excise the ILM precisely.[16]

Recent advancements have enhanced the treatment repertoire for macular hole surgery. PRP has attracted considerable interest in its ability to improve postoperative recovery. PRP, obtained from the patient's blood, is abundant in growth factors that facilitate cellular regeneration and tissue repair.[17] When administered intravitreally, PRP establishes a scaffold for retinal glial cell proliferation, facilitating the closure of the macular hole.[18] Initial research indicates that PRP not only aids in the healing of macular holes but may also enhance

visual and functional results.[19,20] Nonetheless, the incorporation of PRP into standard clinical practice is still restricted, necessitating more study to confirm its effectiveness and safety across various patient demographics.

Beyond Anatomical Success and the Importance of QoL Outcomes

Although increased retinal hole closure rates demonstrate the efficacy of modern surgical techniques, anatomical success does not always result in significant improvements in visual function or quality of life.[21] Vision impairment linked to macular holes transcends diminished visual acuity; it impacts patients' capacity to engage in daily activities such as reading, driving, and facial recognition. The psychological effects of vision loss, such as diminished independence, sadness, and anxiety, highlight the need for comprehensive patient care strategies. Notwithstanding these factors, quality of life outcomes are often disregarded in treatment studies, which typically emphasize objective metrics like closure rates and visual acuity.[22] QoL evaluations, which reflect patients' subjective perceptions of vision-related handicaps, provide significant insights into the overall effects of surgical procedures. These evaluations include areas such as visual capability, social interaction, mental health, and autonomy. Integrating QoL measurements into clinical research corresponds with the increasing focus on patient-centered care, guaranteeing that treatment choices are informed by patients' priorities.[23] The research on quality-of-life outcomes after macular hole repair is limited, indicating a significant gap in comprehending the whole range of advantages and disadvantages linked to these surgeries.

METHOD

Type of Study, Period, and Location

This single-center, prospective cohort research was undertaken at the Kazakh Eye Research Institute, a tertiary eye care institution in Almaty, Kazakhstan. The study period extended from January 2021 to December 2023.

Population, Sample, and Sampling Type

The study population consisted of patients clinically diagnosed with a full-thickness macular hole and referred for surgical treatment at the Kazakh Eye Research Institute. A total of 155 patients were consecutively recruited using a non-probabilistic, consecutive sampling method.

All patients had PPV accompanied by ILM peel, executed by the same surgeon (G.Zh.). The surgical apparatus used was the Constellation Vision System (Alcon, Switzerland), which operated at a frequency of 5 000-10 000 cuts per minute at a vacuum level of up to 650 mmHg. ILM staining was performed using a 0,15 % trypan blue ophthalmic solution (MembraneBlue, DORC, Netherlands), and the stained ILM was meticulously excised with Alcon Grieshaber 25GA+ and 27GA+ forceps (Switzerland).

All patients were administered PRP to facilitate the closure of the retinal hole. Following the drying of the retina, 0,05 ml of autologous PRP, previously derived from the patient's venous blood via the YCEBIO-KIT and a centrifuge, was intravitreally injected into the macular region via a 27G cannula. The distal end of the cannula was positioned superior to the rupture zone. The procedure was completed by normotension and air tamponade of the vitreous cavity.

Inclusion Criteria:

- Age ≥ 18 years.
- Clinical and Optical Coherence Tomography (OCT) confirmation of a full-thickness macular hole.
- Willingness to undergo pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peeling and platelet-rich plasma (PRP) application.
- Provision of written informed consent.

Exclusion Criteria:

- History of previous vitreoretinal surgery in the study eye.
- Presence of other significant ocular comorbidities affecting the macula (e.g., diabetic macular edema, advanced age-related macular degeneration).
- Active ocular infection or uncontrolled systemic disease.

Exit Criteria:

- Withdrawal of consent during the study.
- Intraoperative complications precluding PRP application or ILM peeling.
- Loss to follow-up before postoperative evaluation.

Surgical Procedure

To ensure procedural homogeneity, one surgeon (G.Zh.) performed PPV with ILM peeling on all patients.

With vacuum pressure up to 650 mmHg, the Constellation Vision System (Alcon, Switzerland) made 5 000–10 000 cuts per minute. ILM staining used 0,15 % trypan blue ophthalmic solution (MembraneBlue, DORC, Netherlands). The stained internal limiting membrane was carefully removed with Alcon Grieshaber 25- and 27-gauge forceps.

Platelet-Rich Plasma (PRP) Application

Patients' venous blood was centrifuged to make autologous PRP, which was injected intravitreally into the macular area (0,05 ml). A 27G cannula was inserted above the rupture zone for precise dosing. The therapy ended with air tamponade and normotension.

Quality of Life and Visual Function Assessment

QoL and visual function were assessed using an adapted questionnaire for visual function indicators specifically designed for the population of Kazakhstan. This questionnaire was based on the NEI VFQ-25 scoring method but was customized to better reflect the visual challenges and daily activities relevant to the local population. The assessment was conducted preoperatively and one year postoperatively to evaluate the impact of the surgical intervention on patients' quality of life and visual function. The adapted NEI VFQ-25 questionnaire was translated using a forward-backward method, reviewed by a multidisciplinary expert panel for content validity, and pilot-tested with 20 macular hole patients to ensure cultural relevance and clarity. Internal consistency was assessed with Cronbach's alpha (target ≥0,70), and test-retest reliability was evaluated in a stable subgroup using intraclass correlation coefficients. Construct validity was examined through exploratory factor analysis for structural validity and by testing convergent hypotheses with BCVA and known-groups comparisons. The final version demonstrated acceptable reliability and validity for use in the Kazakh population.

Macular measurements were performed using Optical Coherence Tomography (OCT) preoperatively and one year after surgery to assess anatomical outcomes.

Ethical Aspects

The study adhered to the principles of the Declaration of Helsinki and received approval from the Local Ethics Committee of the Kazakh Eye Research Institute. Written informed consent was obtained from all participants before enrollment, including consent for surgical procedures and use of anonymized data for research purposes.

RESULTS

Patient Demographics and Clinical Characteristics

The research included 155 patients, with a mean age of 65,90 ± 8,84 years. The sample exhibited a feminine preponderance, including 6,2 % male and 38 % females (table 1). This gender distribution corresponds with prior research indicating that women are more susceptible to macular hole development, perhaps owing to physical or hormonal disparities. All patients were clinically diagnosed with a macular hole.

Preoperative Visibility

The mean visibility before surgery was very low at 0,068 ± 0,077. This number highlights the extent of visual deterioration among patients before treatments. Following surgery, sight increased to 0,187 ± 0,155, indicating a substantial gain in functional visual ability (table 1). The significant improvement in vision indicates that the used surgical method, which integrates PPV with internal limiting membrane peeling and PRP injection, successfully reinstated retinal integrity.

Table 1. Demographic characteristics of patients

Parameters	Value (Mean ± SD)	p-value
Age (years), mean ±SD	65,90±8,84	
Male: female	62:38	
Axial eye length (mm)	23,60±1,04	
Visual acuity (logMAR), pre-surgery	0,068±0,077	0,001
Visual acuity (logMAR), post-surgery	0,187±0,155	

Quality-of-Life Improvements

A notable discovery was the considerable improvement in several QoL categories post-surgery. Preoperative visual impairment significantly impacted the participants' capacity to execute everyday tasks, their psychological well-being, and visual functionality. Post-surgery significant improvements were seen in several areas, as shown below.

Visual Functioning

Visual functional scores increased from a preoperative mean of 55,3 to 85,7 postoperatively (table 2).

Table 2. Improvements in Quality-of-Life Domains

Domain	Mean Score Before Surgery	Mean Score After Surgery
Visual functioning	55,3±10,02	85,7±6,87
Daily activities	48,2±9,56	80,4±8,12
Psychological well-being	50,1±8,65	82,9±9,15

This signifies that most patients regained functional vision, allowing them to do activities necessitating visual accuracy. This enhancement highlights the efficacy of surgical surgery in mitigating the impact of visual impairment caused by macular holes.

Daily Activities

Scores for everyday activities rose significantly from 48,2 to 80,4 (table 2). Activities like perusing periodicals, discerning goods on congested shelves, and identifying individuals from a distance got much simpler for the majority of patients. The restoration of these capacities is essential for promoting autonomy and enhancing quality of life.

Psychological Well-Being

Psychological evaluations showed a significant rise from 50,1 preoperatively to 82,9 postoperatively (Table 2). Prior to surgery, several patients articulated sentiments of dissatisfaction, a sense of loss of autonomy, and dependence stemming from their visual impairments. Post-surgery, these emotions were significantly diminished, indicating a substantial effect on mental health.

Detailed QoL Parameter Analysis

The comprehensive examination of quality-of-life (QoL) metrics indicated substantial improvements in several facets of patients' everyday existence and psychological health post-surgery. Prior to surgery, patients indicated significant difficulties in executing tasks necessitating visual acuity, such reading, pursuing hobbies, identifying faces, or partaking in social interactions. These obstacles adversely affected their functional independence and fostered emotions of dissatisfaction, reliance, and diminished control over their life. Postoperatively, practically all parameters exhibited significant enhancement, indicating the profound effect of the surgical procedure.

Significant improvement was seen in close vision tasks, including reading plain text, cooking, crocheting, and repairing things, with scores rising from a mean of 59,51 pre-surgery to 84,03 post-surgery (table 3).

Table 3. Detailed Analysis of QoL Parameters

QoL Parameter	Pre-Surgery Mean	Post-Surgery Mean
Reading plain text	61,61±10,82	64,03±10,05
Work/hobbies requiring near vision	59,51±5,12	84,03±5,61
Recognizing people across the room	83,71±6,25	89,03±7,26
Watching TV	72,90±9,12	95,94±9,05
Sports participation	64,69±7,06	79,19±8,25
Psychological control over actions	47,41±8,15	73,54±7,25

This enhancement underscores the patients' restored capacity to participate in daily and leisure activities essential for preserving autonomy and productivity. The capacity to identify individuals from a distance increased from 83,71 to 89,03, which is notably important for improving social interactions and mitigating the stigma often linked to visual impairments.

Engagement in active sports and other physical activities rose, with scores increasing from 64,69 preoperatively to 79,19 postoperatively. This transition highlights the significance of vision restoration in allowing people to engage in physically active and rewarding lifestyles. Viewing television, a prevalent recreational pursuit became much more accessible, as shown by a rise in scores from 72,90 to 95,94. Improvements in recreational participation indicate larger benefits in patients' overall quality of life.

The psychological markers significantly improved. A significant number of patients reported a diminished sense of control over their activities before surgery, with a mean score of 47,41, which increased to 73,54 after the procedure. This indicates that the restoration of visual function was crucial in restoring confidence and diminishing reliance on others. Emotions of disappointment and shame stemming from inadequate vision markedly decreased, as shown by improved ratings. The concern for actions that can cause embarrassment to oneself, or others decreased from 69,35 to 52,10 (table 3).

Pre-surgery pain or discomfort, identified as a major obstacle, showed marginal enhancement, rising from 64,67 to 70,16 (table 3). This may indicate lingering pain for some individuals, possibly associated with the transient consequences of surgical recovery rather than persistent vision impairment. The data indicates that patients received both functional and psychological comfort, emphasising the comprehensive advantages of macular hole repair.

The thorough investigation of QoL parameters offers an extensive perspective on how vision restoration enhances practical capabilities while also mitigating the psychological and social difficulties encountered by persons with macular holes. These enhancements illustrate the efficacy of the surgical procedure in achieving patient-centered results that are beyond mere anatomical repair.

DISCUSSION

Macular holes represent a significant clinical challenge, leading to substantial visual impairment, particularly in older individuals.[7] The findings of this research shed light on the major influence that macular hole surgery has on the visual function, QoL, and psychological well-being of patients. Underscoring the efficacy of PPV combined with ILM peeling and PRP injection, the findings are consistent with the existing literature, demonstrating that the macular hole closure rate was 94 %. Additionally, the findings demonstrated notable improvements in visual acuity, daily activities, and emotional stability.

The macular hole closure rate of 94 % that was observed in this research is consistent with the findings of other studies that have been published in the past and indicate closure rates ranging from 90 % to 98 % after PPV and ILM peeling. As an example, Michalewska et al.[24] reported closure rates of 95 % in instances that were treated with ILM peeling. They attributed this success to the technique's capacity to alleviate tangential tension and encourage glial cell proliferation for the purpose of closing the macular hole. In a similar vein, previous studies have shown that adjuvant therapy, such as platelet-rich plasma (PRP), which was used in this research, further improve closure rates by establishing a biological framework for retinal restoration. The results of our study lend credence to the notion that platelet-rich plasma (PRP) is an advantageous adjunct to macular hole repair. However, the precise extent to which it contributes to closure rates requires more randomised controlled studies.

After the operation, the patient's visual acuity increased dramatically from a mean value of 0,3 (logMAR) before the procedure to 0,7 (logMAR) after the procedure. This degree of improvement is comparable to the findings that were reported in trials that were quite similar. In one of the primary studies on PPV for macular holes, Scott et al.[25] found an average improvement of two or more lines in visual acuity on the Snellen chart for the majority of patients. This improvement was seen in the majority of patients. Furthermore, according to the findings of a meta-analysis conducted by Ezra et al.[26] 75 % of patients were able to achieve a substantial functional recovery after undergoing surgery. The fact that our results are consistent with those of earlier published publications lends credence to the idea that macular hole surgery may consistently restore functional vision. This is especially true when accomplished via the use of sophisticated surgical methods and complementary treatments. In this particular research, the increases in QoL ratings were among the most striking results since they highlight the advantages that surgery provides in the real world. Visual impairment that was present before the surgery had a significant influence on the patients' capacity to carry out everyday activities, participate in hobbies, and keep their mental health in good standing. Immediately after the surgical procedure, the ratings for visual functioning climbed from 55,3 to 85,7, while the scores for psychological well-being increased from 50,1 to 82,9. The results of this study are consistent with the findings of Tranos et al.[27], who found that QoL indices such as independence, emotional stability, and involvement in social activities dramatically improved after successful macular hole repair. The study highlights recovery domains that remain underexplored, namely patients' ability to recognize faces, participate in sports, and resume domestic responsibilities. Findings suggest that improvements in these areas constitute a component of comprehensive rehabilitation outcomes. By contributing to developing awareness of how surgical therapies address the larger psychological consequences of vision loss, our results contribute to the advancement of this understanding. The remarkable improvement in psychological indicators that patients experienced after surgery is a component of this research that deserves special attention. The feelings of diminished control over one's activities, dependence on other people, and shame brought on by impaired eyesight were significantly improved. Similar tendencies were recorded by Neffendorf et al.[28], who found that patients who had PPV for macular holes experienced less psychological anguish than those who did not have the procedure. Due to the

fact that psychological evaluations provide a more comprehensive perspective on the recuperation process of patients, the increase in QoL ratings underscores the significance of including psychological evaluations in studies that evaluate the results of ocular procedures.

In the context of this investigation, the use of PRP as an adjuvant treatment offers a relatively unique method to improve surgical results. In spite of the fact that PRP has been investigated largely in the context of orthopaedic procedures and wound healing, its use in ophthalmology is garnering increasing interest. There is a belief that the growth factors found in PRP boost macular closure rates and promote retaining repair. Zheng et al.[29] conducted research not too long ago that indicated that PRP accelerates the healing process by fostering an environment that is favourable for the proliferation and migration of cells. These findings are supported by our findings, which indicate that PRP may be an advantageous supplement to the conventional macular hole surgical approaches. Similar regenerative effects have been demonstrated in neuromuscular models, where adipose-derived mesenchymal stromal cell therapy significantly enhanced muscle contractility and delayed fatigue in hereditary peripheral neuropathy.[30]

Unexpectedly, some patients did not experience the anticipated degree of improvement in visual acuity, despite successful anatomical closure of the macular hole. This discrepancy may be attributed to factors such as preoperative macular hole size, duration of symptoms, or the extent of postoperative retinal remodeling. Previous studies have similarly noted that larger macular holes or delayed interventions often result in suboptimal functional recovery. These findings highlight the importance of early diagnosis and intervention to maximize surgical outcomes.[31]

The scientific novelty of this study lies in its holistic approach to evaluating macular hole surgery outcomes. By integrating assessments of visual acuity, QoL, and psychological well-being, this research provides a comprehensive understanding of the benefits and limitations of current surgical techniques. Additionally, the study contributes valuable insights into the potential role of PRP as adjuvant therapy in ophthalmology, an area that has been predominantly explored in orthopedic and wound healing contexts. By demonstrating the feasibility and efficacy of PRP in enhancing retinal repair, this research opens avenues for further investigation into its broader applications in ocular surgery.

Limitations

This research contains a number of shortcomings, despite the fact that the findings are optimistic. The first limitation is that the research was conducted at a single centre, and the patient group was very similar. This may make it difficult to generalise the results of the study. It is necessary to conduct multicenter research with populations that are both bigger and more varied in order to verify the results. Second, while the use of PRP seems to have a great deal of promise, the particular contribution that it makes to the enhancement of quality of life and closure rates was not isolated in this investigation. It is crucial to conduct future randomised controlled studies that compare PPV with and without PRP in order to determine the effectiveness of this treatment. Furthermore, in order to assess the durability of functional and anatomical results, it is necessary to conduct long-term follow-up with a duration of more than one year.

CONCLUSIONS

The results of this research provide more evidence that macular hole surgery is beneficial in enhancing both morphological and functional outcomes, while also drawing attention to the wider quality of life advantages that it offers to patients. A significant improvement in both day-to-day activity and psychological well-being may be achieved via the use of cutting-edge procedures like ILM peeling and PRP injection, which together lead to high closure rates. The dependability of these findings is highlighted by comparison with the current body of literature, which also highlights the possibility for future optimisation of surgical techniques is highlighted. In the future, the incorporation of patient-centered measures and adjuvant treatments such as PRP into conventional therapy has the potential to greatly improve the overall effectiveness of macular hole care.

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ETHICAL APPROVAL

The study was conducted in accordance with ethical standards and approved by the Local Ethics Committee of Kazakh Medical University “KSPH”, Protocol № IRB-A356, № 20-08-92514, dated 05.01.2023.

DATA AVAILABILITY STATEMENT

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

CONFLICTS OF INTEREST

The author declares no conflict of interest.

FUNDING

This research received no external funding.

ACKNOWLEDGMENTS

The author would like to thank the Kazakh Scientific Research Institute of Eye Diseases for institutional support.

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https://doi.org/10.56294/hl2025820 ISSN: 3008-8488