# Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE DOI: 10.53555/05r5mp60

# COMPARATIVE STUDY OF MACULAR HOLE (MH) SURGERY: INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE VS. AMNIOTIC MEMBRANE GRAFT

Nida Khalid<sup>1</sup>, Anusheh Khalid Waheed<sup>2</sup>, Mustafa Khalid Waheed<sup>3</sup>, Nouman Aleem<sup>4</sup>, Amna Rizwan<sup>5</sup>, Muhammad Ayub Khan<sup>6\*</sup>

<sup>1,4</sup>Department of Ophthalmology, Mayo Hospital, Lahore, Pakistan
 <sup>2</sup>Department of Ophthalmology, Services Hospital, Lahore, Pakistan
 <sup>3</sup>Department of Ophthalmology, Lahore Medical and Dental College, Lahore, Pakistan
 <sup>5</sup>Department of Ophthalmology, Avicenna Medical College, Lahore, Pakistan
 <sup>6\*</sup>Department of Ophthalmology, Gomal Medical College, Dera Ismail Khan, Pakistan

\*Corresponding Author: Muhammad Ayub Khan
\*Department of Ophthalmology, Gomal Medical College, Dera Ismail Khan, Pakistan
Email: drayub2310@gmail.com

# **ABSTRACT**

**Background:** Macular holes remain difficult to treat, despite advancements.

**Methodology:** This study has a prospective cohort, comparative study design. The study lasted for 6 months. The study was conducted in the Mayo Hospital, Lahore. 20 patients were included in the study who had macular hole surgery, 10 in each group (ILM Flap and AMG). IBM SPSS 27 v. was used to analyse the data. An independent sample t-test was used to compare the means of two independent groups (ILM flap and AMG) on a continuous dependent variable (BCVA postoperative).

**Results:** The mean age (Mean=65.85 years) with SD=5.95. Females formed a larger proportion of the sample (65%) than males (35%). The internal limiting membrane flap group had a significantly higher mean ETDRS score (Mean=64.84, SD=5.18) than the AMG (Mean=49.78, SD=3.05), p<0.001. 69.2% of study participants with poor satisfaction reported improved quality of life (QoL), compared to 28.6% in the high satisfaction group, with p =0.073.

**Conclusion:** This comparative study demonstrates a significant difference between anatomical success and patient-reported outcomes in MH surgery. The unanticipated inverse association between satisfaction and perceived quality of life (QoL) improvement indicated that psychological variables and disappointed expectations may have a significant impact on postoperative experiences in addition to quantitative visual outcomes.

Key Words ILM flap, Amniotic Graft, Macular holes, Retinal Detachment.

# INTRODUCTION

Macular hole (MH) is an interface of a vitreoretinal illness that can cause blurring of vision(1)Presently, both diagnosis and follow-up following treatment have become definite, both clinically and by using optical coherence tomography (2). Metamorphosia and visual distortion frequently present symptoms caused by central foveal involvement, which may be reversible with complete anatomical closure during surgery.

An idiopathic macular hole is often present. Involvement of both eyes varies greatly from 2 percent to 8 percent, although no conclusive systemic relationship has been established. Females are more likely to participate. The male-to-female ratio was 1:3, in their 6<sup>th</sup> or 7<sup>th</sup> decade of life.(2)It has been proposed that macular holes are caused by both tangential and anterior-posterior vitreoretinal traction of the parafovea. They have been observed during anterior segment laser surgeries, probably because of vitreomacular adhesion traction. MHs are often found in individuals aged greater than 60 years age, and females are commonly affected than males. (3)

MHs affect 3.3 out of every 10.00 individuals over the age of 55, usually in their 6<sup>th</sup> or 7<sup>th</sup> decade, with approximately 2/3 being female. Nearly 50% of MHs are classified as large, with a minimum linear diameter >400 micrometres upon diagnosis.(4). In a prospective experiment, a study was carried out by Michalewska et al. (5) discovered that the anatomical closure rate was greater when employing a new method of inverted internal limiting membrane flap technique than the usual process with ILM peeling for the treatment of large macular holes. Prospective VA was considerably greater when utilising the new approach.(6,7). Large, chronic, or myopic macular holes have increased failure rates due to inadequate glial cell growth and sustained tangential traction.(8,9).

One of the studies examined surgical approaches for treating large idiopathic MHs, including autologous internal limiting membrane flaps, amniotic grafts, lens capsule flaps, platelet plasma, and scleral buckling.(10). Michalewska et al.(5) pioneered the autologous ILM flap approach, which repositions the peeled ILM over the macular hole to scaffold glial cells' migration (11). Amniotic membrane grafts, which are rich in growth regulators and cytokines that inhibit inflammation, serve as a biological scaffold that promotes tissue regeneration and reduces fibrosis.(12)Patients with recurring retinal holes frequently undergo pars plana vitrectomy more than once. Thus, the macular region in these patients may not have an appropriate ILM (13–15).

This aims to compare macular hole surgery by using techniques ILM flap and amniotic graft techniques.

#### **METHODOLOGY**

This prospective, comparative study evaluated surgical outcomes in patients with MHs, recruiting a total of 20 patients over 6 months. The study was conducted in the Mayo Hospital, Lahore. The institutional review board (IRB) provided ethical approval to collect data, and all study participants were provided written informed consent in both their native language and English, guaranteeing complete understanding of the procedures involved. Individuals over 18 years with idiopathic, primary, or macular holes with a minimum linear diameter higher than 400 micrometres were included in the study. Patients having macular holes accompanied by retinal detachment (RD), a history of past macular hole surgery, or media opacities that prevented high-quality OCT imaging were excluded from the study.

A calculated sample size of 20 patients, with 10 in each group, was included to provide 80% statistical power to identify a 30% difference in anatomical closure rates at a 5% significance level based upon effect sizes in a previous study.(13). A convenience sampling method was used.

Study participants were advised to remain face-down for 5 to 7 days post-surgery to ensure proper graft placement and MH closure. IBM SPSS 27 was used to analyse statistical data. An independent sample t-test was used to compare postoperative ETDRS VA between the Internal limiting membrane (ILM) flap and AMG. A paired t-test was used to compare the preoperative and postoperative ETDRS VA. The chi-square test was used to find the comparison between categorical variables. Ordinal logistic Regression was used to predict the overall satisfaction level.

# **RESULTS**

Table 1 reveals the baseline demographic and clinical characteristics of the study participants (N=20). The mean age (Mean=65.85 years) with SD=5.95. Females formed a larger proportion of the sample (65%) than males (35%). The left eye (55%) was more commonly affected than the right

eye (45%). Most of the patients reported symptoms lasting more than three months, and prevalent comorbidities included HTN (60%), Diabetic mellitus (25%), and IHD (50%).

**Table 1: Demographics and Clinical Features of Study Participants** 

Variable	Frequency (n)	Percent	Minimum	Maximum	Mean	Std. Deviation
Age	20		56	74	65.85	5.950
Gender Distribution						
Male Patients	7	35.0 %				
Female Patients	13	65.0 %				
Affected Eye						
• RE	9	45.0 %				
• LE	11	55.0 %				
<b>Duration of Symptoms</b>						
<1 month	4	20.0 %				
1-3 months	3	15.0 %				
3-6 months	7	35.0 %				
>6 months	6	30.0 %				
Comorbidity of Diabetes						
Yes	7	35.0%				
No	13	65.0%				
Comorbidity of HTN						
Yes	12	60.0%				
No	8	40.0%				
Comorbidity of IHD						
Yes	10	50.0%				
No	10	50.0%				

Table 2 compares the postoperative ETRS VA of patients treated with the internal limiting membrane flap and the amniotic graft techniques. The internal limiting membrane flap group had a significantly higher mean ETDRS score (Mean=64.84, SD=5.18) than the AMG (Mean=49.78, SD=3.05), p<0.001. This significant association indicates that the internal limiting membrane flap technique may provide better visual improvement results in MH repair.

Table 2 Comparison of Postoperative ETDRS Visual Acuity between ILM Flap and Amniotic Graft techniques

Surgical Technique	Frequency (n)	Mean ETDRS VA	Standard Deviation	Standard Error Mean	p-value
ILM Flap	10	64.84	5.18	1.64	< 0.001
Amniotic Graft	10	49.78	3.05	0.96	

Table 3 demonstrates a considerable increase in VA following surgery, with the mean ETDRSVA improving from 40.59 to 57.31, p<0.001. The results indicate significant visual improvement following surgery.

Table 3. Comparison of Postop. and Preopt. ETDRS VA

Measure	Mean ± SD	N	Standard Error Mean	Significance (p-value)	
Preoperative ETDRS VA	$40.59 \pm 5.05$	20	1.13	< 0.001	
Postoperative ETDRS VA	$57.31 \pm 8.76$	20	1.96		

According to the table below, 69.2% of patients with poor satisfaction reported an increased quality of life (QoL), compared to 28.6% in the high satisfaction group. This inverse association shows that unhappiness might be associated with apparent improvement. The exact Fisher value was 0.07.

Table 5: Association between Satisfaction and Quality of Life (2x2 Table)

	Improved	Not Improved	Total	p-value
	(Much Better + Better)	(Same + Worse)		
Dissatisfied	9	4	13	0.07
Satisfied/Neutral	2	5	7	
Total	11	9	20	

Table 5 shows the results of an ordinary logistic regression that predicts the total satisfaction level. Age was not a significant predictor, p = 0.0624, and had a nearly neutral Odds Ratio of 0.964. In contrast, the internal limiting membrane surgical approach significantly reduced the likelihood of increased satisfaction odds ratio of 0.027, p = 0.004, indicating that it is associated with lower satisfaction levels than other procedures.

Table 5: Ordinal Logistic Regression Results for Overall Satisfaction Level

Predictor	Estimate	Std. Error	p-value	95% Confidence interval	OR (Exp(B))
Age	-0.037	0.074	0.624	-0.183 – 0.109	0.964
Surgical Technique (ILM)	-3.608	1.261	0.004	-6.0791.137	0.027

### DISCUSSION

The human amniotic membrane (hHM) has been utilised to treat ocular disease. However, the human amniotic membrane lowers inflammation and scarring while also promoting epithelialization, the graft's integration and mechanisms by which it exerts its long-term benefits remain unknown. (16). A study conducted by Caporossi et al.(17) reported structural and functional success with application of human amniotic membrane at a failing MS. Primary surgery for idiopathic MH fails fewer than 10% of the time. In one study, it was discovered that the inverted internal limiting membrane flap technique offers superior morphological and short-term visual results than ILM peeling for big macular holes (MH).(18)Similarly, in our study, patients treated with the ILM flap technique had a superior VA than those who were treated with amniotic grafts. These findings showed that the ILM technique may be more beneficial for the improvement of vision after macular hole surgery. Another study indicated that the ILM flap technique considerably improved the repair of MHs and VA compared to standard internal limiting membrane peeling.(19). The inverted ILM flap technique enhances the MH closure rate associated with peeling; nonetheless, VA improvement is equivalent between the two surgical techniques.(19) In our study, we discovered a significant increase in VA after surgery, indicating a marked functional advantage to patients. The increase in ETDRS scores following surgery demonstrates the intervention's efficacy, and statistical analysis confirms the outcome's dependability. The observed alterations, validated by measures of variability, highlight the surgical techniques' potential to improve visual acuity in affected patients.

In our study, the ordinal logistic regression revealed that age didn't play a major role in predicting overall satisfaction, as evidenced by a non-significant association and an odds ratio around neutrality. In contrast, the internal limiting membrane surgical method was strongly associated with lower satisfaction levels, with a considerably reduced chance of better satisfaction when compared to other surgical procedures. These results indicated the possible impact of the surgical approach on patient-perceived results. (20)The internal limiting membrane surgical technique drastically lowered the probability of increased satisfaction when compared to other surgical techniques.(21)

# **CONCLUSION**

This comparative study demonstrates a significant difference between anatomical success and patient-reported outcomes in MH surgery. While the internal limiting membrane flap method improved vision recovery, it resulted in lower patient satisfaction when compared to amniotic membrane grafting. Overall, surgical intervention resulted in markedly improved functional eyesight, demonstrating its therapeutic effectiveness. The unanticipated inverse association between satisfaction and perceived quality of life (QoL) improvement indicated that psychological variables and disappointed expectations may have a significant impact on postoperative experiences in addition to quantitative visual outcomes. These findings emphasize the requirement of comprehensive patient counselling and individualised surgical planning in balancing technical success with patient well-being. To optimise comprehensive care, further study into the factors that influence satisfaction is required.

# **REFERENCES**

- 1. Gattoussi S, Buitendijk GHS, Peto T, Leung I, Schmitz-Valckenberg S, Oishi A, et al. The European Eye Epidemiology spectral-domain optical coherence tomography classification of macular diseases for epidemiological studies. Acta Ophthalmol [Internet]. 2019 Jun 1 [cited 2025 Jul 7];97(4):364–71. Available from: https://pubmed.ncbi.nlm.nih.gov/30242982/
- 2. Majumdar S, Tripathy K. Macular Hole. StatPearls [Internet]. 2023 Aug 25 [cited 2025 Jul 7]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK559200/
- 3. Gupta OP. American Academy of Ophthalmology. 2025 [cited 2025 Jul 7]. Macular Hole EyeWiki. Available from: https://eyewiki.org/Macular\_Hole
- 4. Ferreira MA, Maia A, Machado AJ, Ferreira REA, Hagemann LF, Júnior PHER, et al. Human amniotic membrane for the treatment of large and refractory macular holes: a retrospective, multicentric, interventional study. Int J Retin Vitr [Internet]. 2021 Dec 1 [cited 2025 Jul 8];7(1):38. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8105940/
- 5. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. Ophthalmology [Internet]. 2010 Oct [cited 2025 Jul 10];117(10):2018–25. Available from: https://pubmed.ncbi.nlm.nih.gov/20541263/
- 6. Sborgia G, Niro A, Sborgia A, Albano V, Tritto T, Sborgia L, et al. Inverted internal limiting membrane-flap technique for large macular hole: A microperimetric study. Int J Retin Vitr [Internet]. 2019 Oct 1 [cited 2025 Jul 8];5(1):1–10. Available from: https://journalretinavitreous.biomedcentral.com/articles/10.1186/s40942-019-0195-6
- 7. Rizzo S, Caporossi T, Tartaro R, Finocchio L, Franco F, Barca F, et al. A Human Amniotic Membrane Plug to Promote Retinal Breaks Repair and Recurrent Macular Hole Closure. Retina [Internet]. 2019 Oct 1 [cited 2025 Jul 8];39:S95–103. Available from: https://pubmed.ncbi.nlm.nih.gov/30312261/
- 8. Meller D, Pires RTF, Tseng SCG. Ex vivo preservation and expansion of human limbal epithelial stem cells on amniotic membrane cultures. Br J Ophthalmol [Internet]. 2002 [cited 2025 Jul 8];86(4):463–71. Available from: https://pubmed.ncbi.nlm.nih.gov/11914219/
- 9. Shiode Y, Morizane Y, Matoba R, Hirano M, Doi S, Toshima S, et al. The role of inverted internal limiting membrane flap in macular hole closure. Investig Ophthalmol Vis Sci [Internet]. 2017 Sep 1 [cited 2025 Jul 8];58(11):4847–55. Available from: https://pubmed.ncbi.nlm.nih.gov/28973331/
- 10. Kalur A, Muste J, Singh RP. A Review of Surgical Techniques for the Treatment of Large Idiopathic Macular Holes. Ophthalmic Surg Lasers Imaging Retin [Internet]. 2022 Jan 1 [cited 2025 Jul 8];53(1):52–61. Available from: https://pubmed.ncbi.nlm.nih.gov/34982003/
- 11. Gu C, Qiu Q. Inverted internal limiting membrane flap technique for large macular holes: a systematic review and single-arm meta-analysis. Graefe's Arch Clin Exp Ophthalmol [Internet]. 2018 Jun 1 [cited 2025 Jul 8];256(6):1041–9. Available from: https://link.springer.com/article/10.1007/s00417-018-3956-2

- 12. Tseng SCG, Espana EM, Kawakita T, Di Pascuale MA, Li W, He H, et al. How does amniotic membrane work? Ocul Surf [Internet]. 2004 [cited 2025 Jul 8];2(3):177–87. Available from: https://pubmed.ncbi.nlm.nih.gov/17216089/
- 13. Rossi T, Trillo C, Ripandelli G. Autologous internal limiting membrane transplant for recurrent idiopathic macular holes. Eur J Ophthalmol [Internet]. 2021 Mar 1 [cited 2025 Jul 8];31(2):656–63. Available from: /doi/pdf/10.1177/1120672120906391?download=true
- 14. Li D, Ye Q, Li C. Auto-transplantation of the anterior lens capsule and blood for a recurrent large macular hole. Int J Ophthalmol [Internet]. 2020 Nov 18 [cited 2025 Jul 10];13(11):1839–40. Available from: https://pubmed.ncbi.nlm.nih.gov/33215020/
- 15. Qiao G, Xie L, Zou Q, He C, Zhang X, Tang Z, et al. The use of biological amniotic membranes in the treatment of recurrent macular holes. Sci Rep [Internet]. 2022 Dec 1 [cited 2025 Jul 10];12(1):1–6. Available from: https://www.nature.com/articles/s41598-022-21754-8
- 16. Zhu D, Jin X, Zhou J. Transplantation of amniotic membrane for choroidal hole to treat suprachoroidal silicone oil migration. Acta Ophthalmol [Internet]. 2017 Sep 1 [cited 2025 Jul 10];95(6):e522–3. Available from: https://pubmed.ncbi.nlm.nih.gov/28696567/
- 17. Caporossi T, Pacini B, Bacherini D, Barca F, Faraldi F, Rizzo S. Human amniotic membrane plug to promote failed macular hole closure. Sci Rep [Internet]. 2020 Dec 1 [cited 2025 Jul 10];10(1). Available from: https://pubmed.ncbi.nlm.nih.gov/33106542/
- 18. Shen Y, Lin X, Zhang L, Wu M. Comparative efficacy evaluation of inverted internal limiting membrane flap technique and internal limiting membrane peeling in large macular holes: a systematic review and meta-analysis. [cited 2025 Jul 10]; Available from: https://doi.org/10. 1186/s12886-019-1271-2
- 19. Baumann C, Kaye S, Iannetta D, Sultan Z, Dwivedi R, Pearce I. Effect of inverted internal limiting membrane flap on closure rate, postoperative visual acuity, and restoration of outer retinal layers in primary idiopathic macular hole surgery. Retina [Internet]. 2020 Oct 1 [cited 2025 Jul 10];40(10):1955–63. Available from: https://journals.lww.com/ retinajournal/fulltext/2020/10000/effect\_of\_inverted\_internal\_limiting\_membrane\_flap.12.aspx
- 20. Spiteri Cornish K, Lois N, Scott N, Burr J, Cook J, Boachie C, et al. Vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with no peeling for idiopathic full-thickness macular hole (FTMH). Cochrane Database Syst Rev [Internet]. 2013 Jun 5 [cited 2025 Jul 10];2013(6). Available from: https://pubmed.ncbi.nlm.nih.gov/23740611/
- 21. Sultan H, Wykoff CC, Shah AR. Five-year outcomes of surgically treated symptomatic epiretinal membranes with and without internal limiting membrane peeling. Ophthalmic Surg Lasers Imaging Retin [Internet]. 2018 May 1 [cited 2025 Jul 10];49(5):296–302. Available from: https://pubmed.ncbi.nlm.nih.gov/29772039/