

Comparative Analysis of Anatomical and Visual Outcomes in Large and Massive Idiopathic Macular Holes Treated with Routine Versus Inverted ILM Flap Techniques

Manisha Agarwal

agarwalmannii@yahoo.co.in

Shroff's Charity Eye Hospital

Pallavi Goel

Shroff's Charity Eye Hospital

Ankit Garg

Shroff's Charity Eye Hospital

Tanya Jain

Shroff's Charity Eye Hospital

Shalini Singh

Shroff's Charity Eye Hospital

Research Article

Keywords: Full thickness macular hole (MH), Best Corrected Visual Acuity (BCVA), optical coherence tomography (OCT), internal limiting membrane (ILM) flap, perfluoropropane gas (C3F8), sulfur hexafluoride gas (SF6), external limiting membrane (ELM)

Posted Date: July 14th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-9360000/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Purpose

To compare the visual and anatomical outcomes following surgical intervention for idiopathic full-thickness macular holes (MH) of large size (500–1000 microns) and massive (> 1000 microns) macular holes at a tertiary eye care center in North India.

Methods

Retrospective study of patients who underwent surgery for large or massive idiopathic MH at a tertiary eye centre of north India between 2009 and 2020. Preoperative and postoperative data was reviewed, including best corrected visual acuity (BCVA) optical coherence tomography (OCT) scans, surgical techniques, functional and anatomical outcomes.

Results

A total of 80 eyes with idiopathic MH were analyzed, with 43 in the large MH group (group A) and 37 in the massive MH group (group B). Preoperative BCVA averaged 0.94 log MAR units in group A and 1.04 log MAR units in group B. Post-operative BCVA averaged 0.514 log MAR units in group A and 0.762 log MAR units in group B. While there was no statistically significant change in BCVA within each group post-surgery ($P < 0.234$), the post-operative BCVA differed significantly between the two groups ($P < 0.05$). Type 1 closure of the macular hole was achieved in 34 eyes in group A and 21 eyes in group B. Notably, anatomical outcomes favored group A.

Conclusion

This study highlights superior visual and anatomical outcomes in large MH compared to massive MH following surgical intervention. Moreover, our findings suggest that while large MHs (500–1000 microns) tend to have better outcomes, surgical intervention benefits patients across both MH sizes. The efficacy of the inverted internal limiting flap (ILM) technique over routine MH surgery was observed. Conversely, routine MH surgery also demonstrated efficacy, indicating improved visual and anatomical outcomes regardless of MH size.

Overall, our study concludes the effectiveness of surgical repair for large and massive MHs in improving visual and anatomical outcomes.

Introduction

A full-thickness macular hole is characterized by a complete retinal defect primarily involving the foveolar area, typically measuring around 500 microns in diameter when fully developed, often accompanied by a rim of sensory retinal detachment.^[1] Macular holes can be broadly classified as idiopathic or secondary to trauma or epiretinal membrane etc.^[2]

Idiopathic macular holes were initially described by Johnson and Gass. These holes are further categorized based on their base diameter as large, measuring < 500 microns, and massive, exceeding 1000 microns. While internal limiting membrane (ILM) peeling has demonstrated approximately 90% anatomical success rates for holes less than 400 microns in diameter, larger macular holes present greater challenge, with reported closure rates below 60%.^[3] Over the past decade, various modifications of the standard technique, including inverted flap, free flap, and retinal transplant procedures, have been explored, with variable outcomes. Notably, the inverted ILM flap technique has shown superior anatomical and functional outcomes in cases of large macular holes.^[3] However, whether this superior outcome extends to massive macular holes remains to be elucidated.^[3, 4]

Timely diagnosis and appropriate intervention are crucial in managing this potentially sight-threatening condition, with larger macular holes (> 500 microns base diameter) often associated with poorer prognosis.^[5] In this study, we aim to compare the visual and anatomical outcomes of large (500–1000 microns) versus massive (> 1000 microns) macular holes on vitreo retinal surgery comprising of either conventional versus the inverted ILM flap techniques.

Methodology

A retrospective review was conducted on medical records of patients diagnosed with large or massive macular holes. Institutional review board approval was obtained prior to the study, and adherence to the principles of the Helsinki Declaration was ensured. The study included all cases of idiopathic macular holes with a base diameter > 500 microns, operated at a tertiary eye care hospital of North India between January 2009 and July 2020. Exclusion criteria comprised patients with associated retinal detachment, secondary macular holes, axial length > 24mm and those with a history of prior surgery for macular holes or any other co-existent retinal pathology.

Primary Outcomes:

Anatomical Outcomes:

1. Rate of Type 1 macular hole closure in both large (500–1000 microns) and massive (> 1000 microns) macular holes.
2. Comparison of closure rates between routine ILM peel and inverted ILM flap techniques for both large and massive macular holes.

Functional Outcomes:

1. Change in Best Corrected Visual Acuity (BCVA) (logMAR) from preoperative to postoperative state in large and massive macular holes.
2. Postoperative visual acuity differences between the two surgical techniques (routine ILM peel vs inverted ILM flap).

Secondary Outcomes:

1. Macular Hole Persistence and Type 2 Closure Rates: Incidence of persistent macular holes and Type 2 closures in large versus massive macular holes.
2. Influence of Surgical Techniques: Assessment of visual acuity gain differences within subgroups undergoing routine or inverted ILM flap techniques for large and massive macular holes.

The base diameter of each macular hole was measured using Zeiss Cirrus optical coherence tomography (OCT) by a single observer. Two readings were taken for each patient to assess intra-observer bias, and the average of these readings was considered as the final base diameter. Based on the base diameter defined as diameter of the macular hole measured by OCT at the level of the retinal pigment epithelium, eyes were categorized into two groups: group A (base diameter 500–1000 microns) and group B (base diameter > 1000 microns).

Patient data collected included age, gender, eye laterality, symptom duration, best corrected visual acuity (BCVA) measured by Snellen's chart, lens status and anterior and posterior segment findings. Surgical details such as gauge of pars plana vitrectomy (23 G or 25 G), internal limiting membrane (ILM) peeling technique (standard ILM peel vs inverted flap), and tamponade agent (14% C3F8 perfluoropropane or 20% SF6 sulfur hexafluoride) were recorded. Standard technique involved peeling of at least 1 disc area around the macular hole.^[6] Patients were instructed to maintain a postoperative prone positioning for 12 hours per day for 5 days.

Postoperative BCVA was assessed at six weeks. Anatomical outcomes were categorized as type 1 closure (complete closure of all retinal layers), type 2 closure (residual defect of the neurosensory layer), and persistence of macular hole (inability to close) based on OCT findings.^[7] OCT interpretation was performed by a single observer to minimize inter-observer bias.

Statistical Analysis

Statistical analyses were conducted using SPSS version 20.0 (IBM Corp.), with significance set at 5% i.e. if the p-value of statistical analysis is less than or equal to 0.05, the result is considered statistically significant. BCVA was converted to logarithm of the minimal angle of resolution (logMAR) for analysis. Improvement in visual acuity between the two groups was compared using independent t-tests, while improvement within each group was assessed using paired t-tests. The distribution of hole closure types between groups was compared using chi-square test.

Results

80 eyes were included in the study and 43 eyes were in group A whereas 37 eyes were in group B. 46 were females and 34 were males. In Group A out of 43 patients 26 (60.46%) were females. Similarly, in group B 20 out of 37 patients (54.06%) were females.

Conventional MH surgery was done in 27 eyes in group A and 18 eyes in group B. Inverse flap technique of ILM peeling was done in 16 eyes in group A and 19 eyes in group B.

Visual Outcome results

In group A, the average preoperative visual acuity (VA) was 0.902 logMAR units whereas in group B, it was 1.034 logMAR units. The difference in the preoperative visual acuity in between the two groups was not statistically significant (p value = 0.088). The average postoperative VA in group A was 0.514 logMAR units and in group B was 0.762 logMAR units. The difference in the postoperative visual acuity in between the two groups was statistically significant (P = 0.001) with group A eyes having better postoperative visual acuity compared to group B. The difference in the change in the visual acuity following macular hole surgery was not found to be statistically significant in group A and group B (P = 0.234). [Table-1]

The difference in the change in the visual acuity following macular hole surgery was found to be statistically significant between routine and inverted flap technique in massive holes with eyes undergoing inverted flap technique having higher post-operative visual acuity gain.

However, there was no statistically significant difference in visual acuity gain between routine and inverted flap technique in large holes. [Table 2]

Anatomical outcome results

Macular hole closure was analysed in the two groups. 34 eyes in group A had type 1 closure. Of these 34 eyes, 18 eyes underwent conventional technique and 16 eyes underwent inverted ILM flap technique of macular hole surgery. In Group B, 21 eyes had type 1 closure. Of these 21 eyes; 11 eyes underwent conventional ILM peel and 10 eyes underwent inverted flap technique of macular hole surgery [Table- 3]. Eight eyes showed type 2 closure and 1 eye showed persistence of the macular hole in group A. In group B- 10 eyes showed type 2 closure and 6 eyes showed persistence of macular hole [Table 3].

A statistically significant difference was observed between inverted ILM flap and routine ILM peel technique in the anatomical closure rate of large macular holes; however, no such statistically significant difference was found in massive macular holes [Table-4 and 5].

In the case of large macular holes, the inverse flap technique demonstrated superior rates of anatomical closure, specifically Type 1 closure, which was statistically significant. Conversely, in massive macular holes, the difference in anatomical closure rates between the two techniques did not reach statistical significance. Irrespective of the ILM peeling technique used, the anatomical closure rate was higher in large macular holes (79%) compared to massive macular holes (57%), and was statistically significant [Table 3].

Discussion

Macular hole surgery, pioneered by Kelly and Wendel in 1991^[8], has evolved significantly over the years, resulting in improved success rates. Base diameter is a crucial prognostic factor influencing postoperative outcomes and closure type. Larger macular holes are generally associated with lower success rates compared to smaller ones. Visual outcomes following macular hole repair are also influenced by the configuration of the closure on optical coherence tomography (OCT), with U-shaped closures associated with the best functional results.^[9] It's noteworthy that a significant proportion of large macular holes close with a flat-open or W-shaped configuration, leading to limited visual acuity gain, particularly if there is a persistent foveal defect.^[10] This study aimed to evaluate and compare functional and anatomical outcomes in patients with large and massive macular holes (base diameter > 1000 microns) following surgery.

Internal limiting membrane (ILM) peeling has become a standard practice in macular hole surgery due to its role in alleviating tangential and anterior-posterior tractions contributing to macular hole formation. Our study found that patients with macular holes smaller than 1000 microns demonstrated better visual and anatomical outcomes compared to those with massive holes (> 1000 microns), with the difference being statistically significant primarily in terms of anatomical outcomes, consistent with previous studies.

Postoperative visual acuity showed a statistically significant difference in both the groups, indicating the influence of macular hole size on functional outcomes. Final closure rates were influenced by macular hole size, with large holes exhibiting higher closure rates compared to massive MH. Notably, a study by Narayanan R et al. comparing routine ILM peeling with inverted ILM peeling technique found no superiority of the inverted technique in terms of closure rates or postoperative visual gain.^[11]

In a meta-analysis by Yu Shen et al., comparing routine ILM peeling with inverted flap technique, better postoperative visual acuity was reported with the inverted flap technique at 3 months' follow-up.^[13] This was attributed to the ILM flap serving as a bridge for cellular migration into the macular hole, facilitating retinal tissue regeneration.^[3] Michalewska et al. found that glial cells proliferated and produced an environment to transfer light from the retinal surface to the photoreceptor cell layer. In the cases after the surgery of inverted ILM flap technique, retinal tissue regenerated from the external limiting membrane (ELM), then regrowth of the ellipsoid layer was observed over the next few months.^[10] A similar study by Dera et. al also suggested the superior anatomical outcomes with ILM flap in large macular holes.^[12] However, contrary to expectations, no significant difference in functional outcomes was observed between the two surgical techniques at long-term follow-up, possibly due to limitations in the restoration of the normal layered structure of the retina even after inverted ILM flap technique.^[14, 15]

Our study reported that the inverted flap technique demonstrated superior closure rates compared to the routine ILM peel technique in patients with holes smaller than 1000 microns; however, this did not translate into higher visual acuity gain postoperatively. Conversely, although holes larger than 1000 microns exhibited similar successful closure rates with both techniques, the inverted flap technique showed greater postoperative visual gain in the massive macular hole group.

In recent years, alternative surgical strategies such as human amniotic membrane graft (AMG) have been explored for refractory and extra-large macular holes, particularly those exceeding 1000–1500 microns or those failing primary surgery. Rizzo et al. demonstrated successful anatomical closure using human amniotic membrane plug transplantation in persistent macular holes, with high closure rates and acceptable visual outcomes.^[16] Similarly, Caporossi et al. reported favorable anatomical success using subretinal AMG placement, suggesting that the amniotic membrane serves as a scaffold promoting retinal gliosis and tissue integration.^[17] Subsequent studies by Felfeli et al. and others have reinforced these findings, highlighting AMG as a viable option in complex and previously failed macular hole surgeries.^[18]

Despite these encouraging outcomes, AMG remains a relatively more invasive intervention with concerns regarding graft handling, positioning, integration, and long-term functional recovery. In contrast, the inverted internal limiting membrane (ILM) flap technique also supported by our findings. It offers a more physiological, less invasive, and reproducible approach with substantial anatomical and functional success. The ILM flap acts as an intrinsic scaffold facilitating Müller cell proliferation and subsequent photoreceptor alignment, thereby preserving retinal microarchitecture more effectively than exogenous grafts.^[10, 13]

Given this, a stepwise surgical strategy appears most appropriate (Fig. 1). The inverted ILM flap technique should be considered the primary intervention for large and massive macular holes. In cases of surgical failure, extremely large holes, or insufficient residual ILM, secondary options such as AMG, autologous ILM free flap, or neurosensory retinal grafts may be considered. This hierarchical approach balances invasiveness with efficacy and may optimize both anatomical and functional outcomes.

Limitations and strengths

Our study is retrospective in nature and has a limited follow up. It is subject to inter-surgeon variation since multiple surgeons were involved in the study. The use of two different type of tamponades and its effect on closure rate is not analysed in our study.

We have not evaluated the intactness of IS-OS junction, ellipsoid zone thereby impacting the final visual outcome.

Conclusion

This study highlights the effectiveness of surgical repair for large and massive idiopathic macular holes, with notable distinctions between the outcomes of routine ILM peel and inverted ILM flap techniques. The superior anatomical closure rates and significant visual gains associated with the inverted flap technique in large macular holes make it a preferred approach. For massive macular holes, the technique provides functional advantages, even when anatomical closure is less consistent. Further research with longer follow-up periods and larger sample sizes is warranted to validate these findings and refine surgical approaches for macular hole repair.

These findings suggest the importance of tailoring surgical strategies to the size of the macular hole to optimize patient outcomes. A stepwise, size-based surgical approach is recommended, wherein the inverted ILM flap technique should be considered the primary intervention, with advanced options such as amniotic membrane graft or retinal grafts reserved for refractory or failed cases.

Declarations

No financial Disclosures

No Conflict of Interest

No Funding Received

Author Contribution

MA: managed patients, made manuscript and edited itPG: wrote manuscript, collected patient data and did statistical analysisTG,AG,SS: collected patient data and helped in statistical analysis. Also helped in proof reading manuscript

References

1. Gass JD. Idiopathic senile macular hole: Its early stages and pathogenesis. *Arch Ophthalmol*. 1988;106:629–39.
2. Le Mer Y, Korobelnik JF, Kodjikian L. Classification of vitreomacular adhesion and macular holes. *J Fr Ophtalmol*. 2015;38:357–64.
3. Morizane Y, Shiraga F, Kimura S, et al. Autologous transplantation of ILM for refractory macular holes. *Am J Ophthalmol*. 2014;157:861–9.
4. Grewal DS, Mahmoud TH. Autologous neurosensory retinal free flap for closure of refractory myopic macular holes. *JAMA Ophthalmol*. 2016;134:229–30.
5. Gupta B, Laidlaw DA, Williamson TH. Predicting visual success in macular hole surgery. *Br J Ophthalmol*. 2009;93:1488–91.
6. Lezzi R, Kapoor KG. No face-down positioning and broad internal limiting membrane peeling in the surgical repair of idiopathic macular holes. *Ophthalmology*. 2013;120:1998–2003.
7. Imai M, Iijima H, Gotoh T, Tsukahara S. Optical coherence tomography of successfully repaired idiopathic macular holes. *Am J Ophthalmol*. 1999;128:621–7.
8. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes: results of a pilot study. *Arch Ophthalmol*. 1991;109:654–9.
9. Michalewska Z, Michalewski J, Cisiecki S, et al. Correlation between foveal structure and visual outcome following macular hole surgery: a spectral optical coherence tomography study. *Graefes Arch Clin Exp Ophthalmol*. 2008;246:823–30.
10. Michalewska Z, Nawrocki J, Adelman RA, et al. Inverted internal limiting membrane flap technique for large macular holes. *Ophthalmology*. 2010;117:2018–25.
11. Narayanan R, Singh SR, Taylor S, Berrocal MH, Chhablani J, Tyagi M, Ohnomatsui K, Pappuru RR, Apte RS. Surgical outcomes after inverted internal limiting membrane flap versus conventional peeling for very large macular holes. *Ophthalmology*. 2017;124:595–610.
12. Dera, A.U., Stoll, D., Schoeneberger, V. et al. Anatomical and functional results after vitrectomy with conventional ILM peeling versus inverted ILM flap technique in large full-thickness macular holes. *Int J Retin Vitre*. 2023; 9, 68
13. 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. *BMC Ophthalmol*. 2020;20:14.
14. Velez-Montoya R, Ramirez-Estudillo JA, de Liano CS, Bejar-Cornejo F, Sanchez-Ramos J, Guerrero-Naranjo JL, Morales-Canton V, Hernandez-Da Mota SE. Inverted ILM flap, free ILM flap and conventional ILM peeling for large macular holes. *Int J Retin Vitre*. 2018;4:1–9.
15. Boninska K, Nawrocki J, Michalewska Z. Mechanism of "flap closure" after the inverted internal limiting membrane flap technique. *Retina*. 2018;38:2184–9.
16. Rizzo S, Caporossi T, Tartaro R, Finocchio L, Franco F, Barca F. Human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure. *Retina*. 2019;39 Suppl 1:S95–S103.
17. Caporossi T, Tartaro R, De Angelis L, Barca F, Rizzo S. Human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure: anatomical and functional outcomes. *Am J Ophthalmol*. 2020;213:178–185.

18. Felfeli T, Mandelcorn ED. Macular hole hydrodissection with human amniotic membrane graft for failed macular hole surgery. *Retin Cases Brief Rep.* 2021;15(3):277–281.

Tables

Table 1: Describes change in visual acuity in both groups and the change in visual acuity with ILM flap versus routine ILM peel methods of macular hole surgery:							
TABLE 1	Macular hole size	Pre-op Mean visual acuity	p value	Post-op Mean visual acuity	p value	Difference	p value
MHSize	Large	0.902 (0.773 – 1.031)	0.088	0.514 (0.407 – 0.621)	0.001	0.391	0.234
	Massive	1.034 (0.905 – 1.163)		0.762 (0.617 – 0.907)		0.289	
	Type of surgical approach	Pre-op Mean visual acuity	p value	Post-op Mean visual acuity	P value	Difference	P value
MHSurgeries	Routine	0.921 (0.803 – 1.039)	0.367	0.645 (0.514 – 0.776)	0.494	0.265	0.024
	Inverse flap	1.014 (0.868 – 1.159)		0.584 (0.462 – 0.707)		0.458	

Table 2:							
Describes the change in visual acuity in both groups with different macular hole surgeries i.e . ILM flap versus routine ILM peel							
Table 2		Pre-Op		Post-Op		PreOp to PostOp	
		Mean LogMar (PreOP)	p-values	Mean LogMar (PostOp)	p-values (Mann Whitney)	Change In LogMar	p-values
Large	Routine	0.867	MannWhitney-0.465	0.535	0.685	0.336	MannWhitney-0.281
	Inverse flap	0.961		0.481		0.480	
Massive	Routine	1.007	MannWhitney-0.743	0.824	0.4792	0.143	MannWhitney-0.017
	Inverse flap	1.057		0.694		0.434	
Total	Routine	0.921	MannWhitney-0.367	0.645	0.6746	0.265	MannWhitney-0.023
	Inverse flap	1.014		0.584		0.458	
The change in visual acuity following macular hole surgery was significantly greater (<i>p value</i> =0.017)in massive holes treated with the inverted flap technique compared to the routine technique. the inverted flap group showing higher post-operative visual acuity of logMar 0.694 versus routine ILM peel group with post op visual acuity of logMar 0.824.							

Table 3: shows anatomical outcomes i.e. type of closure in both groups with different macular hole surgeries											
Table 3		Closure (N)				Closure (%)				p Values	
Macular Hole Size		Type 1	Type 2	Persistent Hole	Total	Type 1	Type 2	Persistent Hole	Total	Fischer's	Chi sq
	Large	34	8	1	43	79%	19%	2%	100%	0.046	0.040
	Massive	21	10	6	37	57%	27%	16%	100%		
	Total	55	18	7	80	69%	22%	9%	100%		
Macular Hole Surgery Routine Flap Inverted Flap Total 29 26 55 11 7 18 5 2 7 45 35 80 65% 74% 69% 24% 20% 22% 11% 6% 9% 100% 100% 100% 0.630 0.575											
In group A, 8 eyes had type 2 closure, and 1 eye showed macular hole persistence. In group B, 10 eyes had type 2 closure, and 6 eyes showed persistence. In group A, 34 eyes had type 1 closure;18 with the routine technique and 16 with the inverted ILM flap technique. In group B, 21 eyes had type 1 closure;11 with the routine ILM peel and 10 with the inverted flap technique.											

Table 4: Describes the anatomical closure rates in Large versus massive macular holes										
		Number				Percent				
Type of MH		Closure Type				Closure Type				
		Type 1	Type 2	Persistent hole	Total	Type 1	Type 2	Persistent hole	Total	p-values
Large	Routine	18	8	1	27	66%	30%	4%	100%	0.023
	Inverse flap	16	0	0	16	100%	0%	0%	100%	0.034
Massive	Routine	11	3	4	18	61%	17%	22%	100%	0.354
	Inverse flap	10	7	2	19	53%	37%	10%	100%	0.318
Total	Routine	29	11	5	45	65%	24%	11%	100%	0.630
	Inverse flap	26	7	2	35	74%	20%	6%	100%	0.575
A significant difference in anatomical closure rates was observed between the inverted ILM flap and routine ILM peel techniques for large macular holes, but not for massive macular holes.										

Table 5: Describes the anatomical outcome between two surgical techniques in large and massive macular holes

Large Macular Holes				
Surgery Technique	Type-1	Type-2	Persistent hole	N
Routine	18 (67%)	8 (30%)	1 (3%)	27 (100%)
Inverse flap	16 (100%)	0	0	16 (100%)
p-value	0.016	0.017	1	
Massive Macular Holes				
Surgery Technique	Type-1	Type-2	Persistent hole	N
Routine	11 (61%)	3 (17%)	4 (22%)	18 (100%)
Inverse flap	10 (53%)	7 (37%)	2 (10%)	19 (100%)
p-value	0.743	0.269	0.405	
A significant difference in anatomical closure rates was observed between the inverted ILM flap and routine ILM peel techniques for large macular holes, bu				

Figures

Clinical Decision-Making Algorithm for Macular Hole Surgery

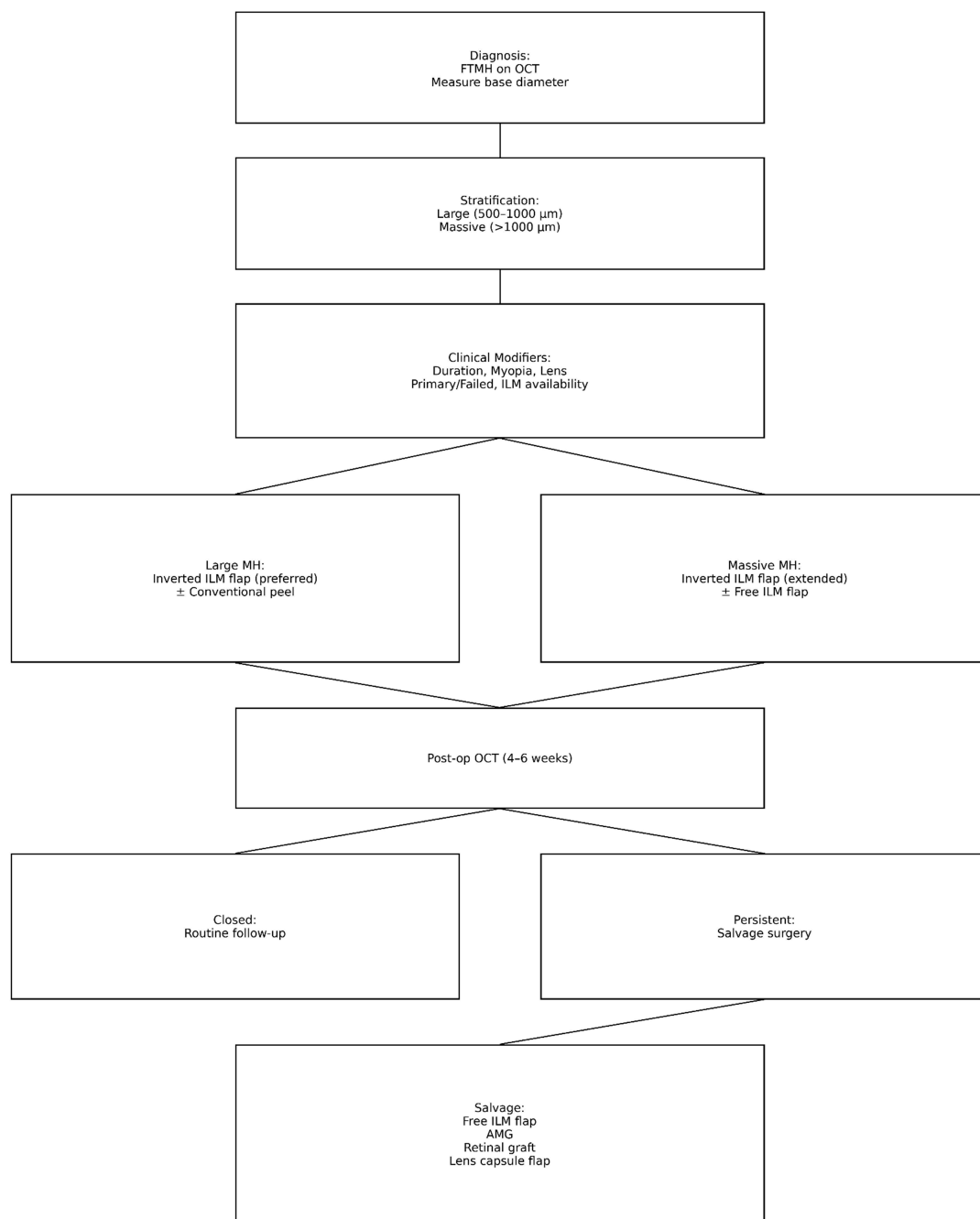


Figure 1

Clinical Decision-Making Algorithm for Surgical Management of Large and Massive Macular Holes