

<https://doi.org/10.31288/oftalmolzh202315260>

Etiology, pathogenesis, and classification of and current methods of treatment for idiopathic macular holes: a review

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This review highlights the surgical treatment of idiopathic macular holes (IMHs). The paper aimed to review (1) the current methods of treatment for IMHs and (2) the prognosis for postoperative hole closure. IMHs are anatomic defects in the fovea resulting in central vision loss. Particular attention was given to studies on the etiology, pathogenesis, and classification of and current methods of treatment for IMHs. Tangential vitreous traction plays a key role in macular hole development. Macular holes are classified based on retinal slit-lamp biomicroscopy and optical coherence tomography findings. Although the available armamentarium of vitreoretinal surgeons includes a variety of techniques for treating IMHs of any size, there is no universal approach for selecting the optimal hole closure technique. Fovea-sparing techniques are feasible options for the treatment of IMHs and allow avoiding certain morphological and functional changes typical of conventional internal limiting membrane (ILM) peeling.

Keywords:

idiopathic macular hole, vitrectomy, ILM peeling

Introduction

The reported prevalence of idiopathic macular holes (IMHs) in the general population ranges between 0.02% and 0.33% [1]. They are a cause of central visual loss and visual disability and significantly deteriorate the quality of life of the affected individuals, which warrants developing effective techniques to treat retinal disorders. This paper aimed to review (1) the current methods of treatment for IMHs and (2) the prognosis for postoperative hole closure.

IMHs are anatomic defects in the fovea resulting in central vision loss, metamorphopsia, and a central scotoma [2].

In the general population, the prevalence of MHs was reported to be around 3.3 per 1,000 people. They typically present in patients older than 60 years and are more common in women than men. The condition is unilateral in around 80% of cases [3].

In 1869 Knapp [4] published the first case description of a macular hole in a patient with ocular trauma. Others reported a similar fundus picture in patients without ocular trauma. Coats (1907) [5] coined the term "idiopathic macular hole" to denote the condition.

Etiology and pathogenesis

Johnson and Gass [6] reviewed 158 eyes with evolving or completed IMHs and postulated that tangential vitreous traction may play a role in macular hole development. The concept is that radial vitreous fibers remaining on the perimacular surface after apparent posterior vitreous

separation contract and slowly tear the macula in a circumferential fashion.

In the opinion of Gass [7], the particular anatomic structure of the macular retina plays a role in the development of macular hole, because the retina is the thinnest in the foveola, the central part of the macula. Foveolar cones are very thin and long. Müller cells are the largest of all cells in the retina, and extend from the external to the internal limiting membranes (ILMs). The retina is the thinnest in the foveola (about 150 μ m), whereas the interface between the retina and the posterior vitreous cortex is relatively strong. Therefore, the structure of the macular retina may make it susceptible to the formation of cysts and foveomacular schisis, leading to retinal holes.

Smiddy and Flynn [8] suggested that the pathogenesis of macular holes is based on degeneration of the inner retinal layers in the central fovea, which results either in the formation of cysts or retinal thinning and weakening at the fovea, leading to macular hole formation.

Classification

The Gass classification [9] was based on careful clinical examination and divided macular holes into four stages (Table 1).

Although the original Gass classification is still relevant, in 2013, Duker and colleagues [10] proposed a

Table 1. Gass classification of macular hole (From Gass JD. Reappraisal of biomicroscopic classification of stages of development of a macular hole. Am J Ophthalmol. 1995 Jun 119(6):752-9)

Stage	1995 Gass biomicroscopic classification of macular hole
Stage 1A: <i>Impending hole</i>	A central yellow spot and moderate loss of the foveal contour
Stage 1B: <i>Impending hole</i>	A yellow ring and loss of the foveal depression
Stage 2	Eccentric round or oval retinal defect inside a yellow ring < 400 µm in size
Stage 3	Central round ≥ 400 µm diameter retinal defect, no detachment of the posterior hyaloid from the optic nerve and macula, no Weiss ring
Stage 4	Central round ≥ 400 µm diameter retinal defect and the presence of (a) detachment of the posterior hyaloid from the optic nerve and macula and (b) Weiss ring

new anatomic classification based on optical coherence tomography (OCT) findings (Table 2).

A small full-thickness macular hole (FTMH) features an aperture size of less than 250 µm. Stalmans and colleagues [11] found that intravitreal injection of the vitreolytic agent ocriplasmin can close an FTMH of this size. Dugel and colleagues [12] reported that, in regards to FTMH, non-surgical hole closure was achieved in 58.3% of holes ≤250 µm which received a single intravitreal injection of 125-µg ocriplasmin.

A medium FTMH is defined by aperture size from 250 to 400 µm. Ip and colleagues [13] explored post-vitrectomy FTMH closure rates by aperture size and showed a very high anatomic closure rate (>90%) with complete removal of residual hyaloid, with or without ILM peeling. The postoperative closure of IMHs following vitreous surgery was related to the preoperative MH diameter, with lesions smaller than 400 µm demonstrating higher success rates.

A trend toward greater visual acuity improvement was demonstrated for idiopathic macular holes smaller than 400 µm.

Ch'ng and colleagues [14], however, suggested that there is a need for a reclassification of large FTMH, and new surgical techniques such as ILM flaps should be reserved for MHs larger than 650 µm. Therefore, the preoperative size of macular hole should be taken into account while predicting the anatomical and functional outcomes of macular hole surgery.

A classification system for focal vitreous traction with and without MH based on spectral domain OCT (SD-OCT), intended to aid in decision-making and prognostication [15], has been developed and validated. The system uses width (W), interface features (I), foveal shape (S), retinal pigment epithelial changes (P), elevation of vitreous attachment (E), and inner and outer retinal changes (R) to give the acronym WISPERR. Width of vitreomacular

Table 2. The international vitreomacular traction study group classification of vitreomacular adhesion, traction, and macular hole (From Duker JS, Kaiser PK, Binder S, de Smet MD, Gaudric A, Reichel E, et al. The international vitreomacular traction study group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013 Dec 120(12):2611-2619)

Vitreomacular adhesion	classified by the size of adhesion	focal (≤ 1500 µm) broad (> 1500 µm)
	subclassified by the absence or presence of association with other macular disease	isolated concurrent
Vitreomacular traction	classified by the diameter of vitreous attachment to the macular surface as measured by OCT	focal (≤ 1500 µm) broad (> 1500 µm).
	subclassified by the absence or presence of association with other macular disease	isolated concurrent
Macular hole	subclassified by size of the hole	small ≤ 250 µm moderate-size 250–400 µm large > 400 µm
	subclassified by the presence or absence of vitreous traction	presence of vitreous traction absence of vitreous traction
	caused by vitreous traction or is the result of pathologic characteristic other than vitreous traction	primary (idiopathic MH) secondary

attachment is the width of the longest continuous length of vitreomacular adhesion (VMA) on any scan that is connected to the foveal centre should be determined. If there are multiple areas of adhesion, the longest single one should be used.

Changes in interface features are graded as grade 0 = none, grade 1 = hyper-reflective inner retinal signal on the VMA itself compared with adjacent retina, grade 2 = any epiretinal membrane (ERM) on any part of the area of retina encompassed by the OCT), and grade 3 = any ERM within the central 1-mm ETDRS circle or contiguous with the zone of vitreous traction.

Changes in foveal shape are graded as grade 0 = none, grade 1 = abnormal profile with loss of smooth contour e.g. notch formation, concave with loss of depression relative to other side, asymmetry of depression, or flat profile and grade 2 = clear eversion of the central foveola with a convex profile of the central fovea.

Pigment epithelial changes are graded as grade 0 = not present and grade 1 = present (could include drusen and/or RPE atrophy).

Elevation of the lowest point of vitreous attachment is determined as the height of maximum central retinal thickness in central 1-mm diameter ETDRS circle—measured from inner surface of retinal pigment epithelium (RPE) to the point of lowest vitreoretinal adhesion and therefore including any subretinal fluid (SRF).

Inner retinal changes (R1) are graded as grade 0 = none and grade 1 = inner retinal cysts or cleavage.

Outer retinal changes (R2) are graded as grade 0 = none, grade 1 = focal outer retinal abnormality without SRF, or dehiscence, grade 2 = SRF, grade 3 = outer retinal dehiscence, and grade 4 = full-thickness macular hole and 'maximum minimum' horizontal linear dimension.

Chung and Byeon [16] proposed a conceptual model of a modified classification system for MHs, with two types of MHs starting from the earliest developmental phases of the condition: A type (dehiscent type) and B type (tearing type).

A type (dehiscent type) is characterized by few outer foveal tissue defects from central dehiscence, foveal pseudocysts and intrafoveal splitting. B type (tearing type) macular holes occur from substantial outer tissue loss as a result of full-thickness tearing (tractional force affects Müller cells eccentric to the centre of the foveolar floor, when traction is large and vitreofoveal adhesion is intensive).

The anterior traction of the incompletely detached posterior hyaloid is a major factor contributing to the progression of holes from A to B type [17].

Historical aspects of surgical treatment for IMHs

IMHs have long been generally considered to be an untreatable condition. In the 1970s and 1980s, there were attempts to treat IMHs with transpupillary retinal laser photocoagulation around the hole to prevent both an increase in hole size and retinal detachment. This approach, however, was found to be unsuccessful because it failed

to provide a favorable functional outcome. In a study by Schocket and colleagues [18], 18 eyes with visual acuity of 20/200 or less were treated with laser for macular hole, and followed for a mean of 34.8 months. Ten eyes (55.6%) improved three to eight lines, five eyes (27.8%) remained the same, and the vision of three (16.6%) deteriorated three to five lines.

In 1991, Kelly and Wendel [19] reported the first series of patients undergoing vitrectomy and gas tamponade with sulphur hexafluoride (SF6) for stage 3 and 4 FTMH. They obtained a closure rate of 58% and an improvement of two or more lines of vision in 73 % of the eyes that had closed holes.

In 1997, Eckardt and colleagues [20] reported on clinical results of vitrectomy with posterior hyaloid removal and ILM peeling for FTMHs. They used specially developed forceps to remove a circular area of the ILM approximately three to four disc diameters in size. Complete closure of the hole was observed postoperatively in 36 of the 39 eyes (92%). A visual improvement of at least two lines was achieved in 77% of eyes with successful closure.

Although the surgical techniques proposed were more advantageous than laser photocoagulation or vitrectomy without ILM peeling in terms of MH closure rate and improvement in visual acuity, others [21–23] noted possible postoperative complications, which required developing less invasive methods of treatment.

In 2011, Rodin and colleagues [24] reported on the results of IMH treatment with expanding intravitreal gas as per the pneumatic retinopexy technique proposed by Rodin and Brazhnikova in 2000 [25]. The technique included injecting a pre-calculated volume of gas into vitreous cisterns through a puncture of the ocular coats in the projection of the pars plana ciliaris without performing vitrectomy. Perfluoropropane (C3F8) was used as a tamponade agent. Patients were asked to position face down for 4–6 weeks after surgery [26]. Functional success rate for MH treatment with expanding intravitreal gas was 100%. Anatomic attachment of the edges of the MH was achieved in 88.6% of eyes, and MH closure, in 58.6% of eyes with stage-2 to stage-4 holes as per the classification by Gass.

Current approaches to treatment of macular holes. Fovea-sparing techniques

A three-port pars plana vitrectomy (PPV) with posterior vitreous detachment and classical ILM peeling is still effective and a gold standard for treating macular holes.

ILM peeling involves mechanical separation of the membrane layers from the underlying layers in a circular fashion. The anatomical success rate of conventional surgery for macular hole was 93–98% [27]. However, this method is considered to be of low efficacy in large macular holes (> 400 µm), possibly, due to the fact that the distance between the broken ends of the retina contains large neural defects which are difficult to fill with the proliferation of glial cells alone unless a scaffold was provided for the migration of glial cells [27]. Therefore, the anatomical

success rate of large macular holes was as low as 50 to 80%, which stimulated the search for improved methods of treatment [28].

Michalewska and colleagues [29] proposed to use an inverted ILM flap technique for large macular holes. They peeled the ILM of approximately two optic disc diameters to the edge of the MH in a circular manner around the MH, leaving a remnant attached to the margins of the MH. This ILM remnant was then inverted upside down to cover the MH. In addition, the authors noted that the ILM flap was found completely detached spontaneously from the MH edge in 14% of cases, which was believed to be a complication associated with the learning curve.

In a comparative study by Rizzo and colleagues [30], among the patients affected by full-thickness MH ≥ 400 μm , success was achieved in 95.6% of the cases in the inverted flap group and in 78.6% in the ILM peeling group. A study by Chen and colleagues [31], evaluated longitudinal changes in multi-focal electroretinogram (mfERG) responses in eyes with large MHs managed by the inverted ILM flap technique. They found that the technique appears to be a safe and effective approach for the management of large idiopathic MHs with favorable short-term anatomical and functional results.

The inverted ILM flap technique and its modifications enable anatomic and functional success in macular holes larger than 400 μm , with macular closure rates as high as 98% [29]. Some concerns with the inverted ILM flap technique have been evoked. The difficulty of the surgical procedure implicates a steep learning curve. Further complications associated with the use of conventional intravitreal dyes (like brilliant blue) in this technique could be difficulties in visualization of the flap by conventional imaging, occurrence of toxic damage to retinal cells, and unintentional ILM flap separation or displacement.

The inverted ILM flap technique provides a smooth and gap-free natural scaffold for the proliferation and migration of glial cells. In addition, Manasa and colleagues [32] reported the ILM flap on MHs can create a closed compartment that enables the retinal pigment epithelium to pump out the subretinal fluid effectively. It prevents further leakage of the fluid into the fovea, thereby keeping the hole dry and contributing to MH closure.

In a study by Yu and colleagues [28], however, the subgroup meta-analysis indicated that the postoperative visual acuity was significantly better in the inverted ILM flap group than the ILM peeling group at the 3-month follow-up, but no significant difference was observed between the two groups at the 6-month follow-up.

Michalewska and colleagues [33] proposed a modification of ILM peeling (a temporal inverted ILM flap technique) associated with temporal peeling, to reduce the occurrence of iatrogenic injury by reducing the area of ILM peeling and preventing possible damage to the retinal nerve fiber layer (particularly, the papillomacular bundle). The study results indicated that the temporal inverted ILM flap technique is as effective as the classic inverted ILM

flap technique for the repair of large Stage IV macular holes.

Few studies proposed using a particular agent perioperatively to stabilize the ILM flap. Shin and colleagues [34] modified the inverted ILM flap technique. They injected perfluoro-n-octane (PFO) into the vitreous to keep the flap in place or displace it in a controlled manner, if required, during fluid-air exchange. This modified technique has some disadvantages such as the requirement for a complete PFO removal from the vitreous cavity, occurrence of incomplete PFO removal, and occurrence of PFO leakage beneath the retina. Song and colleagues [35] investigated the surgical outcomes of Viscoat-assisted inverted ILM flap technique for large MHs associated with high myopia. A small amount of Viscoat (Alcon Laboratories, FortWorth, TX), a low-molecular-weight dispersive viscoelastic material, was applied around the MH and on top of the inverted ILM flap, which had dual effect of adhesive and ballast to stabilize the flap during the fluid-air exchange. An advantage of this modification is that Viscoat can be left in place without causing any toxic effect to the retina.

Lytvynchuk and colleagues [36] reported the efficacy of combination of inverted ILM flap technique and subretinal application of the fluid technique for treatment of refractory FTMHs. The technique involves subretinal injection of balanced salt solution (BSS) in four quadrants with subsequent hydraulic centripetal macular displacement towards the macula and covering the MH with the ILM flap. Final closure of FTMH was achieved in nine of nine cases (100%).

Ghassemi and colleagues [37] evaluated and compared three different techniques of inverted ILM flap in the treatment of large (> 400 μm) IFTMH. Seventy-two eyes from 72 patients with large (> 400 μm) FTMH were randomly enrolled into three different groups: group A (hemicircular ILM peel with temporally hinged inverted flap); group B (circular ILM peel with temporally hinged inverted flap); and group C (circular ILM peel with superior inverted flap). Best-corrected visual acuity (BCVA), anatomical closure rate, and ellipsoid zone (EZ) or external limiting membrane (ELM) defects were evaluated preoperatively, at week 1, and months 1, 3 and 6 after surgery. Differences between groups in postoperative BCVA and rate of successful hole closure were not statistically significant. The rate of successful hole closure was 87.5% vs. 91.3% vs. 100%. The authors concluded that ILM peel with an inverted flap is a highly effective procedure for the treatment of large FTMH, but larger studies with longer follow-up are needed to determine whether different flap orientations affect visual and anatomic success.

Numerous variations of the inverted ILM flap procedure have been described, because central scotoma decreases and visual acuity improves with MH closure. The improvement in visual function, however, depends

on the integrity of outer retinal layers [38]. Some studies on the treatment of large MHs with the inverted ILM flap procedure have found that the recovery period of outer retinal layers is longer in eyes treated with this procedure than in eyes treated with conventional ILM peeling. Thus, Iwasaki and colleagues [39] compared the influence of inverted ILM flap technique with the influence of conventional ILM peeling on the outer retinal layer structures after MH surgery in eyes of the inverted group and ILMP group, respectively. They evaluated the postoperative recovery rate of the ELM and EZ and the BCVA. The postoperative recovery rates of the ELM and EZ in the inverted group were lower than those in the ILMP group. The ELM recovery period in the inverted group was significantly longer than that in the ILMP group. These results indicate that eyes treated for MH with the inverted ILM flap technique may exhibit a delay in functional and morphological restoration. Shiode and colleagues [40] provided an explanation of this delay. Migrating Müller cells express neurotrophic factors which may contribute glial hypertrophy and subsequent MH closure. Therefore, the authors believe that the technique will be useful for large, but not for small to medium-size MHs.

Reports on successful treatment of MHs with the use of autologous plasma [41–42] have evolved in recent years. Thus, Gaudric and colleagues [43] proposed to deposit autologous platelet-rich plasma (PRP) on the macula at the end of FTMH surgery. Preoperatively, blood samples were drawn and centrifuged to collect plasma in special tubes. After vitrectomy, ILM peeling, and fluid-air exchange, some autologous PRP was applied to the macula. The technology has been widely used not only in eye disease patients, but also in orthopedic disease, trauma, and sport medicine and dentistry patients, making it interesting for further research. It has been reported that, unlike PRP, the material for Autologous Conditioned Plasma (ACP) is directly harvested into a syringe and sent for centrifugation.

In a study by Zhu and colleagues [44], patients with a large FTMH underwent PPV and ILM peeling with autologous blood covering the MH at the end of the surgery. No fluid-air exchange or gas tamponade was performed. Postoperatively, all patients were instructed to adopt supine position overnight and thereafter any comfortable posture. Complete MH closure was achieved in all eyes at the end of the follow-up period (range, 3–14 months). A disadvantage of this technique is a toxic effect of hemoglobin on the retinal neuroepithelium. Chakrabarti and colleagues [45] investigated the surgical results of MH surgery without gas tamponade or postoperative posturing in patients with Stage 3 and Stage 4 MHs. Eyes of these patients underwent 23-gauge PPV with broad ILM peel, inverted ILM flap repositioning (ILMR), and use of autologous gluconated blood clumps as a macular plug to close the MH. No fluid-air exchange, endotamponade, or postoperative posturing was used. The anatomical outcome of the procedure was evaluated by fundus examination and OCT. The preoperative and postoperative BCVA

in logMAR units were compared to evaluate functional outcome. Although after a single surgery, hole closure was achieved in 100% of eyes, this methodology had failed to find wide use.

Removal of the ILM increases the elasticity of the denuded macula and improves apposition of hole edges during vitreous cavity tamponade. Morescalchi and colleagues [46], however, reported that ILM peeling may cause progressive macular thinning, leading to dimples on the inner retina. In a study by Wolf and colleagues [47], a human donor retina was subjected to ILM peeling shortly after enucleation and studied by electron microscopy. They found that, within the peeled area, a substantial number of vitreal Müller cell processes was severely damaged. Results of a study by Tadayoni and colleagues [48] suggested that ILM peeling may reduce retinal sensitivity, and significantly increase the incidence of microscotomas. A high incidence of complications like a dissociated optic nerve fiber layer (DONFL) appearance in eyes after idiopathic MH surgery has been reported [49], which may lead to retinal atrophy and visual field defects. This makes developing and implementing the ILM peeling techniques sparing the RNFL especially important.

Electroretinography is used for the quantitative assessment of retinal neuronal function. The changes of each component of the focal macular electroretinograms (FMERGs) were investigated in eyes before and after the ILM were peeled completely in the macular area during surgery for IMHs [50]. In the ILM-off group, the a-wave amplitude and mean oscillatory potential amplitudes were significantly larger 6 months after surgery. The b-wave amplitude, however, did not change significantly. The authors concluded that the selective delay of recovery of the FMERG b-wave 6 months after surgery suggests an alteration of retinal physiology in the macular region.

OCT angiography (OCTA) has been used for quantitative evaluation of vascular and morphological changes following IMH surgery with ILM peeling [51]. There was OCTA evidence of reduced foveal avascular zone (FAZ) area in the superficial and deep capillary plexuses (SCP and DCP, respectively) [52–53] and central retinal thickness (CRT) and increased fovea vessel density (FVDS) compared to preoperative values.

However, currently, regardless of the occurrence of retinal damage induced by ILM peeling, most clinicians favor the use of ILM peeling in MH surgeries, because reoperation rates were found to be lower in MHs treated with ILM peeling [54]. Recent studies [55] have demonstrated that fovea-sparing ILM peeling (FSILMP) does not cause significant anatomical changes to the macula and, compared to complete ILM peeling, is a less traumatic treatment option for MH. In addition, complete ILM peeling does not affect only the thickness of the inner retina but also the middle and outer retinae in the parafoveal region as well as the ganglion cell complex [56–57].

OCT studies [58] demonstrated that retinal thinning was observed soon after the MH surgery mainly in the temporal sector but also in the superior and inferior sectors. The changes in the retinal thickness were significantly correlated with the diameters of the MH. There was a greater displacement of the temporal retina than the nasal retina toward the optic disc postoperatively [59–61].

Morescalchi and colleagues [62] believe that FSILMP technique enables relieving tangential vitreomacular traction while preserving the anatomical integrity of the central fovea. The main outcome measures of MH surgery included the foveal retinal sensitivity, visual acuity, and central retinal thickness. The ILM was peeled as close to the vascular arcades as possible in the complete peeling (CP) group, and in a circumferential pattern for about 1-2 disc diameter around the MH in the fovea-sparing peeling (FSP) group. At the end of surgery, 20% SF6 gas was used as tamponade in all cases. Patients were asked to position face down for 5 days after surgery. The result was in favor of FSP with 100% anatomical closure versus 96% in cases treated with complete ILM peeling. The visual acuity improved postoperative in both groups. Regarding central retinal thickness, there was a significant decrease in the CP group and no change in the FSP group. The authors concluded that both CP and FSP are safe and effective treatments leading to functional and anatomical improvements in patients with all size macular holes. However, the FSP technique may provide better functional outcomes because of a greater improvement in foveal retinal sensitivity.

Ho and colleagues [55] presented the results of a new vitrectomy technique to preserve the foveolar ILM during ILM peeling in early stage 2 MH. A donut-shaped ILM was peeled off, leaving a 400- μ m-diameter ILM over foveola in the FSP group. Smooth and symmetric umbo foveolar contour was restored without inner retinal dimpling in all eyes in the FSP group, but not in the CP group. All eyes (100 %) in the FSP group and 50 % of eyes in the CP group regained the inner segment/outer segment (IS/OS) line. The authors [55] concluded that nonpeeling of the foveolar ILM in early stage 2 IMH surgery prevented inner retinal damages and led to better final visual acuity.

Aurora and colleagues [63] described a new technique of inverted ILM flap in a case of chronic, large, full-thickness macular holes, in which multiple ILM flaps were inverted over each other and the hole-like cabbage leaves. The method was found to be effective in large (> 400 μ m), refractory MHs.

Faizrakhmanov and colleagues [64] described a modified temporal inverted ILM flap technique. After ILM staining, a flap was formed temporally at a distance of one disc diameter to two disc diameters from the MH edge, i.e., the ILM was not removed directly at the MH edge. The rate of MH closure after primary procedure was 96%.

Morizane and colleagues [65] conducted a pilot study to determine the effectiveness of autologous transplantation of the ILM for refractory MHs. The main

outcome measures were MH closure and BCVA. MHs were closed successfully in 9 eyes (90%) after autologous transplantation of the ILM. Postoperative BCVAs improved in 80% and were unchanged in 20% of eyes.

Chen and Yang [66] described lens capsular flap transplantation (LCFT) in the management of refractory MHs from multiple etiologies. Others [67] reported the long-term outcomes of LCFT as initial treatment for large MHs. The MH was successfully closed in all cases, and the authors concluded that LCFT could be an alternative method as primary treatment for large MHs.

Autologous neurosensory retinal free flap transplantation has become an innovative method for the management of refractory large MHs [68]. Grewal and Mahmoud [69] believe that the retinal free flap should be more than 0.5 disc diameters larger than the MH to allow for appropriate handling and flap positioning and permit MH closure despite some flap decentration postoperatively. In a study by Lumi and colleagues [70], the MH was closed with an autologous retinal transplant (ART) of an approximate diameter of 1.5-1.8 mm, harvested outside the vascular arcades. Surgery resulted in the anatomical closure of the macular hole in all cases. The OCT angiography showed normal transplant perfusion, without signs of neovascularization, which was confirmed by other studies [71]. Patients undergoing ART for large primary and refractory MHs achieved good anatomic and functional outcomes, with low complication rates, with the most common complication being ART graft dislocation [72].

OCT images of the repaired macular holes were categorized into the following patterns [73–75]:

U-type (normal foveal contour);

V-type (steep foveal contour);

irregular or W-type (foveal defect of neurosensory retina), and
flat/open.

Good postoperative visual acuity was correlated with U-shape closure.

Conclusion

Although the available armamentarium of vitreoretinal surgeons includes a variety of techniques for treating IMHs of any size, there is no universal approach for selecting the optimal hole closure technique. Each technique has certain indications and limitations, which stimulates the search for and development of improved methods of treatment. Fovea-sparing techniques are feasible options for the treatment of eyes with stages 2 to 4 MHs of 700 μ m or less, and allow avoiding certain morphological and functional changes typical of conventional ILM peeling.

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Disclosures

Received 12.10.2022

Accepted 03.01.2023

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Author Contributions: **ID:** Data collection and analysis, Writing – original draft; **IB:** Data collection and analysis, Writing – original draft; **ZR:** Data collection and analysis, Writing – review & editing; **MU:** Conceptualization, Analysis, Project administration. All authors read and approved the final manuscript.

Funding sources: No financial support was received for this study.

Conflict of interest: The authors have no conflict of interest to declare.