Current Management of Macular Hole

by Sumit Randhir Singh, MD; and Raja Narayanan, MD, MBA

Kelly and Wendel were the first to describe surgery for macular hole (MH), where they did pars plana vitrectomy (PPV), removal of cortical vitreous, and fluid-gas exchange with face-down position for 1 week.\(^1\) Surgery for MH is one of the most successful vitreoretinal procedures in this era, with hole closure rates at more than 90%.\(^2,3\) However, the anatomical or functional success remain a concern in cases of large, chronic, myopic, traumatic, recurrent, or persistent MHs, with hole closure rates ranging from 50% to 80%.\(^2,3\) Numerous modifications have been attempted with variable results to further enhance the surgical results.\(^4-9\) Apart from the standard surgical technique of vitrectomy, internal limiting membrane (ILM) peeling, tamponade agents, and adjuvant agents, a variety of different combinations can be attempted to achieve optimal results in these complex MHs.

EPIDEMIOLOGY

MH is more common in females (3.3:1), with bilaterality in about 10% of cases.\(^10\) The incidence increases with age, and the incidence in the fellow eye is 5% to 10% during a period of 5 years.\(^11,12\)

CLASSIFICATION

Gass initially described the pathogenesis of MH and also proposed a staging system based on the relationship of posterior vitreous with the macula and the size of MH.\(^12,13\) He proposed that remnants of cortical vitreous contract and subsequently lead to MH formation. Therefore, the treatment should also aim at relieving this traction leading to centripetal movements of retinal tissue and hole closure.\(^14\)

The International Vitreomacular Traction Study Group has classified the MH on the basis of minimal hole diameter, which is considered the most predictive parameter for hole closure. MHs have been classified as small (< 250 µm), medium (250 µm to 400 µm), and large (> 400 µm).
The original surgical technique of MH (ie, PPV and gas tamponade) was described by Kelly et al. in 1991. During the next decades, the technique has undergone several modifications. This article intends to present an overview of these innovative techniques (Table 1).

**SURGICAL TECHNIQUES**

**Inverted ILM Flap**

Michalewska et al. introduced the inverted ILM flap technique, in which a rim of ILM was left around the MH margins and this residual ILM was inverted upside-down to cover the MH. The authors reported hole closure rates of 98% compared to conventional technique (88%) in MH, with minimal diameter greater than 400 µm. This technique is especially helpful in large MHs and reduces the chances of type 2 (flat-open) hole closure, which is known to have worse visual acuity. The ILM remnant contains Müller cell fragments, which may induce gliosis, and also provides a scaffold for glial proliferation. A representative case is shown as Figure 1.

Several authors have reported a higher anatomical and functional success rate with this technique and its certain modifications. Andrew et al. used a fragment of ILM, described as “ILM hinge” attached to the hole margin, which is then folded in the hole and allowed to settle at base of the hole. Michalewska et al. developed a modification of the original inverted ILM flap technique, peeling only the area temporal to MH.
and inverting it over the MH. The hole closure rates were similar in both the groups (93%), whereas the modified technique had a reduced incidence of dissociated optic nerve fiber layer. Shin et al. used single-layer inverted ILM flap using perfluoro-n-octane as compared to multilayered ILM flap in the original technique.\(^8\)

For myopic MH without retinal detachment, Michalewska et al. reported hole closure in all 19 eyes

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**Figure 2.** Preoperative spectral-domain optical coherence tomography (SD-OCT) images (A) of 70-year-old patient with best-corrected visual acuity (BCVA) of 20/200. Post-conventional internal limiting membrane peeling and fluid-gas exchange, the hole remained open with lifted edge of the macular hole (MH) (B). Following only a repeat fluid-gas exchange using 10% \(\text{C}_3\text{F}_8\) and face-down position for 5 days, the MH closed, with BCVA of 20/80 at 1 month (C).
using the inverted flap technique, with an improvement in best-corrected visual acuity (BCVA) from 1.2 logMAR to 0.56 logMAR.7

**ILM Free Flap**

Introduced by Morizane et al., this technique involves peeling a portion of free ILM harvested from the edge of already peeled area. The free ILM flap is then tucked in position using viscoelastic.20 This is specifically useful in cases of failed primary surgery for MH. The reported anatomical success rates range from 80% to 100%, with a significant improvement in BCVA.20-22 However, the sample size in all these studies has been small (10 to 12 patients), with absence of a control arm.

**Lens Capsular Flap**

Similar to ILM flap, autologous lens capsular flaps have been used with favorable outcomes. Both the anterior and posterior lens capsule have been used.23 However, harvesting the anterior lens capsule is feasible only in patients undergoing combined cataract and MH surgery, whereas only the posterior capsule can be harvested in pseudophakic eyes.

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**Figure 3.** Preoperative swept-source optical coherence tomography (SS-OCT) of the right eye of an 8-year-old boy showing a large-diameter traumatic macular hole (MH) with relatively flat edges (A). Following 3 months of observation and no spontaneous resolution of MH, the patient underwent vitrectomy, autologous retinal graft, and silicone oil injection. Three-month post-silicone oil removal, SS-OCT shows integrated retinal graft with the donor tissue, with poor delineation of retinal layers (B). The visual acuity improved from 20/400 to 20/200.
**Tapping the Edges of MH**

Kumar et al. used a modification of the conventional ILM peeling technique to achieve a better anatomical hole closure. A soft-tip cannula was used to tap the edges of the MH 360° after ILM peeling. This led to an increase in the height of the MH and, therefore, MH index (MHI; described as ratio of vertical height and basal diameter of MH). This was followed by fluid-gas exchange and prone positioning for 5 days. Hole closure was seen in 89.3% of eyes (25 of 28 patients) along with significant gain in BCVA.

**Extended ILM Peeling**

This technique employed in recurrent or persistent MHs involves extending the previously peeled area of ILM until the vascular arcades, thus reducing the tangential traction. D’souza et al. reported a success rate of 46.7% in 30 eyes with repeat vitrectomy and extended ILM peeling (52% for persistent and 25% for recurrent holes). Valldeperas et al., in their study of 51 persistent and 21 recurrent holes using extended peeling of ILM (in select patients) and autologous platelet concentrate, reported a success rate of 76% and 100%, respectively. Other authors have reported hole closure rates ranging from 60% to 70% in small case series.

**Induction of Macular Detachment**

This surgical technique is based on the assumption that in some cases, the retinal tissue may be adherent to underlying retinal pigment epithelium (RPE). The technique described includes small retinotomies (up to five in number) within the arcades and infusion of balanced salt solution to induce macular detachment. This step releases the adhesions and allows a better approximation of the hole edges. The authors achieved anatomical success in nine out of 10 cases.

**Repeat Fluid–Gas Exchange**

This technique finds use in select cases where just a simple fluid-gas exchange using SF$_6$ or C$_3$F$_8$ with postoperative positioning may lead to closure of hole. Rao et al. have reported anatomical closure in 89% (32 of 36 eyes). Although this is simple and cost-effective, it may not be suitable for all the failed MH surgeries. A representative case is shown as Figure 2.

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**MH Laser**

This technique involves application of laser spots at the base of the MH in addition to the conventional ILM peeling. The mechanism of hole closure involves formation of cytokines by RPE after laser photocoagulation, which in turn leads to formation of glial plug.

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**TABLE 1**

**Various Techniques of MH Repair With Rates of Anatomical Hole Closure**

<table>
<thead>
<tr>
<th>Name of Technique</th>
<th>Indication</th>
<th>MH Closure Rate (%)</th>
</tr>
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<tbody>
<tr>
<td>Inverted ILM flap (Michalewska et al.)</td>
<td>Large, idiopathic / myopic</td>
<td>98% (50 eyes)</td>
</tr>
<tr>
<td>ILM free flap (Morizane et al.)</td>
<td>Persistent / recurrent / traumatic</td>
<td>90% (10 eyes)</td>
</tr>
<tr>
<td>Lens caspular flap (Chen et al.)</td>
<td>Persistent / recurrent</td>
<td>75%* (20 eyes)</td>
</tr>
<tr>
<td>Tapping MH edges (Kumar et al.)</td>
<td>Large, idiopathic</td>
<td>89% (28 eyes)</td>
</tr>
<tr>
<td>Extended ILM peeling (Al Sabti et al.)</td>
<td>Large, idiopathic</td>
<td>100% (2 eyes)</td>
</tr>
<tr>
<td>(D’Souza et al.)</td>
<td>Persistent / recurrent</td>
<td>46.7% (30 eyes)</td>
</tr>
<tr>
<td>Induction of macular detachment (Szigiato et al.)</td>
<td>Persistent / recurrent</td>
<td>90% (10 eyes)</td>
</tr>
<tr>
<td>Repeat fluid gas exchange (Johnson et al.)</td>
<td>Persistent / recurrent</td>
<td>74% (23 eyes)</td>
</tr>
<tr>
<td>Macular hole laser (Del Priore et al.)</td>
<td>Large, idiopathic</td>
<td>100% (1 eye)</td>
</tr>
<tr>
<td>(Cho et al.)</td>
<td>Large, idiopathic</td>
<td>94% (18 eyes)</td>
</tr>
<tr>
<td>Arcuate retinotomy (Charles et al.)</td>
<td>Large, idiopathic</td>
<td>83% (6 eyes)</td>
</tr>
<tr>
<td>Radial incisions (Reis et al.)</td>
<td>Persistent</td>
<td>100% (7 eyes)</td>
</tr>
<tr>
<td>Retinal graft (Grewal and Mahmoud)</td>
<td>Persistent</td>
<td>100% (1 eye)</td>
</tr>
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</table>

*The study included 20 eyes (10 eyes each with anterior and posterior capsular flap with anatomical closure rates of 100% and 50%, respectively).

MH = macular hole; ILM = internal limiting membrane.
This acts as a barrier to fluid movements, thereby aiding in approximation of hole edges to RPE. This technique has been used in failed MH surgeries with reasonable success (13 of 15 eyes). Theoretically, there is a risk of development of central scotoma due to the effect of laser.

**Arcuate Retinotomy**

This was introduced by Charles et al. and involved creation of a full-thickness temporal arcuate retinotomy (90° arc length) to increase the compliance of retina and facilitate better apposition of the hole edges. However, the risk of localized iatrogenic damage to RPE because of close approximation of RPE with neurosensory retina in attached retina always remains. This has been shown to cause retinal thinning and underlying RPE defects on optical coherence tomography (OCT).

**Radial Incisions**

In their series of seven patients, Reis et al. described five perifoveal radial incisions starting one hole diameter from the border of MH extending until the hole margins avoiding the papillomacular bundle. The incisions made were full-thickness and reached to the level of RPE. Hole closure was achieved in all seven eyes. Shah et al. described two horizontal radial incisions in two cases of pediatric traumatic MH and obtained successful hole closure.

**Retinal Graft**

This technique used in large, refractory holes involves harvesting an autologous retinal graft. It involves endolaser around the site earmarked for donor site followed by endocautery to the edges of the graft to coagulate the bleeder vessels. Intraocular vertical cutting scissor and forceps were used to manipulate the graft and position it over the base of hole and tuck it in position. The latter step can be facilitated using a perfluorocarbon liquid bubble. Although the anatomical results are encouraging, functional integration may be suboptimal, indicating that the graft tends to act as a mechanical scaffold. Furthermore, there is always an inherent property of the retinal graft to shrink with time (Figure 3).

**POSITIONING**

Eckardt et al. reported that hole closure in the majority of cases (76%) occurred by 48 hours. A few authors have also reported that for MH 400 µm or smaller, face-down positioning for a prolonged period may not be required. Conversely, positioning may be of benefit in holes larger than 400 µm. With the near universal use of ILM peeling in MH surgeries, the tangential traction is relieved. Moreover, the use of adjuvants (described later) may further obviate the need for positioning.

**ADJUVANT AGENTS**

Smiddy et al. described the role of transforming growth factor-beta, which acts as in vivo biological glue and helps in closure of MH. Similarly, autologous whole blood, serum and platelet concentrates, thrombin, and glucuronated blood clumps have been used in various studies with variable outcomes. These adjuvant agents circumvent the use of ILM peeling, thus minimizing the retinal trauma and obviate the need for any tamponade agents or postoperative positioning. However, the benefit of these adjuvants has not been proven in large studies.

**TAMPONADE**

Since the inception, intraocular gases have been favored in cases of uncomplicated MH due to better apposition of the gas to the hole surface. Gas has the additional advantage of spontaneous absorption, whereas silicone oil has to be removed by performing another surgery. The duration of the tamponade has always been a matter of controversy with the availability of various agents such as air, SF6, C2F6, C3F8, and silicone oil. In their study using OCT, Eckardt et al. documented hole closure in 75.7% eyes at 48 hours using air tamponade. Similarly, encouraging results with greater than 90% closure rates using air with 3 to 4 days of positioning has been reported. An isoexpansile concentration of SF6, C2F6, and C3F8 has been shown to yield similar anatomical outcomes, ranging from 87% to 93%. Both conventional (1,000 centistokes) and heavy silicone oil (HSO) have been used as a tamponade in MH. However, their use has not found much favor. The select indications include retinal detachment with MH and patients unable to maintain postoperative positioning like the elderly, children, or those with spinal disability. In their study of 54 eyes, Lai et al. reported an inferior hole closure rate (65% vs. 91%; P = .022), higher reoperation rate with silicone oil, and better BCVA with gas tamponade. Smiddy et al. reported comparable hole closure rates in 82.6% (19 eyes) and 86.9% (20 eyes), with silicone oil and gas tamponade, respectively. However, BCVA gain was better with gas tamponade. Multiple case series have reported good anatomical outcomes with HSO in cases with MH retinal detachment (Oxane HD [Bausch + Lomb, Rochester, NY]: 10 out of 12 eyes) or persistent MHs after failed initial surgery (Densiron 68 [Fluoron GmbH, Ulm, Germany] ranging from 82% to 91%). However, the issues with emulsification of RPE with neurosensory retina in attached retina always remains.
fication, secondary glaucoma, and need for a repeat surgery to remove silicone oil are always a concern. At present, use of silicone oil in MH is reserved for few select indications.

NON-SURGICAL TECHNIQUES

Intravitreal ocriplasmin (125 µm / 0.1 mL) (Jetrea; ThromboGenics, Iselin, NJ) has been successfully used to treat MHs of minimal diameter (< 400 µm) with presence of vitreomacular adhesion. However, the success rates have not been highly encouraging. The hole closure rates vary from 18% to 40%, with worse outcomes associated with large holes of minimal diameter (> 250 µm). Several adverse events have been reported, such as increase in traction or subretinal fluid at fovea, dyschromatopsia, outer retinal changes, retinal tears, and detachment. Moreover, the cost of ocriplasmin may be even higher than vitrectomy in few of the health care settings. Therefore, routine use of ocriplasmin may not be feasible in current scenario.

CONCLUSION

Among the various surgical options available for MH repair, the optimum technique depends on a number of factors, including size and duration of MH, primary or failed surgery, postoperative positioning, and surgical expertise and experience. For primary surgeries with MHs 400 µm or smaller, PPV, ILM peeling, and gas tamponade still remain the standards of choice. For larger MHs, inverted flap may provide a better alternative, with desirable anatomical and functional outcomes. For recurrent or persistent MHs, the choice becomes difficult. Extended peeling of ILM with fluid-gas exchange or ILM flaps can be considered in these recurrent or failed cases. Postoperative positioning of 4 to 7 days may suffice for most of the routine cases. The role of silicone oil as tamponade remains controversial and needs consideration in very few selected cases. Adjuvant agents, though not routinely practiced, are a matter of choice of the treating physician. Currently, MHs can be treated with success due to the availability of a variety of surgical options. The need for face-down position is probably the biggest challenge that remains to be solved.

REFERENCES

Practical Retina


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