ABSTRACT

Primary surgery for macular hole (MH) closure has a high success rate with current methods of pars plana vitrectomy and internal limiting membrane (ILM) peeling. When primary surgery fails, there are several options available for secondary repair, including extension of the ILM peel, creation of an ILM flap, pedunculated ILM flap, lens capsule flap transplantation, autologous retinal transplantation, use of a human amniotic membrane plug, adjuvant autologous platelet concentrate, induction of macular detachments with subretinal blebs, and creation of retinal incisions. In this review, we discuss the practical approach to each of these surgical techniques for the management of recurrent or persistent MHs.

Key Summary Points

- A full-thickness macular hole (MH) is a full-thickness break within the fovea that can cause decreased vision.
- Primary surgery for MH has a high success rate with current methods of pars plana vitrectomy and internal limiting membrane (ILM) peeling.
- When primary surgery fails, several secondary surgical options exist for recurrent or persistent MHs.
- In this review, we discuss each surgical technique in detail.

INTRODUCTION

A full-thickness macular hole (MH) is defined as a full-thickness break within the fovea that can cause a significant decrease in vision. The annual incidence has been reported to be between 4.05 and 8.69 eyes per 100,000 population per year [1, 2]. The prevalence is reported to be between 0.14 and 0.7% in the general population [3–7]. There is a female-to-male...
predominance, and the incidence of MHs appear to increase with age [1, 8–11].

The primary closure rate for macular holes is greater than 90% with current methods, which consist of a pars plana vitrectomy with or without internal limiting membrane (ILM) peeling, and gas endotamponade [12–18]. Peeling of the ILM has been significantly associated with lower rates of reoperation in a recent, large, retrospective, cross-sectional study [19].

The management of recurrent and persistent MHs can be challenging for vitreoretinal surgeons. After closure, macular holes may reopen in approximately 3.3–9.2% of cases, and larger holes are more likely to fail primary surgery [20–25]. Fortunately, a second surgery can result in anatomic closure. In one study by Valdeperas and Wong, reoperation on reopened macular holes resulted in anatomic closure in 100% of 21 cases [20]. In the same case series, 76% of patients who had persistent holes without initial closure achieved successful anatomic closure after the second surgery but final vision was poorer than in those with initial closure. In another study of 103 patients with failed primary macular hole surgery, 85% of 53 reoperated eyes showed hole closure. Vision improved but may take some time to occur [26].

RISK FACTORS FOR FAILURE OF PRIMARY MACULAR HOLE SURGERY

Primary surgical repair may fail due to various factors, including persistent vitreoretinal and epiretinal traction, chronicity of the hole, inadequate gas endotamponade, large aperture diameter, high myopia, or MHs with a flat-open configuration [27–31]. The benefit of face-down positioning after MH surgery remains unclear, but it is possible that it may benefit MHs larger than 400 microns [29, 32, 33].

In general, the prognosis for closure is correlated with the size of the hole [27, 34, 35]. The larger the base diameter and minimal extent of the hole, the higher the likelihood of surgical failure and poorer postoperative visual function [35]. If a second surgery is pursued, the type of surgical technique utilized may depend on the surgeon’s comfort and experience. In our review, we describe the current literature on surgical management options for recurrent and persistent MHs. Table 1 provides a summary of studies.

SURGICAL TECHNIQUES

Internal Limiting Membrane Peel

In 1991, Kelly and Wendel reported the first series of patients to undergo successful vitreous surgery for idiopathic MHs [36]. After their cohort of 52 patients underwent pars plana vitrectomy, epiretinal membrane (ERM) stripping, a gas-fluid exchange, and face-down positioning for at least 1 week, 30 (58%) experienced MH closure. Of these 30 patients, 73% (22/30) had at least a two-line improvement in visual acuity. Seven had no significant change in vision and one showed a significant decline in vision. They also showed a slight negative correlation between visual acuity and duration of symptoms.

Surgery for MH closure was revolutionized when Eckardt et al. introduced internal limiting membrane (ILM) peeling in 1997 [15]. Specially-designed forceps were used to remove a circular area of ILM measuring three to four disc diameters in size from around the hole. This was followed by C3F8 gas endotamponade and face-down positioning. With this technique, 36 of 39 eyes (92%) had full closure of their MH and 77% achieved at least two lines of visual acuity improvement. Similar results were found when Park et al. looked at 58 eyes that underwent ILM peeling (at least 1000 µm from the MH edge) followed by air endotamponade and face-down positioning [37]. With a single surgery, 91% of eyes had successful MH closure. The number of eyes that had a visual acuity of at least 20/50 increased from 5 (9%) eyes preoperatively to 31 (53%) eyes postoperatively. In this study, 14% of eyes were classified as stage 2, 83% as stage 3, and 3% as stage 4. Long term, ILM peeling has proven to be safe. In 64 eyes with follow-up of at least 36 months (median 62 months, mean 56 months), 95% achieved anatomical MH closure without late reopening and best-corrected
| Surgical method  | Authors                        | # of eyes \((n)\) | MH size/stage | Closure rate | Improvement in vision (pre-op to post-op) | Follow-up period |
|------------------|--------------------------------|-------------------|---------------|--------------|-------------------------------------------|------------------|
| ILM peeling      | Kelly and Wendel [36]           | 52                | Not reported  | 58%          | 73% of holes that closed—2 lines or better| Not reported     |
|                  | Eckardt et al. [15]             | 39                | Not reported  | 92%          | 77% of hole that closed—2 lines or better | Not reported     |
|                  | Park et al. [37]                | 58                | 14% stage 2, 83% stage 3, 3% stage 4 | 91%          | 9% initial visual acuity 20/50 or better; 53% final visual acuity 20/50 or better | At least 6 months; mean 696 days (range, 180–1869 days) |
|                  | Haritoglou et al. [17]          | 64                | 8% stage 2, 73% stage 3, 19% stage 4 | 95%          | Median visual acuity improved from 20/100 to 20/32; median gain of 5 lines | At least 36 months; mean 56 months (range, 36–75 months) |
| Enlargement of ILM rhexis | D’Souza et al. [44]             | 30                | Not reported  | 47% (reoperation) | 88% no improvement, 8% improved by 2 lines, 4% improved by 4 lines \((n = 25\) with follow-up data) | Not reported     |
|                  | Che et al. [46]                 | 13                | Mean 584 ± 89 µm | 62% (reoperation) | Mean logMAR visual acuity improved from 0.98 to 0.84 | 6 months         |
| Inverted ILM flap | Michalewska et al. [47]         | 50 (7 failed attempts) | Mean minimum hole diameter 759 µm, mean maximum hole diameter 1595 µm | 98% \((n = 43)\) | Mean visual acuity improved from 0.078 to 0.28 | 12 months        |
|                  | Rizzo et al. [48]               | 320               | MH size subcategorized into 2 groups: < 400 µm and > 400 µm | 92% overall; 97% for MH < 400 µm, 96% for MH > 400 µm | Mean visual acuity improved from 20/110 to 20/54 | Mean 9.3 months ± 2.0 SD |
|                  | Kannan et al. [52]              | 30                | Mean base diameter 1395.17 ± 240.56 µm | 90%          | Mean improvement 2.1 lines of visual acuity | 6 months         |
|                  | Narayanan et al. [53]           | 18                | Mean diameter 1162.8 ± 206.0 µm | 89%          | Mean visual acuity improved from 20/270 to 20/120 | 6 months         |
| Surgical method         | Authors                  | # of eyes (n) | MH size/stage                                                                 | Closure rate | Improvement in vision (pre-op to post-op)                                                                 | Follow-up period |
|-------------------------|--------------------------|---------------|-------------------------------------------------------------------------------|--------------|----------------------------------------------------------------------------------------------------------------|------------------|
| Free ILM flap           | Morizane et al. [57]     | 10            | Mean diameter 509.3 ± 137.8 μm                                               | 90%          | Mean visual acuity improved from 0.99 ± 0.25 to 0.57 ± 0.36                                                  | Mean 12 ± 5 months |
|                         | Dai et al. [60]          | 13            | Mean minimum diameter 814.4 ± 255.0 μm, mean base diameter 1637.6 ± 412.7 μm | 92%          | Mean visual acuity improved from 1.15 ± 0.21 to 0.99 ± 0.17                                                  | 12 months        |
|                         | Pires et al. [58]        | 12            | Mean minimum diameter 654.9 ± 196.5 μm, mean base diameter 1662.7 ± 688.5 μm  | 91% (reoperation) | Mean visual acuity improved from 20/400 to 20/160                                                            | 12 months        |
| Lens capsule transplant | Chen and Yang [64]       | 20            | Mean diameter 788.8 ± 198.1 μm                                               | 75% (reoperation) | Mean logMAR visual acuity improved from 1.53 ± 0.39 to 1.07 ± 0.35                                         | Not reported     |
|                         | Peng et al. [65]         | 50            | Mean diameter 1102.0 ± 561.6 μm                                              | 96%          | Median logMAR visual acuity improved from 1.78 to 1.00                                                       | Mean 18.5 ± 6.1 months |
| Autologous retinal transplant | Grewal et al. [67]      | 41            | Mean inner-opening diameter 825 ± 422.5 μm, mean base diameter 1468.1 ± 656.4 μm | 87.8% (reoperation) | Mean logMAR visual acuity improved from 1.11 ± 0.66 to 1.03 ± 0.51                                          | Mean 11.1 ± 7.7 months |
|                         | Chang et al. [69]        | 10            | Mean diameter 1404.2 ± 562.9 μm                                              | 90% (reoperation) | Mean logMAR visual acuity improved from 1.65 ± 0.43 to 0.88 ± 0.49                                         | 12 months        |
|                         | Tanaka et al. [70]       | 7             | Mean minimum hole diameter 643 μm, mean maximum hole diameter 1214 μm          | 100%         | Mean logMAR visual acuity improved from 1.10 to 0.68                                                        | 12 months        |
|                         | Rojas-Juárez et al. [71] | 13            | Mean minimum diameter 964.38 ± 709.77 μm, mean base diameter 1615.38 ± 689.19 μm | 76.9%        | Mean logMAR visual acuity improved from 0.92 ± 0.28 to 0.75 ± 0.29 (not statistically significant)           | 12 months        |
| Surgical method                  | Authors                        | # of eyes | MH size/stage                          | Closure rate | Improvement in vision (pre-op to post-op)                      | Follow-up period |
|---------------------------------|-------------------------------|-----------|---------------------------------------|--------------|-----------------------------------------------------------------|------------------|
| Amniotic membrane transplant    | Caporossi et al. [73]         | 20        | SF6 group: mean minimum diameter 779.8 ± 142.53 µm; air group: mean minimum diameter 799 ± 175.18 µm | 100%         | SF6 group: mean visual acuity improved from 20/400 to 20/63; air group: mean visual acuity improved from 20/250 to 20/63 | 12 months       |
|                                 |                               | (10 in SF6 group, 10 in air group) |                                       |              |                                                                 |                  |
|                                 | Ferreira et al. [75]          | 19        | Mean base diameter 1301 ± 742 µm, mean minimum diameter 856 ± 459 µm | 100%         | Mean logMAR visual acuity improved from 1.30 ± 0.44 to 1.0 ± 0.72 | Mean 9 ± 3.87 months |
| Autologous platelet concentrate | Gaudric et al. [78]           | 20        | 15% stage 2, 55% stage 3, 30% stage 4 | 95%          | Mean visual acuity improved from 0.18 to 0.43                  | 6 months         |
|                                 | Paques et al. [79]            | 53        | 85% stage 3                            | 98%          | Mean gain of 7.3 ETDRS (Early Treatment Diabetic Retinopathy Study) letters compared to baseline | 1 month          |
|                                 | Vote et al. [80]              | 70        | 20% stage 2, 74% stage 3, 6% stage 4   | 98.5%        | 77% improved at least 2 Snellen lines; mean improvement of 4 lines | Not reported     |
|                                 | Cheung et al. [81]            | 56        | 8 were stage 2, 36 were stage 3, 12 were stage 4 | 98.2%        | 66.1% improved at least 2 Snellen lines                        | Variable: < 6 months in 37 patients, 12 months in 16 patients, 18 months in 1 patient, > 18 months in 2 patients |
| Subretinal blebs                | Meyer et al. [85]             | 41        | Mean aperture diameter 1212 µm, mean base diameter 649 µm | 85.4%        | Mean visual acuity improved from 0.1 to 0.22                   | 6 weeks          |
|                                 | Felfeli and Mandelcorn [87]   | 39        | Mean aperture diameter 549.1 ± 159.47 µm, mean base diameter 941.97 ± 344.14 µm | 87.2%        | 79.5% improved at least 2 Snellen lines                        | Mean 320.33 ± 269.04 |
visual acuity improved in 92% of eyes [17]. In this study, there was a median gain of five lines of vision postoperatively. Eight percent of these eyes were stage 2, 73% were stage 3, and 19% were stage 4.

A subsequent comparative study found that ILM peeling significantly improved primary closure rates when compared to eyes that did not undergo ILM peeling [38]. When comparing 44 eyes without ILM peeling to 116 eyes with ILM peeling, only 36 of 44 eyes without ILM peeling achieved primary closure versus 100% of 116 eyes that achieved primary closure when ILM was peeled ($p < 0.00001$). In eyes without ILM peeling, a greater percentage of stage 3 holes (24% of 25 eyes) had primary failure compared to stage 2 holes (12% of 17 eyes) [39]. In addition, visual acuity after ILM peeling was significantly better compared to eyes without ILM peeling. Other comparative studies found a similar advantage to ILM peeling versus no ILM peeling. In a series by Sheidow et al., 43 of 44 (97.7%) of eyes with ILM peeling without indocyanine green (ICG) staining and 34 of 35 (97.1%) of eyes with ICG-assisted ILM peeling had primary MH closure compared to only 75 of 97 (77.3%) eyes in a group without ILM peeling [13]. ILM peeling also increased the patients’ chances of developing at least 20/50 vision (odds ratio 2.4; 95% confidence interval 1.06–5.45; $p = 0.04$). While the anatomic benefit of ILM peeling has been corroborated in several other comparative trials, its effect on functional outcomes is less clear, with several studies finding no significant difference in ILM-peeled and non-ILM-peeled eyes [14, 16, 40].

More recently, the use of indocyanine green (ICG) dye to stain the ILM has facilitated its visualization, which may improve MH closure rates [41, 42]. In eyes that fail primary surgery despite ICG-assisted ILM peeling, re-staining and enlarging the prior peel may result in an increase in closure rate. In a series of nine eyes with persistent/recurrent MH that underwent additional ILM peeling, all eyes had closure of the MH after the second surgery and experienced statistically significant improvement in postoperative visual acuity [43]. In another study of 55 patients who had failed primary closure or had reopened during follow-up, 30

| Table 1 continued |
|---------------------------------|
| Surgical method | Authors | # of eyes $(n)$ | MH size/stage | Closure rate | Improvement in vision (pre-op to post-op) | Follow-up period |
| Retinal relaxing incisions | Charles et al. [88] | 6 | Mean diameter: 658 ± 180 μm | 83% (reoperation) | 3 patients experienced improvement in vision | Mean 26.5 months (range: 1 to 70 months) |
| | Reis et al. [89] | 7 | MH diameter range: 455 to 750 μm | 100% (reoperation) | All patients experienced improvement in vision | Mean 12 months (range: 5–24 months) |

ILM, internal limiting membrane; MH, macular hole.
underwent a second surgery with enlargement of the ILM rhexis [44]. Fourteen of the 30 eyes (46.7%) achieved secondary closure and an improvement in best corrected visual acuity (p = 0.02). Two other series in which eyes underwent additional ILM peeling showed a secondary closure rate between 61.5 and 68.9% with an improvement in vision [45, 46].

**Internal Limiting Membrane Flap**

Providing a scaffold over the MH for tissue proliferation is another approach that has been shown to lead to MH closure in difficult cases. In 2010, Michalewska et al. described the use of an inverted ILM flap for MH closure and found that it improved both anatomic and functional outcomes for MHs greater than 400 μm in diameter [47]. In their study of 43 eyes that successfully underwent the inverted ILM flap technique, the mean minimum and maximum MH diameters were 759 μm and 1595 μm, respectively. There was a 98% MH closure rate after the first surgery and patients experienced a statistically significant improvement in vision 12 months after surgery. In this technique, ERM peeling is followed by circumferential peeling of ILM two disc diameters around the MH. The ILM is left attached to the MH edge and trimmed down, then the ILM remnant is gently inverted upside-down over the MH until it is covered. The authors believe that this technique works by introducing Müller cells that induce glial cell proliferation. Compared to standard ILM peeling, the ILM flap technique improved closure rate, the anatomic configuration of the fovea, and the postoperative visual acuity. Additional studies found a similar anatomic benefit of the inverted ILM flap over conventional ILM peeling in myopic eyes with MHs [48–50]. While another study by Manasa et al. also found superior outcomes for the inverted ILM flap technique in holes of at least 600 μm in size, additional trials looking at similarly sized MHs did not find a benefit in anatomical or visual outcomes, and the results appear mixed for these larger MHs (at least 600 μm in diameter) [51–53].

Several variations of the ILM flap have been described, including a semicircular ILM peel with a temporally hinged inverted flap, a circular ILM peel with temporally hinged inverted flap, and circular ILM peel with superior inverted flap, with studies suggesting comparable results amongst the different techniques [54, 55]. Another variation is called the “Texas taco” technique and involves a semicircular peel of the nasal ILM beyond the temporal edge of the hole followed by draping of the ILM flap over the hole [56]. In all of these techniques, the principle is the same: to provide a scaffolding over the hole.

In cases with previously complete ILM peels, creation of an ILM flap may not be possible. In these eyes, the use of a free ILM flap or a pedunculated flap are options [57]. Morizane et al. described a technique in which a small piece of ILM peeled from the peripheral macula is used to create a free flap similar in diameter to the macular hole [57]. This is followed by stabilization of the flap with a viscoelastic tamponade within the hole. In their prospective series of 10 eyes, 9 eyes had successful closure and 8 eyes had significant improvement in visual acuity an average of 12 months after surgery [57]. The mean MH diameter in their series of patients was 509.3 ± 137.8 μm. Similar results with high closure rates and improvements in vision have been reported in other similarly sized series with large MHs [58–60]. Maintaining the tissue within the hole may be difficult during air-fluid exchange, but use of perfluorocarbon or viscoelastic, as previously mentioned, can help tamponade the flap in place during this step of the surgery [61, 62]. The pedunculated flap is where an ILM flap larger than the radius of the hole to the edge of the previous ILM peel is fashioned with the hinge at the edge of the previous ILM peel. This allows the flap to lay across both the original ILM peel area and the hole. It goes without saying that this may be technically difficult as the ILM is increasingly thinner the further from the fovea one goes.

**Lens Capsule Transplant**

When ILM peeling or an ILM flap are difficult or not possible, the tissue of the lens capsule may
provide an alternative scaffold to facilitate MH closure in recurrent or persistent cases [63, 64]. Chen and Yang first described this technique in 2016 in a series of 20 eyes (mean MH diameter 788.8 ± 198.1 μm) with prior history of a failed pars plana vitrectomy with ILM peel [64]. The procedure was performed by first staining the anterior (AC) or posterior capsule (PC) with ICG, followed by the creation of a capsule flap dependent on the patient’s lens status. In phakic patients, combined cataract surgery was performed and the AC was harvested, and in pseudophakic patients, the PC was used. The flap was trimmed to a size slightly larger than that of the MH and placed within the hole with microforceps. Ten of 10 eyes with AC flap transplantation and 5 of 10 eyes with PC transplantation achieved complete hole closure, and vision was significantly improved [64].

The long-term results of this technique appear favorable. In a series of 50 eyes that had undergone either autologous or allogeneic lens capsule transplantation, the closure rate was 96.0% after a mean follow-up period of 18.5 months (mean MH diameter 1102.0 ± 561.6 μm) [65]. This series also demonstrated an improvement in vision. Thirty-one of the 50 eyes also had simultaneous autologous whole-blood application which may reduce lens capsule dislocation during the procedure.

**Autologous Retinal Transplant**

In 2016, Grewal and Mahmoud introduced the use of an autologous full-thickness retinal free flap for closure of refractory myopic MHs [66]. Similar to the ILM flap and lens capsule flap, the retinal tissue provides a scaffold and plug for MH closure. They describe this technique in their first published case of a -15-diopter myopic woman with a complex history of failed vitrectomy with ILM peel for a MH followed by a scleral buckle and vitrectomy for retinal detachment repair. Additional ILM could not be harvested and she was pseudophakic with an open PC. During the procedure, they applied endolaser barricade and diathermy in a circular pattern around a 2-disc diameter area of retina and used a bimanual approach with vertical scissors and forceps to obtain a retinal free flap. This was followed by instillation of perfluoro-n-octane heavy liquid (PFC; Perfluoron; Alcon) over the flap and direct PFC-silicone oil exchange. After 3 months, her MH remained closed and vision improved.

In a multicenter case series of 41 eyes with macular holes refractory to prior vitrectomy with ILM peeling, 87.8% achieved anatomic hole closure after autologous retinal transplantation [67]. The study included MHs with a mean inner-opening diameter of 825 ± 422.5 μm and a mean base diameter of 1468.1 ± 656.4 μm. The mean visual acuity improved in 36.6% of eyes, remained stable in 41.5% of eyes, and worsened in 21.9% of eyes. Similar anatomic success rates have been found in additional case series, though results for functional improvement have been less consistent [68–71]. In a recent prospective case series of 13 eyes with refractory MHs (mean minimum diameter 964.38 ± 709.77 μm, mean base diameter 1615.38 ± 689.19 μm), closure rate after 12 months was 76.9% with this technique but there was no statistically significant improvement in vision [71].

**Amniotic Membrane Transplant**

Rizzo et al. first reported the use of a human amniotic membrane (hAM) for MH closure in 2019 [72]. In their series of eight eyes with recurrent MH despite prior vitrectomy with ILM peeling, hAM was manipulated under fluid or perfluorocarbon (perfluorodecalin, Biofluor, Bucine [AR], Italy) and transplanted through the MH into the subretinal space. Afterwards, the patients underwent an air-fluid exchange and gas endotamponade, yielding a 100% closure rate at 6 months of follow-up. It is believed that the hAM induces retinal pigment epithelium (RPE) cell proliferation and secretion of growth factors that facilitate retinal growth, as optical coherence tomography (OCT) scans obtained during the postoperative period demonstrated a fully stratified retinal layer over the patch of hAM. In a comparative study of 10 eyes with a hAM plug and 20% SF6 gas endotamponade versus 10 eyes with hAM plug and air endotamponade, all MHs were found to be closed after 12 months [73]. Both groups maintained face down positioning for 3 days.
and there was no statistically significant difference in MH size or postoperative visual acuity between the two groups. The mean minimum MH diameter was $779.8 \pm 142.53 \, \mu m$ in the SF6 group and $799 \pm 175.18 \, \mu m$ in the air group. Similar success rates have been reported in additional case series with the use of hAM for MH closure, though studies comparing this technique to others have not been published [74–76].

**Autologous Platelet Concentrate**

Autologous platelets are believed to contain growth factors and cytokines that may promote tissue healing [77]. Gaudric et al. decided to test the effects of autologous platelet concentrate (APC) by comparing two groups of patients with MHs, one with (group 1) and one without (group 2) an injection of autologous platelet concentrate (APC) after standard MH surgery [78]. They found a statistically significant difference in MH closure rate (95% in group 1 versus 65% in group 2) but no difference in vision for successfully operated eyes between the two groups. They then studied 110 patients with stage 3 or 4 MHs and randomized them to receive an APC injection or no APC injection after standard vitrectomy, posterior hyaloid separation, and fluid-gas exchange [79]. Their results were similar: the group that received an APC injection ($n = 53$) had a 98% MH closure rate one month after surgery while the control group without an APC injection ($n = 57$) had an 82% closure rate ($p = 0.009$). However, when comparing successfully closed MHs, visual acuity was not significantly different between the groups.

In a study of 70 eyes that underwent vitrectomy with APC, primary anatomical closure rate was 95.7%, though 8.5% of holes reopened a mean of 12.7 months after the initial surgery [80]. In this subset of patients, 14 eyes were classified as stage 2 holes, 42 as stage 3 holes, and 4 as stage 4 holes. After reoperation on reopened holes, final surgical success was 98.5%, and 77.0% of patients experienced an improvement in visual acuity at final follow-up. Another review of 56 patients revealed a similar anatomical success rate of 98.2% with 66.1% experiencing functional improvement, defined as at least two lines of improvement in Snellen vision [81]. Of the 56 eyes, 8 were classified as stage 2, 36 as stage 3, and 12 as stage 4 MHs. More recently, a comparative study evaluating ILM peeling versus ILM peeling plus platelet-rich plasma (PRP) showed a significant improvement in anatomic and functional results in eyes that had adjuvant application of PRP [82]. While these results are encouraging, larger prospective comparative studies are necessary to corroborate these results.

![Fig. 1 FTMH closure after enlargement of the ILM rhexit](image_url)
Subretinal Blebs

Induction of a localized macular detachment around the macular hole has also been shown to be a viable option for the closure of recurrent or persistent holes [83, 84]. In this technique, a small-gauge subretinal cannula (38-gauge or 41-gauge) is connected to a syringe filled with balanced salt solution (BSS), and multiple BSS blebs are injected into the subretinal space surrounding the MH. After additional BSS is injected and a confluent perifoveal serous detachment is induced, a Tano diamond dusted scraper or a Flex Loop is used to massage the released paracentral retina towards the fovea center. This is followed by an air-fluid exchange and either gas or silicone oil endotamponade. The technique is believed to work by releasing any firm adhesions of photoreceptors to the retinal pigment epithelium (RPE), allowing mobilization of the parafoveal retina. These adhesions are hypothesized to be one potential reason initial MH surgery fails despite the release of epiretinal traction.

Using this method, Meyer et al. achieved a closure rate of 85.4% in a case series of 41 eyes with large MHs (mean base diameter of 649 microns) [85]. In another series of ten eyes with persistent or recurrent MH after prior ILM peeling, 90% experienced closure 6 months postoperatively with a statistically significant improvement [86]. Another study reported a similar closure rate of 87.2% in a series of 39 eyes with a mean MH base diameter of 941.97 ± 344.14 μm [87]. The mean postoperative vision was significantly improved and better in the closure compared with the non-closure group.

Retinal Relaxing Incisions

Charles et al. presented a technique involving the creation of a full-thickness arcuate retinotomy temporal to a MH in a series of six eyes with large MHs (mean diameter 548 ± 180 μm) that had failed primary repair [88]. Using this approach, five (83%) of those eyes had successful MH closure and three (50%) demonstrated an improvement in visual acuity. His technique is limited by its potential damage to the underlying RPE as evidence by postoperative retinal thinning and underlying RPE defect in some patients. Variations of this technique include the creation of five peri-foveal radial full-thickness incisions beginning one hole diameter away and ending at the margin of the hole or the creation of 120 degree arcuate relaxing retinotomies near the superotemporal and inferotemporal vascular arcades [89, 90].
CONCLUSIONS

While primary anatomic closure rates for macular holes are high, complex cases that are recurrent or refractory can be challenging for vitreoretinal surgeons. Fortunately, there are numerous techniques that have been developed that may portend good anatomic and functional outcomes. Currently, there are no large, randomized studies directly comparing these techniques to one another, so the selection generally rests on the surgeon’s personal preference and experience.

Case Examples

Case 1: Enlargement of the ILM Rhexis
A 73-year-old Caucasian woman with a history of non-exudative age-related macular degeneration (AMD) presented with decreased vision in

Fig. 3 FTMH closure after subretinal blebs
her right eye for 3 months. Vision was count fingers, which had declined significantly from 20/30 1 year prior. On examination, she had a full-thickness MH and OCT confirmed a MH with a base diameter of 1020 μm and a minimum diameter of 740 μm (Fig. 1A). She underwent cataract surgery with intraocular lens placement, pars plana vitrectomy, ERM removal with creation of an ILM flap, and C3F8 gas endotamponade. Three months later, the hole remained open with a base diameter of 1230 μm and a minimum diameter of 410 μm (Fig. 1B). She underwent a second surgery with enlargement of the ILM rhexis and the hole remained closed at the postoperative month 6 visit and vision was 20/500 (Fig. 1C).

Case 2: ILM Flap
A 68-year-old Caucasian man presented for a second opinion for a persistent MH in his right eye. He had decreased vision for 2 months prior to undergoing pars plana vitrectomy with membrane peel and SF6 gas endotamponade. After the MH failed to close, he underwent repeat pars plana vitrectomy, membrane peel, and C3F8 gas endotamponade, which also failed to close the hole. He subsequently presented to the Cole Eye Institute with a vision of 20/200. An OCT revealed a full-thickness MH with a base diameter of 910 μm and minimum diameter of 470 μm (Fig. 2A). He underwent cataract surgery with intraocular lens placement, pars plana vitrectomy, an ILM flap, and C3F8 gas endotamponade. One week after surgery, an ILM flap was visible over a closed MH (Fig. 2B). The hole remained closed 8 months after surgery and vision improved to 20/50 (Fig. 2C).

Case 3: Subretinal Blebs
A 63-year-old African-American woman presented with declining vision in the right eye for 1 year. Vision was 20/80 and OCT showed a MH with a minimum diameter of 970 μm and a base diameter of 1290 μm (Fig. 3A). After pars plana vitrectomy with a membrane peel, ILM flap, and C3F8 gas endotamponade, the hole decreased in size but remained open (Fig. 3B). Two months after surgery, vision was 20/100. OCT showed a persistent MH with a minimum diameter of 770 μm and a base diameter of 1520 μm (Fig. 3C). The patient underwent repeat pars plana vitrectomy with an ILM free flap, but the hole remained open on OCT 10 days after surgery (Fig. 3D). Three months after the second surgery, the MH persisted with a base diameter of 1710 μm and a minimum diameter of 890 μm (Fig. 3E). Vision remained unchanged at 20/100. The patient then underwent repeat pars plana vitrectomy with injection of BSS into the subretinal space surrounding the MH. The MH was shown to be closed at postoperative month 1 and remained closed 3 months after surgery (Fig. 3F). Vision remained stable at 20/100.

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