Clinical Management of Myopia in Adults: Treatment of Retinal Complications

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Key Points
- MTM is an important treatable cause of visual loss among individuals with high myopia.
- A certain proportion of cases of MTM do not progress. Treatment should be offered to patients with more advanced disease with progressive visual loss.
- Fovea-sparing instead of complete peeling of the ILM and avoidance of gas tamponade could prevent the formation of secondary macular hole in MTM.
- Surgical adjuncts should be considered for macular hole especially in high-risk cases (persistent macular hole despite initial surgery, large and chronic macular hole, atrophic macula, etc.)

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12.1   Introduction

As described in the previous chapter, myopic foveal retinoschisis was first described in 1958 [1], then by Takano and Kishi in 1999 through the advent of optical coherence tomography (OCT) [2]. Subsequently, the various pathological effects of traction on the macula in patients with high myopia were collectively termed *myopic traction maculopathy* (MTM) by Panozzo and Mercanti in 2004 [3]. It was estimated to occur in approximately 8–34% in individuals with high myopia [4–6]. The term MTM originally encompassed retinal thickening, macular retinoschisis, foveal detachment, and lamellar macular hole with or without epiretinal membrane and/or vitreomacular traction [3]. The spectrum was extended to include full-thickness macular hole (HM) with or without retinal detachment.

Central to the pathogenesis of MTM is traction, which was postulated to arise from one or more of the following mechanisms [7]: vitreomacular traction associated with perifoveal posterior vitreous detachment (PVD) [8–10]; relative incompliance of inner retinal structures (e.g., internal limiting membrane [ILM] [11–15], epiretinal membrane [ERM] [6, 8, 16–18], and cortical vitreous remnant after PVD [19]) to the outer retina which conforms to the shape of the posterior staphyloma; and traction exerted by retinal arterioles [14, 20, 21].

Not all patients with MTM require interventions [10, 22, 23]. A study on the natural history of MTM with 207 eyes found that while 12% of cases progressed during a mean follow-up period of 36 months, the majority (84%) remained stable and a small proportion (4%) even had improvement or complete resolution of the disease [24]. The extent of macular retinoschisis was identified as a predictor of progression, with stage 4 disease (i.e., involving the entire macula) having the higher chance of progression than any other stages [24]. It is generally accepted that eyes with complications such as foveal detachment or full-thickness MH with or without retinal detachment, or eyes with significant progression in the extent of macular retinoschisis on OCT should undergo intervention early. On the other hand, an early macular retinoschisis involving only a limited area of the macula with preserved vision should be monitored with OCT for any progression.

There are numerous reported interventions for MTM. The principles of the treatment are: (1) to relieve traction, mainly achieved through pars plana vitrectomy (PPV) with or without ILM peeling; (2) to minimize surgical damage to the weakened macula through technique modifications in order to prevent the formation of postoperative MH; and (3) in the presence of full-thickness MH to maximize the chance of hole closure through the use of various surgical adjuncts.

12.2   Surgical Procedures

12.2.1 Pars Plana Vitrectomy

PPV serves several purposes in the treatment of MTM. It allows removal of all premacular tractional forces, including posterior vitreous cortex and ERM. It also creates a potential space in the posterior segment for gas tamponade to be performed.

12.2.1.1   Microincision Vitrectomy Surgery

With the advent of microincision vitrectomy system, PPV can be performed with small sclerotomy wounds and instruments in the size of 23 gauge, 25 gauge, or 27 gauge. Small sclerotomy wounds tend to be self-sealing and do not require sutures. It has the advantages of reduced ocular trauma, reduced inflammation, less conjunctival scarring, shorter operation time, better patient comfort, and faster postoperative recovery [25]. The design of closer opening near the tip of vitreous cutter probe also facilitates engagement and induction of PVD.

12.2.1.2   Induction of Posterior Vitreous Detachment

Since the pathogenesis of MTM involves abnormal vitreoretinal traction at the macula, induction of PVD is crucial to a successful operation. After core vitrectomy, induction of PVD is performed by using an aspiration port, usually the vitreous cutter probe, to engage the posterior hyaloid just anterior to optic disc. Once the posterior hyaloid is engaged by applying aspiration, the port is lifted upward to detach the posterior hyaloid from the retinal surface.

Induction of PVD can be difficult in MTM due to tight vitreoretinal adhesion and presence of vitreoschisis. Vitreoschisis refers to splitting of posterior vitreous cortex which occurs when there is vitreous gel liquefaction but without dehiscence at the vitreoretinal interface [26]. Vitreoschisis is common in MTM and is present in around half of the patients with MH [27]. To facilitate induction of PVD, triamcinolone acetonide [28] or trypan blue can be injected to stain the posterior hyaloid to improve visualization. If PVD cannot be induced by aspiration, intraocular forceps or diamond-dusted membrane scraper can be used to lift and assist detachment of the posterior hyaloid [29, 30].

12.2.1.3   Epiretinal Membrane Peeling

It is necessary to remove all ERM if any present on the macula. Removal of ERM allows removal of tractional forces on the macula, and allows access and identification of the underlying ILM with vital dyes.

Trypan blue is useful to stain the ERM to enhance visualization [31, 32]. Trypan blue is often injected after fluid-air exchange [33], or it can be mixed with 10% glucose isovolumetrically to create a heavy dye denser than balanced salt solution so that it will fall onto the macula with less dispersion in vitreous cavity [34]. There are also products combining trypan blue, brilliant blue, and polyethylene glycol with increased molecular weight so that the dye falls onto the macula to enhance tissue staining.

12.2.1.4   Internal Limiting Membrane Peeling

ILM is the innermost layer of a normal retina. It has significant contribution to retinal rigidity [35]. ILM peeling therefore improves retinal compliance and allows the retina to restore its normal anatomy [35]. The potential complications of ILM peeling include iatrogenic damage to retinal nerve fiber layer, retinal hemorrhage, and retinal defect formation, especially at sites of ILM flap creation and grasping points [35]. Due to the thinner retina and longer distance required to reach the posterior pole, ILM peeling is more technically challenging in highly myopic eyes than normal eyes and complications may be more common.

ILM is barely visible and requires staining with vital dyes for identification. Triamcinolone acetonide and trypan blue do not stain ILM well. The better dyes for ILM staining are brilliant blue and indocyanine green (ICG) [31, 32]. ICG adheres well to the extracellular matrix of ILM such as collagen type 4 and laminin and allows good visualization of ILM [31]. However, there are concerns of potential retinal toxicity, especially when ICG is in direct contact with the photoreceptors and retinal pigment epithelium through a MH [31]. ICG retinal toxicity has been shown with electrophysiology and histological studies in animal models [36, 37]. The risk increases with endoillumination light exposure [32]. In comparison, brilliant blue is a much safer alternative. A recent meta-analysis showed that postoperative visual acuity was better with brilliant blue than ICG in MH surgeries [38].

After ILM staining, an ILM flap can be created at the extrafoveal region using intraocular forceps by direct pinch method [35]. Alternatively, a pick, diamond-dusted membrane scraper or flexible nitinol loop can be used to create an ILM flap by scrapping [11]. The ILM flap is then lifted with intraocular forceps and moved in a circular fashion so that the whole ILM is peeled off from the macula.

Full-Thickness Macular Hole

In full-thickness MH, ILM peeling helps to reduce retinal rigidity and improve retinal compliance and thus the chance of MH closure [35]. It also helps to reduce postoperative ERM formation and risk of MH reopening [35]. A meta-analysis of four randomized controlled trials showed that ILM peeling for stages 2, 3, and 4 full-thickness MH has a significantly higher closure rate than without ILM peeling [39]. Another meta-analysis showed that MH reopening rate reduced from 7 to 1% when ILM peeling was performed.

Concerning the extent of ILM peeling, there is no consensus on the optimal size required [35]. Extended ILM peeling up to arcade is often performed for large MH to ensure traction has been sufficiently removed. Extended ILM peeling, however, is performed at the expense of longer operation time and higher risk of iatrogenic retinal trauma due to repeated ILM grasping [35]. Dissociated optic nerve fiber layer (DONFL) and swelling of arcuate retinal nerve fiber layer (SANFL), which can be shown on imaging modalities such as OCT scan and infrared fundus photographs, are two known structural changes secondary to ILM peeling [40, 41]. ILM flap initiation techniques might affect the chance of these structural complications, with pinch technique shown to be less damaging than diamond dust membrane scraping [40].

Myopic Foveoschisis

For myopic foveoschisis, ILM peeling helps to ensure that all tractional forces from premacular glial cells and vitreous cortex are completely removed [42]. It increases retinal compliance and allows the retina to better conform to the posterior staphyloma [42].

Favorable anatomical and visual outcomes have been reported for combined PPV, ILM peeling, and gas tamponade. However, development of postoperative full-thickness MH is not uncommon and occurs in around 13–28% of patients [43].

Shimada et al. [44] and Ho et al. [45] introduced the technique of *fovea-sparing ILM peel* in 2012. Instead of complete ILM removal, this technique involves removal of the perifoveal ILM only and leaving the ILM over the central foveola intact. It is believed that preservation of foveolar ILM would preserve foveolar Muller cells integrity and therefore reduce the risk of postoperative MH development [46]. Although studies suggested this technique might be useful to reduce the risk of MH development and foveolar thinning [46], leaving ILM on the fovea could result in late ILM contraction and retinal thickening [44]. This technique is also more technically demanding and requires more tissue manipulation than conventional complete ILM peeling.

In view of the risk of secondary macular hole development in foveoschisis patients undergone ILM peeling, conservative treatment can be considered in foveoschisis patients without foveal detachment.

12.2.1.5   Gas Tamponade

The commonly used gases for tamponade include air, sulfur hexafluoride (SF_6), and perfluoropropane (C_3F_8). Gas tamponade is commonly performed for MTM, particularly in cases with FTMH. For myopic foveoschisis without FTMH, it is still controversial whether gas tamponade is necessary. Gas tamponade may help the retina to adhere better to the posterior staphyloma and tamponade against unnoticeable macular holes [47]. In the presence of outer retinal detachment, the subretinal fluid (SRF) could be displaced toward areas with healthier retinal pigment epithelial (RPE) cells, which can facilitate SRF absorption [48–50]. More rapid resolution of foveoschisis was also reported by a study [51]. However, the study showed that the chance of successful resolution was similar between the group with gas tamponade and that without gas tamponade [51]. Indeed, a meta-analysis showed that for eyes undergoing vitrectomy for myopic foveoschisis, gas tamponade did not have significant impact on visual acuity or the rate of resolution of foveoschisis, yet it was associated with more complications [42]. Several studies also reported the paradoxical occurrence of FTHM from the use of gas tamponade, which could squeeze SRF within the limited space through the weak point of fovea [52–54]. The use of gas tamponade as an adjunct for FTMH would be discussed below.

12.2.2   Additional Measures (Adjuncts) to Improve Outcome of Macular Hole Surgery

12.2.2.1   Endotamponade

PPV with endotamponade agents is the most commonly employed technique for the management of myopic macular hole with or without retinal detachment. Gas tamponade with long-acting gases, commonly SF_6 and C_3F_8, has the advantages of high surface tension and buoyancy compared to silicone oil. A study comparing C_3F_8 and silicone oil as a tamponade agent for myopic MH retinal detachment (MHRD) showed higher initial success rate for C_3F_8 than silicone oil [55]. Due to lower buoyancy, silicone oil is less conforming to posterior staphyloma, rendering

it less effective for MHRD. However, silicone oil still has advantages over gases for longer duration of tamponade, shorter duration of face down posturing, earlier visual recovery as well as allowing immediate air travel.

12.2.2.2 Inverted Internal Limiting Membrane Flap

Even with extended ILM peeling, a proportion of large chronic MH remains open after operation. Michalewska et al. introduced the *inverted ILM flap technique* in 2009 and reported closure rate of large MH reached 98% [56]. Instead of complete ILM removal, this technique involves leaving a hinge of ILM flap at the edge of MH during ILM peeling. This ILM flap is then inverted upside-down to cover or fill the MH. Some surgeons would inject an ophthalmic viscosurgical device on the inverted ILM flap in order to keep it in place. It is postulated that this technique facilitates MH closure by (1) providing a flap which contains Muller cell fragments to induce glial cells proliferation, and (2) providing a scaffold for retinal tissue to approximate [56]. Despite an apparently promising closure rate for large or persistent MH, it has been reported that the visual recovery and recovery of retinal microstructures such as external limiting membrane and the ellipsoid zone are worse among cases managed with inverted ILM flap when compared to conventional complete ILM peeling [57]. This can possibly be due to mechanical obstruction of functional recovery of retinal layers by the presence of an ILM plug in the MH.

12.2.2.3 Autologous Internal Limiting Membrane Transplantation

Although the inverted ILM flap technique proposed by Michalewska and associates seems to be a good surgical adjunct for anatomical closure of large MH, this method cannot be applied to patients who suffer from persistent macular hole after vitrectomy and conventional ILM peeling, since ILM surrounding MH has already been removed in the previous procedure. In view of this limitation, Morizane et al. introduced a new method of ILM flap, which is the autologous ILM transplantation (free ILM flap) [58]. Brilliant Blue G solution is used to stain the remaining ILM in those refractory MH cases. Subsequently appropriately sized ILM is peeled off, which is supposed to match the size of the macular hole, and is placed as a free flap onto the persistent MH. Infusion should be turned off during the procedure in order to avoid accidental loss of the ILM flap. In order to stabilize the flap, an ophthalmic viscosurgical device is injected on the top of the flap before fluid-air exchange is performed. It has been demonstrated that with this method of autologous ILM transplantation, up to 90% of refractory MH (with previous vitrectomy and ILM peeled) could achieve MH closure [58, 59].

12.2.2.4 Autologous Blood

In order to prevent subretinal migration of dye and the resultant retinal toxicity associated with vital stains, it was proposed to use autologous blood to cover the MH before injection of brilliant blue dye. Ghosh et al. collected autologous heparinized whole blood from patients' antecubital vein and injected to MH before injection of brilliant blue dye assisted ILM peeling. It has been demonstrated that compared to conventional method, the use of prestaining autologous blood led to better visual

acuity outcomes and continuity of ellipsoid zone at all postoperative time points; and the outer retinal layer is thicker as well [60].

Apart from being used in the prevention of subretinal migration of dye, the therapeutic effect of autologous blood in persistent and refractory MH has also been investigated. It has been shown that injection of autologous blood or platelet concentrate into MH after ILM peeling can improve closure rate of macular hole and visual recovery [61–63]; and the efficacy of autologous platelet concentrate might even be better than whole blood. In one study in which 75 subjects were included, MH closure rate after revitrectomy plus autologous platelet concentrate was 85.2% versus 7.1% in the group using autologous whole blood instead [64].

12.2.2.5   Lens Capsular Flap Transplantation

Due to the possible lack of residual accessible ILM in reoperative cases of persistent MH, transplantation of lens capsules to MH have been proposed to increase the surgical success rate. In patients with cataract, phacoemulsification would be performed in the same setting and capsular flap would be harvested during continuous curvilinear capsulorhexis and stained with indocyanine green solution or brilliant blue solution for better visualization. In aphakic or pseudophakic patients with insufficient anterior capsule, capsular flap can be harvested from their fellow eyes requiring cataract operations. Alternatively, posterior capsular flap can be used instead. Since capsular flaps are more rigid than ILM flap, it is easier to manipulate during the operation. Moreover, due to the higher specific gravity of capsular flap, it will sink in balanced salt solution, therefore shall fall nicely onto the preretinal surface, unlike ILM flap that is tended to float inside the vitreous cavity. Chen et al. demonstrated a 100% MH closure rate with anterior capsular transplantation among patients with refractory MH, whereas the complete closure rate of MH after posterior capsular transplantation was only 50% and with another 30% enjoyed partial MH closure [65]. Similarly, Peng et al. reported a 90% MH closure rate after transplantation of anterior capsule to refractory MH [66].

12.2.2.6   Macular Buckle

One of the major etiological factors of MTM is the elongation of axial length of the globe leading to tension and traction on retinal layers. The aim of vitrectomy is to remove vitreous traction and ILM peeling to reduce the rigidity and improve the compliance of retina. Nevertheless, none of these procedures tackle the primary pathology, which is the long axial length in high myopes.

Macula buckles have been used to shorten the axial length of myopic eyeballs in conditions such as MHRD, myopic foveoschisis with or without foveal detachment and MH with foveoschisis. There are many types of macular buckle, including scleral sponge, T-shaped or L-shaped buckle, Ando Plombe, wire-strengthened sponge exoplant, and even donor sclera and suprachoroidal injectable long-acting hyaluronic acid. Chandelier light is attached to the indenting head of macular buckle when necessary for better localization and positioning of the buckle. The purpose of all the aforementioned macular buckles is to shape the globe back to normal length along the visual axis, thereby reducing the anteroposterior traction on retina and the tension within retinal layers [67].

Studies have been carried out to compare the efficacy of vitrectomy and macular buckle in inducing retinal reattachment and MH closure in patients suffering from MHRD. Fifty to seventy-nine percent of patients with previous vitrectomy had their retina successfully reattached whereas 93.3–100% of the patients managed with macular buckles enjoyed flattening of the retina [68–70]. The differences in MH closure rates between the two treatment modalities are even higher. Similarly, comparing to less than 50% MH closure rate by vitrectomy, macular buckle surgeries achieved a 100% closure rate in patients with MH and concomitant foveoschisis, and more than 80% of these patients had improvement in final visual acuity [67]. In patients with very poor MTM, combined vitrectomy and macular buckle surgeries can be considered.

Despite the high success rate in the latest macular buckle surgeries, these procedures are technically demanding and are not without risks. Complications of macular buckles include globe perforation, problems with extraocular movement, squint, choroidal effusion, changes in retinal pigment epithelium and the need for removal of buckle.

12.2.2.7 Autologous Neurosensory Retinal Transplantation

In 2016, Grewal and Mahmoud reported the technique of autologous neurosensory retinal free flap transplantation for the closure of refractory macular hole after initial PPV with peeling of ILM [71].

The technique involves bimanually harvesting a free flap of neurosensory retina superior to the superotemporal arcade, with the harvest site first secured by endolaser barricade and endodiathermy. The free flap was translocated in its correct orientation over the macular hole and perfluoro-*n*-octane heavy liquid (PFC) was instilled over it, followed by direct PFC-silicone oil exchange.

In order to prevent flap dislocation intraoperatively and postoperatively, the intraocular pressure should be lowered to reduce fluid turbulence [72]. The edge of the flap could be tucked underneath the edge of MH [72]. A technique combining autologous blood and autologous retinal free flap transplantation was described to secure the flap with blood clot [72].

There were small case series using similar techniques with good results, in terms of both anatomical closure rate and visual recovery [73–75]. The recovery of vision was postulated to be in part due to integration of the free flap to the surrounding retinal tissue with partial recovery of the ellipsoid zone and external limiting membrane, as observed postoperatively using OCT. It was hypothesized that the flap served more than a scaffold, providing glial cells and growth factors for structural and functional restoration. The implications of this observation to other macular diseases are yet to be determined.

12.3 Conclusion

The pathological changes associated with high myopia lead to a range of retinal complications, including MTM. An understanding of the pathogenesis and natural history of the disease sheds light on its management. Advances in surgical instruments and skills have shown promises in the management of this challenging condition.

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