Chapter

Peeling of Epiretinal Membrane: Analysis of Prognostic Factors and Surgical Complications, Impacting Visual Outcome

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Abstract

An epiretinal membrane (ERM) is the most common pathology of the vitreoretinal interface. First-line therapy for a symptomatic ERM is vitrectomy with ERM peeling. Clinical prognostic factors for postoperative visual acuity improvement include baseline visual acuity, age, duration of symptoms, and baseline pseudophakia. Postoperative optical coherence tomography (OCT) shows improvement in the integrity of the inner/outer segment junction and a reduction in the thickness of the ganglion cell complex and foveola. Retinal changes after ERM peel are also described using OCT angiography, fluorescein angiography, fundus autofluorescence, and multifocal retinography. Complications of ERM peeling include cataract formation, retinal breaks/detachments, ERM recurrence, and macular holes.

Keywords: epiretinal membrane, epiretinal membrane peeling, ganglion cell complex, central foveal thickness, spectral-domain optical coherence tomography

1. Introduction

The epiretinal membrane (ERM) is a layer of fibrous, contractile tissue that develops on the interface of the vitreous and the internal limiting membrane (ILM). ERM formation is associated with increased age, diabetes, retinal vein occlusions, uveitis, and other diseases of the retina and vitreous [1]. In the majority of cases, ERMs do not significantly interfere with visual functions and may be observed [2]. However, patients who experience decreased visual acuity, metamorphopsia, or diplopia secondary to the ERM may benefit from vitrectomy with membrane peeling, which is the treatment of choice for symptomatic ERMs [2]. Postoperative complications of ERM peeling include cataract formation, retinal tears/detachments, vitreous hemorrhage, macular holes, and recurrence of ERM, therefore a thorough, individualized review of clinical and imaging prognostic factors must be performed prior to consideration for surgery [2]. Clinical factors such as age, lens status, severity, and duration of symptoms may affect postoperative visual recovery [3]. Imaging modalities, such as spectral-domain optical coherence tomography (SD-OCT), fluorescein angiography (IVFA), and fundus autofluorescence (FA) can also guide clinicians in decision-making [3]. SD-OCT characteristics, such as the thickness of the ganglion cell layer and foveola, have prognostic value in postoperative visual acuity [4–14]. OCT angiography, fluorescein angiography, fundus autofluorescence, and multifocal retinography are additional imaging modalities which have been used to predict retinal changes after ERM peeling [15–22].

This chapter will review the epidemiology, classification, effect on visual function, natural disease course, and management of epiretinal membranes. Special attention will be paid to the preoperative clinical factors, imaging characteristics, and postoperative complications, most associated with epiretinal membrane peeling, that determine final visual outcome.

2. Methods

A Medline and Excerpta Medica database (EMBASE) search was conducted for all English language publications from 1947 to 2021 using the search term: ("ERM" OR "epiretinal membrane" OR "macular pucker"OR "pre-retinal fibrosis" OR "pre-retinal membrane" OR "cellophane maculopathy") AND ("epidemiology" OR "classification" or "staging" OR "progression" OR "management" OR "vitrectomy" OR "peeling" OR "optical coherence tomography" OR "OCT" OR "IVFA" or "OCT-A" or "OCT angiography" OR "fluorescein angiography" OR "multifocal electroretinogram" OR "mfERG" OR "complication"). All relevant abstracts and the articles were reviewed. The search was also supplemented by manual search primarily using additional references from key articles.

3. Epidemiology

An epiretinal membrane is a common condition estimated to affect approximately 7–9% of the general population [23, 24]. Certain ethnicities seem to be affected more than others; prevalence can be as high as 29% among Latinos and 39% among people of Chinese descent [25]. This condition is more common in the elderly population—one study found that 12% of people in their 70s are affected yet only 2% of people under 60 years of age are affected. Women have slightly higher rates of epiretinal membrane formation than men, and bilaterality is estimated to be 20–30% [24, 26].

4. Classifications

An epiretinal membrane may be classified as being either idiopathic or secondary, with most cases being idiopathic [24]. Secondary causes of ERMs include retinal vein occlusions, diabetic retinopathy, uveitis, retinal tears or detachments [27]. Secondary epiretinal membranes may also be iatrogenic, triggered by both invasive (e.g., cataract, vitrectomy) and noninvasive (e.g., laser photocoagulation and cryopexy) procedures [28].

In addition to etiology, epiretinal membranes may be staged based on clinical or OCT severity. Clinically, epiretinal membranes vary from a minimal cellophane light reflex to a more opaque membrane with retinal folds [29]. The most widely used clinical classification scheme for ERMs was proposed by Gass—Grade 0: cellophane maculopathy, in which a translucent epiretinal membrane is not associated with retinal distortion; grade 1: crinkled cellophane maculopathy, in which the inner retinal surface is distorted by irregular retinal folds; grade 2: macular pucker, in which a grayish membrane causes marked retinal crinkling and macular puckering [30]. Various OCT-guided staging schemes have also been proposed based on the presence of foveal involvement, macular edema, macular holes, schisis, and the integrity of the inner foveal layers [31, 32].

5. Effect on visual functions

Most people with epiretinal membranes have little to no visual symptoms, whereas others are more symptomatic and have progressive visual changes, including central vision loss, diplopia, metamorphopsia, and aniseikonia [2]. Metamorphopsia and diplopia can be especially debilitating, and they complicate essential daily activities such as reading and driving. Patients commonly report needing to close one eye to eliminate the distortion [2]. In addition to distortion, visual acuity is also degraded through light-filtering and scattering effects of the membrane, disruption of photoreceptor outer segments, obstruction of axoplasmic flow, tractional separation, and deformation of the outer retina [33]. Aniseikonia is caused by a traction-induced change in the distribution of photoreceptors, whereas metamorphopsia is related to tractional changes in the inner retina [33].

6. Natural disease course

Anatomically, about a third of ERM cases remain stable, a third progress, and a third improve when observed for >5 years [34, 35]. Functionally, visual acuity remains stable in the majority of patients, worsens in 10% of patients, and improves in 7%, over a 2 year period [36]. Significant factors that predict progression are a lack of posterior vitreous detachment (PVD), an ERM that is attached fully (rather than focally) to the retina, and an early stage of ERM [33, 36]. In cases that do progress, ERM contraction causes retinal thickening, disappearance of the fovea pit, and disruption on the ellipsoid zone [33]. The timescale for progression is slow, spanning several years [33].

7. Management

The majority of patients with ERMs do not require treatment and may be observed due to minimal symptoms at baseline and slow rate of progression [2, 34, 36]. For symptomatic patients, the mainstay of treatment is surgical requiring a pars plana vitrectomy with epiretinal membrane peeling [2]. In general, visual outcome after ERM peeling is favorable. Patients who elect to undergo vitrectomy with ERM peeling experience an average improvement in visual acuity of two or more lines and improvement in vision-related quality of life [2, 37]. Additionally, 70% of patients experience an improvement in metamorphopsia after ERM peeling, with 20% reporting a complete resolution of visual distortion [37].

Treatment with enzymatic or pneumatic vitreolysis may be used for isolated vitreomacular traction; however, these therapies have not been found to improve functional outcomes in patients with concurrent ERM [2]. Ocriplasmin, a recombinant proteolytic enzyme, has been found to release vitreomacular traction (VMT) in 8.7% of patients who have VMT in addition to an ERM (compared to 1.5% with placebo injection) without improvement in visual acuity [38]. C3F8 gas injection has been shown to release VMT in 50–83% of patients with concurrent ERMs, but also without improvement in visual acuity [39, 40].

8. Clinical prognostic factors

Despite overall favorable outcomes, 10–20% of patients will have unchanged or worse vision following surgery; therefore, a review of each patient's prognostic factors is advised prior to considering surgical intervention [2].

Both severity and duration of visual symptoms may be useful factors in predicting postoperative visual acuity. In a systematic review of prognostic factors for ERM peeling, Miguel and Legris discovered a heterogeneity regarding baseline visual acuity as a prognostic factor, finding that a low baseline VA appeared to be a poor prognostic factor in the majority of studies [3, 41]. Low baseline VA was also correlated with ERM recurrence [3, 42]. Duration of ERM-induced visual symptoms is inversely correlated to postoperative VA improvement—patients with symptoms of less than 1 year have the greatest improvement in VA [43, 44].

Age also impacts VA improvement after ERM surgery. Patients younger than 75 years old have a higher chance (42% in one study) of achieving postoperative BCVA of 20/20, compared with the patients who are older than 75 years of age [43]. However, older age should not be a deterrent for undergoing ERM peeling, since 66% of patients older than 75 years of age gained more than two Snellen lines in visual acuity postoperatively [43, 45]. In another study, which evaluated prognostic factors based on ERM etiology, younger patients with the secondary ERM as a result of previous retinal detachment surgery were found to have more significant visual improvement than the older patients [44].

Patients with preoperative pseudophakia were found to have better improvement in postoperative VA compared with phakic patients [41]. Cataract formation is the most common complication of PPV with ERM peeling (47–89% develop cataracts), so this finding may be at least partially due to phakic patients developing cataracts postoperatively [46, 47].

9. Imaging characteristics and prognostic value

9.1 Spectral-domain optical coherence tomography

Spectral-domain optical coherence tomography (SD-OCT) captures the reflection of a broad-bandwidth light source to provide a high-definition image of the retinal layers [48]. Anatomical retinal changes after ERM peeling have been studied extensively by spectral-domain optical coherence tomography (SD-OCT).

9.1.1 Ganglion cell complex

The ganglion cell complex (GCC) consists of the three innermost retinal layers: the nerve fiber layer, the ganglion cell layer, and the inner plexiform layer. ERM peeling is associated with thinning of the GCC, most prominently in the temporal region [4–6]. A greater GCC reduction was found to be correlated with worse postoperative VA in some studies [4, 7] and improved postoperative VA in another study [8]. Postsurgical GCC thinning is correlated with retinal displacement of the fovea toward the optic disc [6].

9.1.2 Foveola

The thickness of the foveola also carries a prognostic value. Eyes with the highest postoperative reduction in central foveal thickness were found to have the best improvement in VA and more significant reduction of metamorphopsia [9, 10]. In a comparison between each retinal layer thickness and its ratio of the central foveal thickness, a higher central foveal thickness/GCC ratio postoperatively was shown to be the most significant factor that is associated with the improved VA [11].

9.1.3 Inner/outer segment junction

The rods and cones make up one of the outermost layers of the retina, known as the photoreceptor layer. Baseline integrity of the inner/outer segment junction (IS/OS) of the photoreceptor layer is associated with improved postoperative visual acuity and reduction in metamorphopsia. [10, 12, 13]. Similarly, postoperative incidence of an intact IS/OS junction is correlated with a higher VA improvement [14]. The gradual improvement in the IS/OS junction postsurgically most likely results from the slow functional recovery of the photoreceptors, leading to the VA improvement. The best improvement in VA after the ERM surgery usually occurs approximately 1 year after the surgery [14, 49].

9.1.4 Macular edema

Cystoid macular edema (CME) has the potential to affect all retinal layers—it can induce thinning of the GCC, cause disruption of the IS/OS junction, increase in the central foveal thickness, and lead to the development of cystic spaces primarily in the outer nuclear layer (ONL) [12, 50–52]. CME is a poor prognostic factor for VA improvement both when it is present at baseline and when it occurs postsurgically [12, 51].

Microcystic macular edema (MME), a distinct process from CME, is characterized by the absence of fluorescein leakage on FA [53]. Unlike CME, MME does not change foveal thickness and consists of more uniform, ellipsoidal cystic spaces localized to the inner nuclear layer (INL) [54]. MME typically occurs postsurgically after ERM peeling, possibly as a result of the damage to Müller cells and subsequent changes in the osmotic gradient, however, it does not seem to have an impact on visual recovery [50, 53, 54].

9.2 Fundus autofluorescence

Lipofuscin is the by-product of the metabolism of photoreceptor external segments. Its density and distribution in the retinal pigment epithelium (RPE) can be demonstrated by fundus autofluorescence (FA) imaging [15]. Patients with normal autofluorescence were found to have the best postoperative improvement in visual acuity when compared with patients with hypoautofluorescent patterns [16]. Baseline hypoautofluorescence is associated with IS/OS segment disruption, while hyperautofluorescence is correlated with a greater reduction in postoperative central foveal thickness without affecting postoperative VA [16, 17].

9.3 OCT angiography

OCT-A is a noninvasive technology which utilizes laser reflectance of the surface of moving red blood cells to depict vessels of the retina and choroid [18]. No differences in the superficial vascular plexus were found on OCT-A, when compared before and after the ERM surgery by Romano et al. [19]; however, a postoperative decrease in vessel density was demonstrated by Mastropasqua et al. [20]. The deep perifoveal capillary-free zone was found to increase postsurgically in patients with diabetic ERM, unlike with idiopathic ERM. Both those changes do not seem to affect postoperative VA recovery [19].

9.4 Fluorescein angiography

Unlike the OCT-A, fluorescein angiography (IVFA) maps out chorioretinal vasculature using the fluorescence of an intravenous dye. Patients with RPE abnormalities, demonstrated on preoperative FA, had a higher central foveal thickness preoperatively, a higher macular volume preoperatively, a more extensive ERM, and a greater BCVA improvement postoperatively [17]. This may be explained by the fact that the macular traction (with resultant macular thickness and RPE abnormalities) seems to be a reversible cause of visual loss, or by the ceiling effect, related to the data showing that patients with better preoperative BCVA have lower rates of improvement [17].

9.5 Multifocal electroretinography

The multifocal electroretinogram (mfERG) is a noninvasive, objective measure of retinal electrical activity in response to a light stimulus. It is used for detection of localized abnormalities within the macula. It was found that mean, P1, and N1 mfERG amplitude were decreased in the eyes with ERMs preoperatively, but no significant change was noted after ERM peeling [21, 22]. There was also no correlation found between the multifocal ERG values and the central foveal thickness and visual acuity [21].

10. Postoperative complications

10.1 Cataract formation

Cataract formation is the most common complication after ERM peeling—de Bustros et al. found that 47% of patients developed nuclear sclerosis within 3 years, and Reilly et al. found that 89% of patients developed nuclear sclerosis within 1 year [46, 47]. There was no change in the incidence of anterior subcapsular cataracts, and only 4% of patients developed posterior subcapsular cataracts [46].

10.2 Recurrence and macular holes

Recurrence of ERM is another possible complication of ERM peeling. About 4–5% of all patients undergoing ERM peeling develop a recurrence within 1 year of surgery, while half of them would require a reoperation due to visually significant symptoms [42, 47].

Some surgeons choose to peel the underlying internal limiting membrane, while peeling an ERM. Although visual outcomes and anatomical retinal changes of ERM peeling with or without ILM removal seem to be equivalent, a lower ERM recurrence, a lower reoperation rate, but a higher rate of macula hole development were observed in patients who undergo ILM peeling in addition to ERM removal [55, 56]. Sandali et al. compared the two methods and found that only 2.6% of patients in the group of both ERM and ILM removal developed an ERM recurrence within 1 year, and 8.6% of ERM recurrence was noted in a group of patients who underwent only ERM peeling without ILM peeling [42]. A proposed explanation for this observation is that ILM peeling removes the scaffold for myofibroblast proliferation, and this can contribute to the recurrence of ERM [57].

Of patients who underwent ERM removal with ILM peeling, 1.7% were found to have macular holes postoperatively, while very few cases of macular hole development were noted in patients with ERM removal without ILM peeling [56]. The majority of macular holes were outside the fovea and appeared to be non-visually significant [56].

10.3 Retinal breaks and detachments

Retinal breaks and detachments are uncommon while utilizing current vitrectomy surgical methods [2]. Retinal detachments occur in 1% of cases during PPV with ERM peeling performed using a 23-gauge cannula system and in 3.5% of cases undergoing 20-gauge vitrectomy [2, 58, 59]. The incidence of retinal breaks ranges from 1 to 6% in the literature [60, 61].

11. Conclusion

Epiretinal membranes are a common finding, especially in the geriatric population. The majority of patients with ERMs do not require any treatment, but those who develop symptoms such as blurred vision or metamorphopsia may benefit from vitrectomy with ERM peeling. Vitrectomy with membrane peeling, although effective in relieving symptoms in most cases, has complications such as cataract formation, retinal breaks/detachments, ERM recurrence, and macular holes. Complications can be minimized and good outcomes maximized, through the careful consideration of prognostic factors in selecting surgical candidates. Clinical characteristics correlated with better postoperative VA include younger age, baseline pseudophakia, and shorter duration of symptoms. Physicians should also consider performing imaging tests such as OCT, IVFA, and autofluorescence (FA) to assist with decision-making. Patients who have a baseline integrity of the IS/OS junction on OCT, lack of cystic macular edema, normal autofluorescence on FA, and presence of RPE abnormalities on IVFA tend to have better postoperative visual outcomes and therefore may be good surgical candidates. With appropriate optimization and patient selection, epiretinal membrane peeling represents the best therapeutic intervention for this disabling disease. As trials continue to move forward, there remains the promise of continued improvements in technique and technologies, which will one day serve as a cure.

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