

FOVEA-SPARING VERSUS COMPLETE INTERNAL LIMITING MEMBRANE PEELING IN VITRECTOMY FOR VITREOMACULAR INTERFACE DISEASES

A Systematic Review and Meta-Analysis

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Purpose: To evaluate fovea-sparing internal limiting membrane (ILM) peeling in vitrectomy compared with traditional complete ILM peeling in vitreomacular interface diseases, including macular hole (MH), epiretinal membrane, macular foveoschisis, myopic traction maculopathy, and the like.

Methods: PubMed, EMBASE, Cochrane, CNKI Databases, and the ClinicalTrials.gov website (PROSPERO number CRD42020187401) were searched. Controlled trials comparing fovea-sparing with complete ILM peeling were included. Postoperative changes in best-corrected visual acuity, central retinal thickness in vitreomacular interface diseases, the incidence of MH closure in MH cases, full-thickness macular hole development in non-MH cases, and retinal reattachment in retinoschisis cases were extracted.

Results: Fourteen studies (487 eyes) were eligible. Compared with complete ILM peeling, the fovea-sparing technique revealed significant improvement in best-corrected visual acuity (logarithm of the minimum angle of resolution; weighted mean difference = -0.70 ; 95% confidence interval, -1.11 to -0.30), and a reduced incidence of full-thickness macular hole was noted in non-MH cases (risk ratios = 0.25 ; 95% confidence interval, 0.08 – 0.76). However, no significant differences in mean change in central retinal thickness, incidence of MH closure in MH cases, and retinal reattachment in retinoschisis cases were noted.

Conclusion: Based on current evidence, fovea-sparing ILM peeling significantly improve visual outcomes and decrease complications of full-thickness macular hole development in vitreomacular interface diseases.

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Vitreomacular interface (VMI) diseases are an umbrella term used to describe a series of disorders occurring in association with vitreomacular adhesion.^{1–4} The vitreous body, a semisolid gel structure, fills the central space of eyeball and functions in retinal attachment and the composition of dioptric media. With aging, the vitreous liquefies and collapses, causing complete or incomplete posterior vitreous detachment. Incomplete posterior vitreous detachment is associated with abnormal vitreomacular adhesion, which leads to the development of VMI diseases.³

Myopic macular traction could also increase the occurrence of VMI disorders.⁵

In 2013, a panel of scientists developed an optical coherence tomography (OCT)-based anatomical classification system for VMI diseases.¹ Vitreomacular interface diseases are classified into three major branches, namely, vitreomacular adhesion, vitreomacular traction, and macular hole (MH). Vitreomacular adhesion is characterized by perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphological features. Vitreomacular traction is

defined as posterior vitreous detachment accompanied by anatomical distortion of the fovea. Pseudocysts, macular retinoschisis, macular edema, and subretinal fluid are included in this category. Macular hole is defined as a defect in the neural retina of the fovea. Full-thickness macular hole (FTMH), a subtype of MH, manifests as interruption of all retinal layers from the internal limiting membrane (ILM) to the retinal pigment epithelium (RPE).

At present, some concerns have emerged that VMI diseases could stimulate the growth progression of retinal glial cells and RPE cells, resulting in the formation of a proliferative membrane on ILM, which is also known as the epiretinal membrane (ERM). In 1988, Gass et al⁶ proposed the hypothesis that ERM has a tangential pulling effect on the macular area, explaining the rapid progress of such diseases.

Presently, pars plana vitrectomy and ILM peeling are considered to be effective in the management of VMI diseases by relieving retinal traction anatomically and blocking RPE cell migration.^{7,8} However, peeling the ILM off from the fovea could induce a break of the central foveal tissue and cause anatomical damage to the macula.

To solve this problem, Ho et al⁹ proposed preserving the epifoveal ILM during ILM peeling in 2012,^{10–13} which help to prevent postoperative development of FTMH. The proposed technique has been widely used, but the efficacy varies from different researches.^{14,15}

Despite a large number of articles on this topic, no published meta-analysis has focused on fovea-sparing ILM peeling techniques in VMI diseases, especially on the clinical outcomes like best-corrected visual acuity (BCVA) or central retinal thickness (CRT). To address this gap, we conducted a meta-analysis of studies to

improve understanding of the effectiveness of fovea-sparing ILM peeling in vitrectomy.

Methods

This study applied the Cochrane Collaboration's Preferred Reporting Items for Systematic Reviews and Meta-Analyses method for the meta-analysis.¹⁶

Eligibility Criteria

We included controlled studies that reported the comparison of effectiveness between fovea-sparing and complete ILM peeling in vitrectomy for VMI diseases. Eligible observational studies met the following criteria: 1) subjects of the study were eyes with VMI diseases, such as vitreomacular adhesion, vitreomacular traction, MH, ERM, retinoschisis, etc., 2) intervention referred to applying fovea-sparing and complete ILM peeling in vitrectomy, and 3) eligible studies should have at least one of the following outcomes: changes in BCVA or CRT from baseline to postoperative follow-up.

The following exclusion criteria were employed: 1) noncomparative studies, single-arm studies, animal studies, or case reports and 2) abstracts, letters, editorials, and conference proceedings without original data or published results.

Search Strategy

We searched PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, CNKI (the largest database of science in China), and the clinicaltrials.gov website from inception to May 1, 2020, without language restrictions. The selected keywords were used as free words, truncations, and subject morphology. Detailed search strategy is shown in **Supplemental Digital Content 1** (see **Content**, <http://links.lww.com/IAE/B422>) (PROSPERO number CRD42020187401). One author (Y.W.) executed the search strategy, and another author (X.Z.) independently peer-reviewed the strategy. An independent researcher (W.Z.) peer-reviewed the strategy.

To identify studies and determine eligibility, two authors (Y.W., X.Z.) independently reviewed titles and abstracts for inclusion, and full manuscripts and further relevant references were examined if necessary. If two authors disagreed, a third researcher (Y.C.) participated in the discussion.

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Data Extraction

The name of the author, year of publication, study design, and outcomes were extracted from each study. The primary outcomes were 1) mean change in BCVA (logarithm of the minimum angle of resolution) from baseline to the last follow-up and 2) mean change in CRT from baseline to the last follow-up. The secondary outcomes were 1) incidence of MH closure in MH cases, 2) incidence of FTMH developed in non-MH cases, and 3) incidence of retinal reattachment in retinoschisis cases (resolution both internal and external detected by OCT).

Risk for Bias

The quality of included randomized control trials (RCTs) was assessed using the Cochrane Collaborative's risk for bias assessment tool.¹⁷ The quality of included non-RCTs was assessed using the Newcastle–Ottawa Scale.¹⁸ Any disagreement was solved by discussion.

Statistical Analysis and Exploration of Heterogeneity

Statistical analysis was performed using Stata (SE v12, StataCorp, TX). We used weighted mean difference with 95% confidence intervals (CI) for the estimation of continuous outcomes (postoperative change in BCVA, CRT). We used pooled risk ratios (RR) and 95% CI for dichotomous outcomes (incidence of MH closure, FTMH developed, retinal reattachment). We used the inverse variance (IV) or Mantel–Haenszel (M-H) method to combine the summary statistics and assessed the statistical heterogeneity using the I^2 method with the χ^2 test to calculate P values. Heterogeneity was evaluated using I^2 statistic. If $I^2 < 50\%$, a fixed-effects model would be applied to perform meta-analysis; otherwise, a random-effects model would be used. Potential publication bias was assessed by Egger test with $P > 0.05$ indicating negative publication bias.

Results

Description of the Evidence

Initially, a total of 280 studies were retrieved. After excluding 231 records by screening the titles and abstracts, a total of 49 manuscripts were fully examined (Figure 1). We ultimately included 14 studies (487 eyes) in our meta-analysis (Table 1). Of the included studies, 11 studies^{14,19–28} were retrospective observational studies, 1 study²⁹ was a prospective trial,

and 2 studies^{15,30} were RCTs. Among the types of diseases involved in these studies, 5 studies^{22,24–26,28} assessed macular foveoschisis (MF), four studies^{20,23,29,30} assessed MH, three studies^{14,21,27} assessed myopic traction maculopathy (MTM, defined as VMI disorders caused by myopic, which included ERM, vitreomacular traction, macular retinoschisis, retinal detachment, etc.), 1 study¹⁵ assessed epiretinal membrane, and 1 study¹⁹ assessed lamellar macular hole. Literature quality evaluation revealed low risks of bias in two RCT studies, and prospective or retrospective studies were varied from moderate to high quality. The literature quality evaluation is shown in **Supplemental Digital Content 2** (see **Content**, <http://links.lww.com/IAE/B423>).

Primary Outcomes

Mean change in best-corrected visual acuity. Changes in BCVA were reported in 8 studies with a total of 308 eyes. The pooled results revealed a visual acuity improvement in BCVA from baseline for patients who received fovea-sparing ILM peeling versus complete ILM peeling (weighted mean difference = -0.70 , I-V random-effects; 95% CI, -1.11 to -0.30 ; Figure 2A). Egger regression intercepts were -5.30 (95% CI, -9.48 to -1.13 ; $P > |t| = 0.02$), which indicated publication bias. Significant heterogeneity was found among these studies ($I^2 = 64.2\%$; $P = 0.007$), and we performed subgroup analyses to assess the heterogeneity (see **Content**, **Supplemental Digital Content 3**, <http://links.lww.com/IAE/B424>).

Mean change in central retinal thickness. Mean change in CRT, which was reported in 6 studies with a total of 187 eyes, is presented in Figure 3. The meta-analysis revealed no statistically significant differences among patients who received fovea-sparing ILM peeling versus complete ILM peeling (weighted mean difference = 0.06 ; I-V fixed-effects; 95% CI, -0.23 to 0.35 ; heterogeneity, $I^2 = 0\%$; $P = 0.999$; Figure 2B). Egger regression intercept (-1.32 ; 95% CI, -2.75 to 0.12 ; $P > |t| = 0.06$) revealed no publication bias.

Secondary Outcomes

Incidence of macular hole closure in macular hole cases. The incidence of MH closure in MH cases was reported in 4 studies of 186 eyes. Compared with complete ILM peeling, foveal-sparing ILM peeling achieved no significant difference in the incidence of MH closure (RR = 1.05 , M-H fixed-effects; 95% CI, 0.99 – 1.12 ; heterogeneity, $I^2 = 0\%$; $P = 0.974$; Figure 3A). Because of the lack of included studies, publication bias was not evaluated.

Incidence of full-thickness macular hole development in non-macular hole cases. Six studies of 221 eyes reported the incidence of FTMH in non-MH cases. The pooled results revealed a significant difference in the incidence of FTMH for patients who received fovea-sparing ILM peeling versus complete ILM peeling (RR = 0.25, M-H fixed-effects; 95% CI, 0.08–0.76; heterogeneity; $P = 0.996$; $I^2 = 0\%$; Figure 3B). Egger regression intercept (−1.14; 95% CI, −3.54 to 1.24; $P > |t| = 0.255$) revealed no publication bias. A subgroup analysis showed a significant reduction of incidence of FTMH development in MTM diseases (see **Content, Supplemental Digital Content 4**, <http://links.lww.com/IAE/B425>).

Incidence of retinal reattachment in retinoschisis cases. Four studies of 147 eyes reported the incidence of retinal reattachment in retinoschisis cases. The pooled results revealed no significant difference in the incidence of retinal reattachment for patients who received fovea-sparing ILM peeling versus complete ILM peeling (RR = 1.00, M-H fixed-effects; 95% CI, 0.72–1.38; heterogeneity; $P = 0.536$; $I^2 = 0.0\%$; Figure 3C). Egger regression intercept (−0.69; 95% CI, −19.04 to 20.42; $P > |t| = 0.894$) revealed no publication bias.

Discussion

Our meta-analysis reported the efficacy of fovea-sparing ILM peeling in VMI diseases compared with complete ILM peeling. The exact mechanism of fovea-sparing ILM peeling remains undetermined, but a potential mechanism can be hypothesized. The photoreceptor layer in the fovea of the macula mainly consists of densely arranged cone cells, and the axons of these photoreceptors are shifted to the surrounding areas to form the structure of the macula.³¹ Such a structure helps to maximize vision by reducing the interference of other retinal cells, which enables cone cells to receive more light.³² The role of the ILM is to form the inner boundary of the retina, which is considered to be the basement membrane of Müller cells that connect tightly with the photoreceptor cells via the end feet.³³ When the ILM is peeled off, these end feet are also removed, causing the damage of Müller cells and triggering a cascade of reactions that result in postoperative macular alterations.³⁴ Physiological and morphological changes, such as the swelling of retinal nerve fiber, the appearance of unstable retinal fiber tissue, are noted. The purpose of the fovea-sparing ILM peeling technique is to interrupt the continuity of the ILM around the macular fovea with the

Fig. 1. Flowchart of selection process in the comparison of the fovea-sparing ILM peeling group and the complete ILM peeling group.

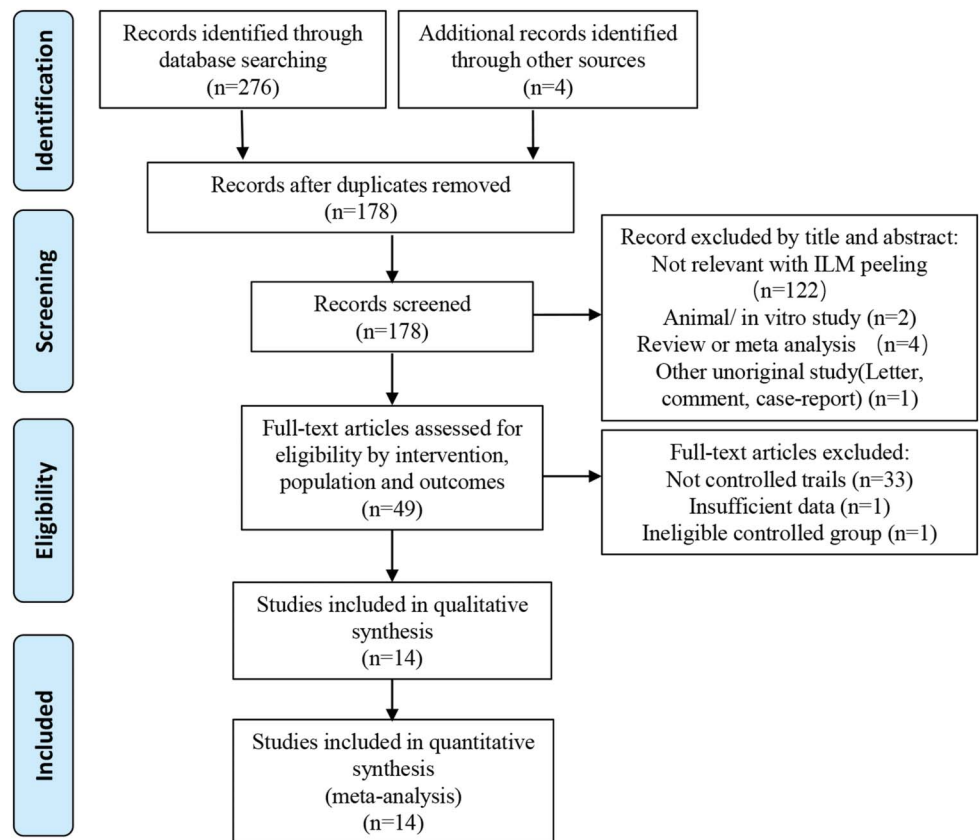


Table 1. Characteristics of the Studies Included in this Meta-Analysis

Study	Study Design	Disease	n	Participants		Intervention and Comparison	
				Inclusion	Exclusion	Fovea-Sparing ILM Peeling	Complete ILM Peeling
Murphy et al ²⁷	PS	MH	68	Symptoms less than 12 months, MLD of macular hole less than 630 μ m on OCT	Myopia < -6.00 D, visually significant cataract, trauma, severe glaucoma, retinal detachment, and stage 4 MHs with complete vitreoretinal separation from the optic disk	P + I + 27G PPV + BBG + fovea-sparing ILM peeling + C ₂ F ₆	P + I + 27G PPV + BBG + complete ILM peeling + C ₂ F ₆
Russo et al ¹⁴	RCT	ERM	38	Age more than 60 years, presence of idiopathic macular pucker documented by OCT	Any prior intraocular surgery; pathological myopia (< -7.00 D); significant cataract; age-related macular degeneration, glaucoma, diabetic retinopathy or any other retinal vascular disease	P + I + 25G PPV + fovea-sparing ILM peeling + SF ₆	P + I + 25G PPV + complete ILM peeling + SF ₆
Morescalch et al ²⁸	RCT	MH	44	Age more than 60 years, presence of MH documented by OCT	Any prior intraocular surgery; pathological myopia (< -7.00 D); age-related macular degeneration, glaucoma, diabetic retinopathy or any other retinal vascular disease	P + I + 25G PPV + fovea-sparing ILM peeling + SF ₆	P + I + 25G PPV + complete ILM peeling + SF ₆
Shimada et al ¹³	RS	MTM	45	Underwent PPV with ILM peeling to treat a foveal RD attributable to myopic traction maculopathy, myopic \geq 8.00 D or an AL \geq 26.5 mm	Full-thickness MH, myopic CNV, macular atrophy affected the central vision, other retinal diseases; ocular trauma history; dense opacities of the media	25G PPV + ICG + fovea-sparing ILM peeling + SF ₆	25G PPV + ICG + complete ILM peeling + SF ₆
Ho et al ¹⁹	RS	MTM	19	Myopic > -6.00 D, MTM as the main cause of VA decrease	Diffuse macular chorioretinal atrophy or large fuchs spots	20/23G PPV + ICG + donut-shaped ILM peeling + gas	20/23G PPV + ICG + complete ILM peeling + gas

(continued on next page)

Table 1. (Continued)

Study	Study Design	Participants				Intervention and Comparison	
		Disease	n	Inclusion	Exclusion	Fovea-Sparing ILM Peeling	Complete ILM Peeling
Ho et al ¹⁸	RS	MH	28	Early Stage-2 MH according to the Gass classification	NA	Standard 3 PPV + ICG + donut-shaped ILM peeling + C ₃ F ₈	Standard 3 PPV + ICG + complete ILM peeling + C ₃ F ₈
Tian et al ²⁰	RS	MF	36	Myopic >−8.00 D or AL >26 mm, progressive visual loss caused by foveoschisis	Dense opacities of the media; preoperative FTMH observed by OCT, macular chorioretinal atrophy or a large Fuchs spot, CNV, trauma history, and retinal diseases	23G PPV + BBG + fovea-sparing ILM peeling + C ₃ F ₈	23G PPV + BBG + complete ILM peeling + C ₃ F ₈
Wang et al ²³	RS	MF	33	Myopic <−6.00 D or AL >26.00 mm, BCVA (LogMAR) <0.2, macular retinoschisis shown by OCT	MH; choroidal neovascularization; history of photocoagulation; with other retinopathies	25G PPV + BBG + fovea-sparing ILM peeling + C ₃ F ₈	25G PPV + BBG + complete ILM peeling + C ₃ F ₈
Elwan et al ²⁶	RS	MF	28	Spherical equivalent ≥8.00 D, AL >26 mm, recent visual deterioration related to foveoschisis	Eyes with full-thickness MH, myopic CNV, diffuse macular chorioretinal atrophy, large Fuch spots, trauma history, eyes with opaque media	23G PPV + BBG + fovea-sparing ILM peeling + C ₃ F ₈	23G PPV + BBG + complete ILM peeling + C ₃ F ₈
Ho et al ¹⁷	RS	MH	33	Presence of lamellar macular hole with related epiretinal proliferation	With other macular diseases, retinal vascular diseases, hereditary macular diseases or previous vitreoretinal surgeries	23/25G + PPV + ICG + LHEP-filled retinal defect + fovea-sparing ILM peeling + C ₃ F ₈	23/25G + PPV + ICG + LHEP-filled retinal defect + complete ILM peeling + C ₃ F ₈
Itoh et al ²⁴	RS	MF	15	Myopia <−8.00 D or AL >26.5 mm. The presence of a myopic retinoschisis at the fovea was confirmed in the preoperative examinations by spectral-domain OCT	The presence of preoperative FTMH, other retinal diseases, such as diabetic retinopathy and retinal vein occlusion, previous vitrectomy, postoperative follow-up of <12 months, and lack of iOCT imaging	P + I + 25/27G PPV + BBG + fovea-sparing ILM peeling + SF ₆	P + I + 25/27G PPV + BBG + complete ILM peeling + SF ₆

Table 1. (Continued)

Study	Study Design	Participants				Intervention and Comparison	
		Disease	n	Inclusion	Exclusion	Fovea-Sparing ILM Peeling	Complete ILM Peeling
Wang et al ²²	RS	MF	33	Myopic > -6.00 D or ocular AL > 26.00 mm, BCVA (logMAR) > 0.7 but decreased significantly, macular retinoschisis shown by OCT	MH; choroidal neovascularization; history of photocoagulation in the macular region; with other retinopathies	25G PPV + BBG + fovea-sparing ILM peeling + C ₃ F ₈	25G PPV + BBG + complete ILM peeling + C ₃ F ₈
Wang et al ²¹	RS	MH	45	Early Stage 2-4 MH according to the Gass classification	Choroidal neovascularization; history of photocoagulation in the macular region; with other retinopathies	23G PPV + ICG + fovea-sparing ILM peeling + C ₃ F ₈	23G PPV + ICG + complete ILM peeling + C ₃ F ₈
Iwasaki et al ²⁵	RS	MTM	22	Presence of foveal MTM in high myopia	Presence of amblyopia, a preoperative macular hole, preoperative MHRD, AMD, foveal choroid retinal atrophy, and history of vitreous surgery or scleral buckle	P + I + 25/27G PPV + BBG + fovea-sparing ILM peeling + gas	P + I + 25/27G PPV + BBG + complete ILM peeling + gas

AL, axial length; BBG, brilliant blue G; ICG, indocyanine green; LHEP, lamellar macular hole with related epiretinal proliferation; MLD, minimum linear diameter; NA not available; logMAR, logarithm of the minimum angle of resolution; PPV, pars plana vitrectomy; PS, prospective study; RS, retrospective study.

peripheral ILM.³⁵ As a result of this procedure, traction forces change their direction from centrifugal to centripetal, and the integrity of the end feet of the foveal Müller cells and macular structure is preserved.^{13,36}

The proposed technique is easy to operate (see **Content, Supplemental Digital Content 5**, <http://links.lww.com/IAE/B426>). Shimada et al¹⁴ decomposed the procedure into two steps: 1) use the vitreoretinal forceps to peel ILM peeling from several new sites around the macula and 2) trim the ILM that remains around the fovea with a vitreous cutter.

Regarding the primary outcomes in our meta-analysis, fovea-sparing ILM peeling exhibits a significant difference in the mean change in BCVA. This finding indicates that retaining the ILM of the central fovea of the macula is more helpful in improving vision. One possible explanation is that the visual function of the macular area mainly depends on the integrity of the cone cells and the nerve fiber layer connected to it. Internal limiting membrane removal with foveal retention does

not disturb the nerve fiber layer in the macular area to the same extent as complete ILM removal; thus, the vision can be improved to a greater extent. Besides, fovea-sparing can enhance retinal sensitivity detected by the microperimetry,^{15,30} which is another proof of its efficacy in vision improvement.

Compared with complete ILM peeling, fovea-sparing ILM peeling showed no significant difference in CRT changes; however, slight reductions were noted compared with preoperation. Central retinal thickness changes often occur in retinal detachment as the distance between the retinal neuroepithelium and RPE increases. Fovea-sparing ILM peeling and complete ILM peeling exhibit no significant differences in reducing this distance. This finding is interesting because vision changes occur before macroscopic structure changes in the retina. This finding may be attributed to the fact that vision was highly dependent on the integrity of the cone cells and the nerve fiber layer, not just the thickness change of the retina.

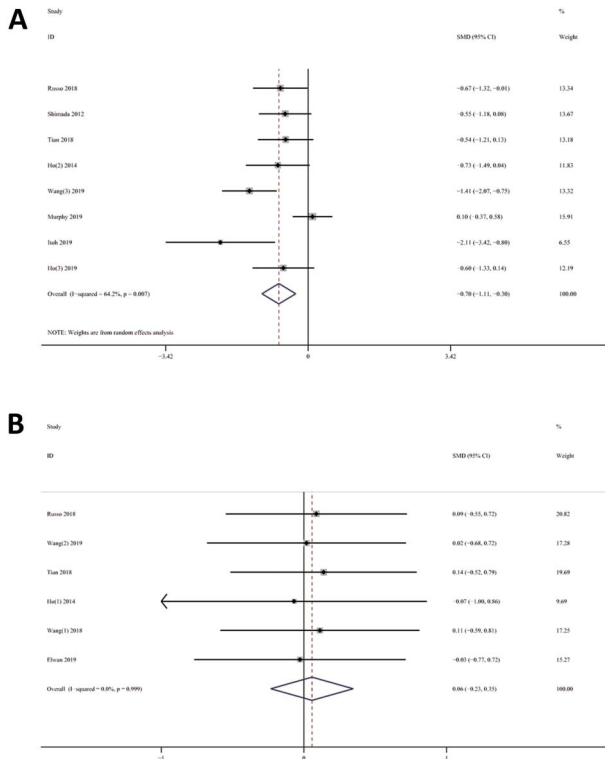


Fig. 2. Forest plot demonstrating changes of best-corrected visual acuity (A), and changes of CRT (B) for fovea-sparing versus complete ILM peeling.

Regarding secondary outcomes, in non-MH cases, such as MTM, ERM, MF, and lamellar macular hole, the incidence of FTMH is significantly reduced with fovea-sparing ILM peeling. During the ILM peeling surgery, some surgeons may remove too much ILM with the underlying retina, causing iatrogenic damage to the macular fovea, such as FTMH. Fovea-sparing ILM peeling preserves the ILM of the foveal area, which enables maintenance of the integrity of the macular structure and subsequently improves the patient's vision. Fovea-sparing and complete ILM peeling exhibited no significant difference in the incidence of MH closure in MH cases and the incidence of retinal reattachment in retinoschisis cases. The results indicated that fovea-sparing does not affect MH closure and does not increase the risk of retinal detachment. For MH cases, fovea-sparing ILM peeling changes gliosis and traction forces from centrifugal to centripetal. The holes in the macular area are not subject to the surrounding traction, which may aid in the closure of MH. For retinoschisis cases, fovea-sparing ILM peeling reduces the centrifugal tension of the ERM on the retina and the traction of the retina toward the vitreous, thus reducing the risk of retinal detachment. However, our study found that fovea-sparing and complete ILM peeling exhibited no sig-

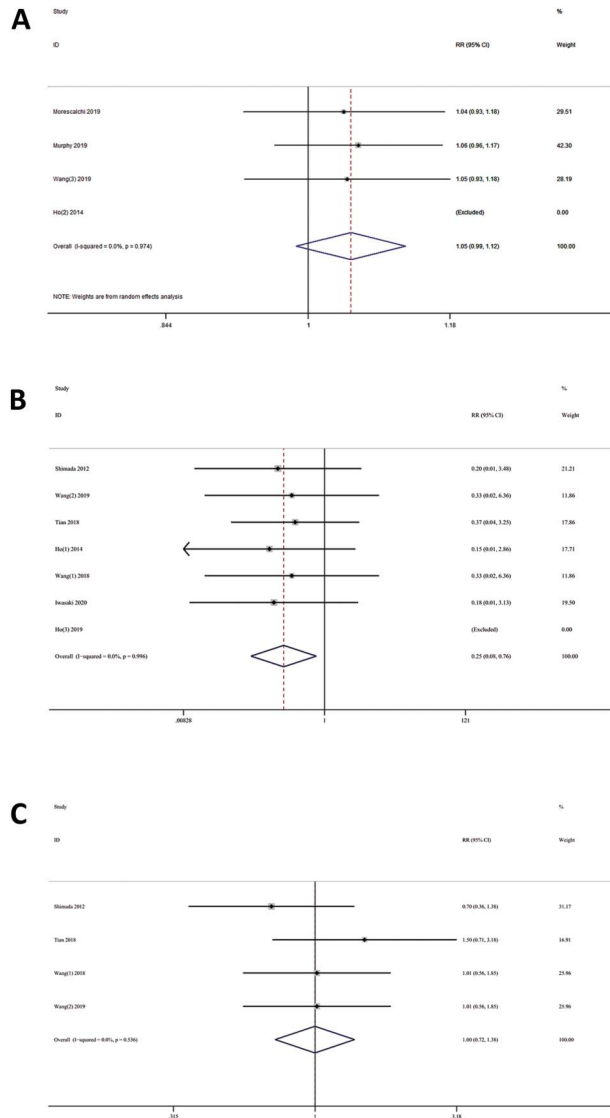


Fig. 3. Forest plot demonstrating the incidence of MH closure in MH cases (A), the incidence of FTMH development in non-MH cases (B), and the incidence of retinal reattachment in retinoschisis cases (C) in fovea-sparing versus complete ILM peeling.

nificant differences in the closure rate of MH and the incidence of retinal reattachment. Complete ILM peeling seems to lift more areas of ILM than fovea-sparing ILM peeling in these two diseases, which could reduce more tension on the retina and promote MH closure and retinal reattachment.¹³ However, the fovea-sparing technique has several problems: 1) Potential recurrent of ERM, as the remaining RPE cells and glial cells may continue proliferation, which may need reoperations, 2) unclosure of MH, as tractions of the retina has not been completely relieved, 3) occurrence of ILM shrinkage, which may lead secondary MH, 4) no studies have compared the efficacy of fovea-sparing ILM peeling

and ILM flap preservation, more study should be conducted,^{37,38} and 5) the staining of ILM needs to be concerned. Indocyanine green has the risk of RPE toxicity and atrophy, whereas brilliant blue G (BBG) is reported less toxic to the retina, although some research found brilliant blue G yield a less well visibility.^{39,40}

Our study has some limitations. 1) Only two RCTs were rated as high quality, and the other studies were either prospective or retrospective studies that varied from moderate to high quality. High heterogeneity of primary outcomes was noted. 2) Among these studies, only Russo et al¹⁴ reported the recurrence rate of ERM. More research on other complications of ERM is needed. 3) Publication bias exists in some of our studies, which may be attributed to the limited number of studies. 4) The majority of the included studies were related to myopia, which may exaggerate the beneficial effect of the fovea-sparing technique.

Conclusion

The results from the present meta-analysis showed that vitrectomy with fovea-sparing ILM peeling resulted in better visual outcomes when treating VMI diseases and reduced the incidence of FTMH in non-MH cases. Long-term follow-up studies are necessary to clarify the usefulness and safety of fovea-sparing ILM peeling.

Key words: best-corrected visual acuity, central retinal thickness, fovea-sparing ILM peeling, meta-analysis, vitreomacular interface disease.

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