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일차적 열공성 망막박리 환자에서 유리체절제술 후 망막전막의 발생 및 위험인자에 대한 연구

Incidence and Risk Factors of Epiretinal Membrane Formation After Pars Plana Vitrectomy for Primary Rhegmatogenous Retinal Detachment

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Purpose: Formation of an epiretinal membrane (ERM) is a major cause of decreased visual acuity after surgical treatment of rhegmatogenous retinal detachment (RRD). This study analyzed the incidence and risk factors of ERM formation after primary vitrectomy of RRD.

Methods: This retrospective and interventional case series included 217 eyes from 217 patients who underwent vitrectomy by a single surgeon to repair a primary RRD from March 2012 to August 2022. Eyes were excluded if they underwent combination surgery of scleral buckling and vitrectomy, had a history of scleral buckling or vitrectomy, or had a prior ERM. Eyes with retinal detachment caused by a macular hole were also excluded. Data on demographics, ocular status, and intraoperative techniques were collected. At 1 week and 1, 3, and 6 months after surgery, fundus photography and macular optical coherence tomography were used to investigate the status of retinal reattachment and development of an ERM over the macula. Additional ERM surgery was performed in patients with ERM formation if there were symptoms such as visual disturbance or metamorphopsia.

Results: Of the 217 eyes, a macular ERM occurred in 42 eyes (19.3%). Additional ERM surgery was performed in 18 eyes (8.3%) of patients with ERM formation. The ERM group was significantly older ($p = 0.020$) and had a greater proportion of patients with large retinal break before RRD surgery ($p < 0.001$) than the non-ERM group. The additional ERM surgery group had a significantly greater proportion of patients with large retinal break before RRD surgery ($p = 0.023$) than the non-ERM group. There was no significant difference in sex, macular detachment, smoking history, diabetes mellitus history, high myopia, intraoperative techniques or postoperative vitreous hemorrhage between the non-ERM group and the ERM group or the additional ERM surgery group.

Conclusions: Patients who underwent vitrectomy to repair a RRD should be carefully monitored, especially in older patients or cases with a large retinal break.

Keywords: Epiretinal membrane; Macular pucker; Rhegmatogenous retinal detachment; Vitrectomy

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Introduction

Rhegmatogenous retinal detachment (RRD) is the most common form of retinal detachment and occurs due to retinal breaks. The two main techniques used to treat RRD include pars plana vitrectomy and scleral buckling [1]. These two surgical methods show no significant differences in the reattachment rate and visual prognosis [2]. Because of continuous improvement of the vitrectomy system, equipment, and techniques, however, vitrectomy has emerged as the preferred method in recent years [3,4].

Reports have indicated that the formation of an epiretinal membrane (ERM), also known as macular pucker, frequently causes decreased visual acuity after the surgical treatment of RRD [5-7]. Some patients with an ERM may be asymptomatic, while others may present with decreased visual acuity or metamorphopsia. The reported incidence of ERM after the primary surgical repair of RRD with scleral buckling varies greatly, ranging between 3% and 32.6% [5,6,8]. The incidence of ERM after vitrectomy was performed as the primary surgical repair of RRD also varies significantly, ranging from 6.1% to 12.8% [9-11]. Despite this wide variance, the risk factors that contribute to ERM formation are not well understood.

In this study, we investigated the incidence and risk factors of ERM formation after primary surgical treatment of rhegmatogenous retinal detachment with vitrectomy performed by a single surgeon.

Materials and Methods

A retrospective review of medical records was conducted on 217 eyes from 217 patients diagnosed with RRD from March 2012 to August 2022. A single surgeon performed pars plana vitrectomy on the patients with a follow-up at least six months later. Eyes were excluded from the study if they had a combination surgery of scleral buckling and vitrectomy, a history of previous scleral buckling or vitrectomy, or prior ERM. We also excluded eyes with retinal detachment due to a macular hole. Information on patient sex, smoking habits, diabetes mellitus history, age at the time of retinal detachment diagnosis, and postoperative vitreous hemorrhage was obtained from medical records.

The first diagnosis of the retinal detachment involved an examination of the anterior segment and lens status using slit lamp microscopy. Fundus photography (Topcon TRC-NW8; Topcon) was used to visualize the optic disc, retina, and macula. The posterior pole and peripheral fundus examination were performed using the Goldmann three-mirror contact lens (Ocular Instruments Inc.) and an indirect ophthalmoscope. Spectral domain optical coherence tomography (OCT) was performed with Cirrus HD OCT® Model 4000 (Carl Zeiss Meditec Inc.). Axial length was measured using A-scan (Tomey AL-100; Tomey); high myopia was defined as an axial length of 26 mm or longer.

A single surgeon performed all operations using general anesthesia. The scleral incision was made using a 23 or 25-gauge vitrectomy trocars, and vitrectomy was performed using the Accurus® Surgical System (Alcon Laboratories Inc.) or the CONSTELLATION® Vision System (Alcon Laboratories Inc.). In cases of comorbid cataracts, both phacoemulsification and intraocular lens implantation were performed. All patients underwent core vitrectomy, followed by peripheral vitrectomy using scleral indentation. Endolaser photocoagulation around the retinal break was performed. If deemed necessary, the surgeon performed additional procedures such as perfluorocarbon liquid injection or retinotomy. Surgical treatment was completed by air-fluid exchange and following 5% or 10% C_3F_8 gas or air or silicone oil (Arciolane 1300; BVI Medical) injection.

During the procedure, the number and size of the retinal breaks were recorded using a scleral indentation used for finding breaks in the peripheral retina. Retinal breaks larger than two-disc diameters were categorized as large retinal breaks [12].

We conducted examinations at 1 week and 1, 3, and 6 months after surgery using fundus photography and macular OCT to determine the status of retinal reattachment and ERM formation on the macula. The OCT with macular cube 512 × 128 scans determined the development of ERM in a 6 × 6 mm area on the macula (Fig. 1). The cases with ERM development on this area were classified into the ERM group, and the rest were classified into the non-ERM group. In the ERM group, additional ERM surgery was performed in patients with deterioration of visual acuity and deterioration of ERM. To evaluate whether visual acuity improved before and after ERM surgery, the best corrected visual acuity (BCVA) before and after surgery (3 months) was compared by converting to logarithm of minimal angle of resolution

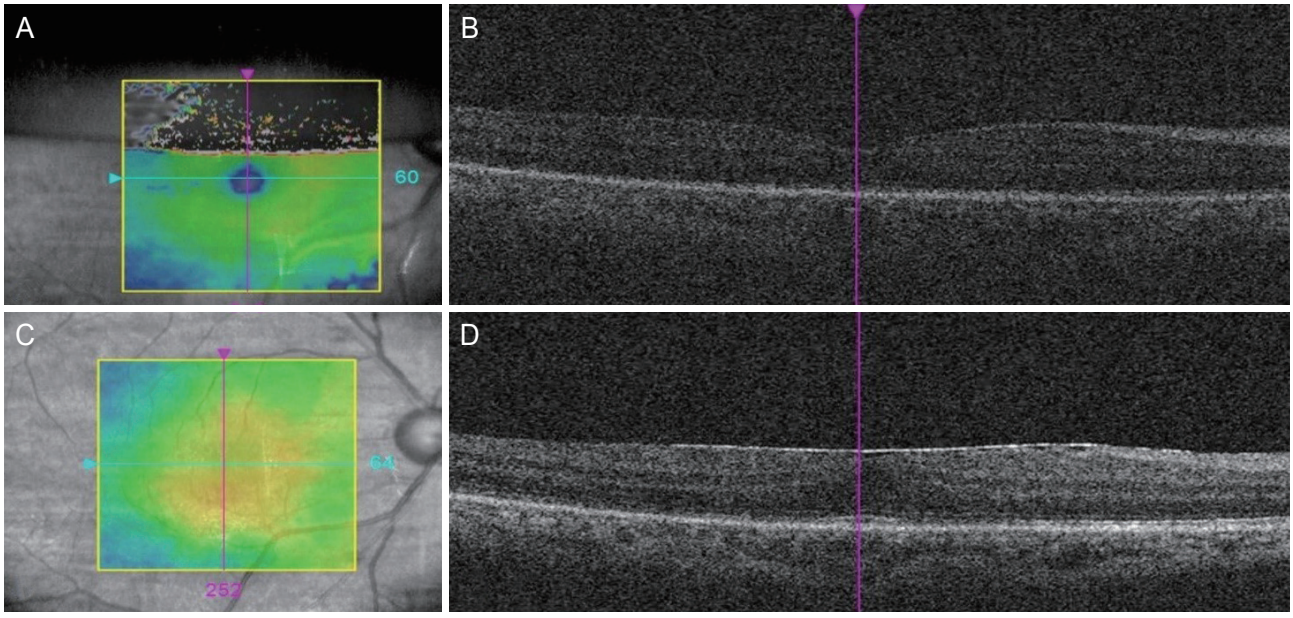

Figure 1. Representative images of macular optical coherence tomography (OCT) from a patient that developed an epiretinal membrane (ERM). OCT was carried out with macular cube 512 × 128 scans to determine the development of ERM in the 6 × 6 mm area around the macula. (A, B) There was no ERM at 1 week after primary retinal detachment surgery. (C, D) ERM was discovered 2 months after primary retinal detachment surgery.

Table 1. Characteristics of patients in the non-ERM group and ERM group

	Non-ERM Group	ERM Group	*p*-value
Number	175	42	
Sex, male:female	103:72	24:18	0.679
Mean age* (years)	53.20†	57.40†	0.020†
High myopia‡	72 (41.14)	9 (21.42)	0.052
Macular detachment	102 (58.28)	21 (50.0)	0.125
Diabetes mellitus	20 (11.42)	4 (9.52)	0.412§
Smoking history	39 (22.28)	9 (21.42)	0.881
Tamponade agent			0.813
5% C_3F_8	40 (22.85)	9 (21.42)	
10% C_3F_8	72 (41.14)	20 (47.61)	
Air	35 (20.00)	8 (19.04)	
Silicone oil	28 (16.00)	5 (11.90)	
Multiple retinal break	88 (50.28)	26 (61.90)	0.211
Large retinal break∏	42 (24.00)†	25 (59.52)†	<0.001†
Retinotomy	46 (26.28)	9 (21.42)	0.372
PFCL	107 (61.14)	25 (59.52)	0.818
Postoperative vitreous hemorrhage	25 (14.28)	5 (11.90)	0.824

Values are presented as number (%) unless otherwise indicated.
ERM = epiretinal membrane; C_3F_8 = octafluoropropane; PFCL = perfluorocarbon liquid.
*Median; †*p*-values indicate statistical significance; ‡axial length ≥ 26 mm; §Fishers exact test; ∏≥ 2 disc diameter.

Table 2. Characteristics of patients in the non-ERM group and ERM with surgery group

	Non-ERM Group	ERM with Surgery Group	*p*-value
Number	175	18	
Sex, male:female	103:72	11:7	0.902
Mean age* (years)	53.20	54.29	0.741
High myopia†	72 (41.14)	4 (22.22)	0.184
Macular detachment	102 (58.28)	8 (55.55)	0.266
Diabetes mellitus	20 (11.42)	1 (5.55)	0.697‡
Smoking history	39 (22.28)	4 (22.22)	0.767‡
Tamponade agent			0.881‡
5% C_3F_8	40 (22.85)	4 (22.22)	
10% C_3F_8	72 (41.14)	9 (50.00)	
Air	35 (20.00)	3 (16.66)	
Silicone oil	28 (16.00)	2 (11.11)	
Multiple retinal break	88 (50.28)	11 (61.11)	0.430
Large retinal break§	42 (24.00)∏	9 (50.00)∏	0.023∏,‡
Retinotomy	46 (26.28)	5 (27.77)	> 0.999‡
PFCL	107 (61.14)	10 (55.55)	0.551
Postoperative vitreous hemorrhage	25 (14.28)	2 (11.11)	> 0.999‡

Values are presented as number (%) unless otherwise indicated.
ERM = epiretinal membrane; C_3F_8 = octafluoropropane; PFCL = perfluorocarbon liquid.
*Median; †axial length ≥ 26 mm; ‡Fishers exact test; §≥ 2 disc diameter; ∏*p*-values indicate statistical significance.

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scale.

This study was approved by the Institutional Review Board and Ethics Committee. The study procedures adhered to the tenets of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using Fisher's exact test, chi-square test, Mann-Whitney test, and the paired sample *t*-test using SPSS statistics ver. 12.0 (SPSS Inc.). Statistical significance was defined as $p < 0.05$.

Results

Among the total 217 eyes, 42 eyes (19.3%) showed ERM formation after six months from primary vitrectomy. The average period of ERM formation after RRD surgery was 48.6 weeks. Eighteen eyes (8.3%) underwent secondary vitrectomy due to deterioration of the ERM. The average period from ERM formation to additional ERM surgery was 29.5 weeks.

Patient age was significantly different ($p = 0.020$) between the ERM group (57.4 ± 9.0 years) and the non-ERM group (53.2 ± 13.7 years). The prevalence of large retinal break was also significantly different ($p < 0.001$) between the ERM group and the non-ERM group. There was no significant differences in sex, high myopia, macular detachment, smoking, diabetes mellitus, tamponade agent, multiple retinal break, retinotomy, perfluorocarbon liquid, or postoperative vitreous hemorrhage between the two groups (Table 1).

In the comparison of the non-ERM group and the ERM with surgery group, only the prevalence of large retinal break was significantly different between the groups ($p = 0.023$); none of the other factors showed significant differences (Table 2).

In comparison with the ERM without surgery group and the ERM with surgery group, there were no significant differences between factors (Table 3). The ERM with surgery group tended to be slightly younger than the ERM without surgery group, but without significance ($p = 0.055$).

In the ERM with surgery group, BCVA was improved after surgery ($p = 0.005$) (Table 4).

Table 3. Characteristics of patients in the ERM without surgery group and ERM with surgery group

	ERM without Surgery Group	ERM with Surgery Group	*p*-value
Number	24	18	
Sex, male:female	13:11	11:7	0.584
Mean age* (years)	59.86	54.29	0.055
ERM formation period (weeks)	59.14 ± 76.27	32.53 ± 47.00	0.189
Period from ERM formation to ERM surgery (weeks)		29.52 ± 63.07	
High myopia†	5 (20.83)	4 (22.22)	> 0.999‡
Macular detachment	13 (54.16)	8 (55.55)	0.584
Diabetes mellitus	2 (8.33)	1 (5.55)	> 0.999‡
Smoking history	5 (20.83)	4 (22.22)	0.709‡
Tamponade agent			> 0.999‡
5% C_3F_8	5 (20.83)	4 (22.22)	
10% C_3F_8	11 (45.83)	9 (50.00)	
Air	5 (20.83)	3 (16.66)	
Silicone oil	3 (12.50)	2 (11.11)	
Multiple retinal break	15 (62.50)	11 (61.11)	0.987
Large retinal break§	15 (62.50)	9 (50.00)	0.332
Retinotomy	5 (20.83)	5 (27.77)	0.677‡
PFCL	15 (62.50)	10 (55.55)	0.546
Postoperative vitreous hemorrhage	3 (12.50)	2 (11.11)	> 0.999‡

Values are presented as number (%) or mean ± standard deviation.
ERM = epiretinal membrane; C_3F_8 = octafluoropropane; PFCL = perfluorocarbon liquid.
*Median; †axial length ≥ 26 mm; ‡Fishers exact test; §≥ 2 disc diameter.

Table 4. Comparison of BCVA before and after surgery in ERM with surgery group (n = 18)

	Before ERM Surgery	After ERM Surgery (3 M)	*p*-value
Mean BCVA (logMAR)	0.48 ± 0.44	0.21 ± 0.41	0.005*,†

Values are presented as mean ± standard deviation.
BCVA = best corrected visual acuity; ERM = epiretinal membrane; logMAR = logarithm of minimal angle of resolution; M = months.
*Paired sample *t*-test; †*p*-values indicate statistical significance.

Discussion

The ERM is a major complication that reduces visual acuity even after successful reattachment of a retinal detachment [5-7]. The incidence of ERM after surgery for RRD has been extensively studied. Early studies without OCT reported that the incidence of ERM development after scleral buckling ranged from 3.0 to 15.6% [5,6]. More recently, Cacioppo et al. [8] performed a prospective study using OCT and reported a much higher rate (32.6%) of ERM development in the macula within 6 months from scleral buckling to retinal detachment repair. Several studies reported the incidence of ERM development after vitrectomy for RRD repair ranging from 6.1%-12.8%. A retrospective study by Katira et al. [9] reported that ERM formation developed in 12.8% of 141 patients who had vitrectomy performed by 15 surgeons. In this study, biomicroscopy was used instead of OCT to observe ERM development. In another retrospective study, Heo et al. [10] investigated 264 eyes that underwent vitrectomy performed by three surgeons. The authors reported that approximately 6.1% of the eyes developed macular ERM. In a prospective study, Martínez-Castillo et al. [11] investigated 312 eyes with either aphakia or intraocular lens that underwent vitrectomy for retinal detachment and found ERM formation in 8.97% of the eyes.

In our study, the incidence of ERM in vitrectomy with primary RRD was 19.3% (42 out of 217 eyes), which was slightly higher than rates in previous studies. The studies varied in diagnostic methods, using biomicroscopy or variable OCTs for ERM detection and surgery methods. These factors are presumably responsible for the differences in incidence rates. Szigiato et al. [13] reported that approximately half of the ERM formation following vitrectomy was detected after the first post-operative year. The long follow-up period of our study may have affected the results.

In our study, postoperative ERM was more likely to occur in older patients. This result may come from the differences of state of the vitreomacular interface. A higher mean age of the ERM eyes may reflect the presence of posterior vitreous detachment, which is more likely to occur in an elderly population.

The ERM group had a larger proportion of patients with large retinal break before RRD surgery than the non-ERM group. Heo et al. [10] reported that the number or size of retinal breaks and vitreous hemorrhage can be risk factors of ERM development [14]. Martínez-Castillo et al. [11] reported that the duration of retinal detachment and the presence of equatorial and retinal holes are associated with ERM development.

In previous studies, a variety of factors (e.g., old age, long duration of macular detachment, large retinal breaks, multiple retinal breaks, preoperative or accompanying vitreous hemorrhage, use of cryopexy, retinotomy) have been suggested to be risk factors for ERM formation in patients who underwent vitrectomy for primary RRD [5,14-17]. However, in our patient cohort, we found that macular detachment, high myopia, intraoperative tamponade materials, smoking, and diabetes mellitus did not increase the risk of ERM formation.

Several studies also explored the correlation between ERM formation and postoperative BCVA. Matoba et al. [18] reported no significant difference in postoperative BCVA between eyes with ERM formation and those without ERM formation. However, Martínez-Castillo et al. [11], Soares et al. [19], and Perente et al. [20] reported that BCVA was significantly improved in the group with secondary ERM surgery. In our study, we also observed a significant improvement of BCVA between after surgery.

In our study, there was no significant difference in the period of ERM formation between the ERM surgery group and ERM without surgery group. Ishida et al. [16] reported that the occurrence and progression of ERM were detected relatively early after RRD surgery in the ERM formation group. Therefore, in high-risk patients, careful follow-up may be required, especially in the early period after RRD surgery.

The main limitations of our study are the use of a retrospective approach and a relatively small cohort of patients. Moreover, the use of 5% or 10% C_3F_8 gas was determined according to the degree of RRD under the judgment of the

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operator, and this might be a limitation of our study. However, this study has several advantages, including that the operations were performed by a single surgeon, eliminating the confounding surgical variables due to different surgeons. Furthermore, this study used close monitoring of the status of the macular ERM and early detection of ERM based on both OCT and fundus photography performed at every follow-up visit. These methods provided consistent diagnostic methods throughout the study period and early detection of ERM development.

This study suggests that patients who receive vitrectomy to repair a primary RRD require continuous monitoring using both fundus photography and OCT. Additionally, elderly patients and patients with large retinal breaks before RRD surgery may need closer monitoring.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this article.

Author Contribution

Conception (Y.H.K.); Design (Y.H.K.); Data acquisition (S.Y.C., Y.H.K.) Analysis (S.Y.C., Y.H.K.); Interpretation (S.Y.C., Y.H.K.); Writing (S.Y.C.); Review (Y.H.K.); Final approval of the article (All authors)

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