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Original Article

Assessment of Risk Factors Affecting Refractive Outcomes after Phacovitrectomy for Epiretinal Membrane

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Purpose: To investigate factors associated with refractive outcomes after phacovitrectomy for epiretinal membrane (ERM).

Methods: Retrospective review of patients undergoing phacovitrectomy for ERM was done. The main outcome measure was predictive refraction error (PE), defined as observed refraction error – target refraction error, calculated by the SRK/T, Haigis, and SRK II formulae. PE was measured at postoperative 1, 3, and 6 months. Simple and multiple linear regression analysis were used to evaluate factors associated with PE.

Results: A total of 53 eyes of 53 patients were included. The mean PEs at postoperative 1, 3, and 6 months were all negative, implying myopic shift in all patients regardless of the intraocular lens formula used. Haigis formula showed the least myopic shift among the three formulae (p = 0.001, Friedman test). There was no significant difference in PE depending on preoperative central macular thickness (CMT) in subgroup analysis. On stepwise multiple linear regression analysis, ERM etiology (β = 0.759, p = 0.004, SRK/T formula; β = 0.733, p = 0.008, Haigis formula; β = 0.933, p < 0.001, SRK II formula), preoperative anterior chamber depth (β = –0.662, p = 0.013, Haigis formula; β = –0.747, p = 0.003, SRK II formula), and decrease of CMT (β = –0.003, p = 0.025, SRK/T formula) were significantly associated with PE at postoperative 6 months.

Conclusions: Myopic shift in PE was observed after combined phacovitrectomy for epiretinal membrane. ERM etiology, preoperative anterior chamber depth, and decrease of CMT were significantly associated with PE at postoperative 6 months. There was no difference in PE after surgery between the two groups defined by CMT (≥500 and <500 µm).

Key Words: Epiretinal membrane, Myopia, Refractive errors, Vitrectomy

Epiretinal membrane (ERM) refers to the growth of semi-translucent avascular membranes on the inner surface of the retina. Although most ERMs are idiopathic, common secondary causes include trauma, previous intraocular surgery, retinal vascular disease, uveitis, and retinal tears [1]. The prevalence of ERM is 7% [2] to 11.8% [3], with increasing age being the most important risk factor [1].

For patients with coexisting cataract and ERM, combined simultaneous phacovitrectomy is recommended as a

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safe and effective treatment option, with functional and anatomical outcomes comparable to those of staged sequential surgery [4–9]. It is cost-effective, reduces the number of necessary surgeries and improves intraoperative macula visualization by removing the opacified lens [4]. However, previous studies have reported that combined phacovitrectomy for ERM may result in myopic shift of the target postoperative refraction [10–14], but few studies were able to identify factors associated with such myopic shift [15,16]. Thus, the purpose of this study is to evaluate postoperative refractive outcome accuracy after combined phacovitrectomy for ERM and determine risk factors affecting refractive outcomes.

Materials and Methods

Ethical statements

The study protocol was approved by the Institutional Review Board of the Seoul Metropolitan Government Seoul National University Boramae Medical Center (No. 30-2022-70) and was conducted with adherence to the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

Study design and participants

Retrospective review of patients who underwent combined phacovitrectomy for ERM between March 2013 and January 2020 were done. Inclusion criteria were patients who underwent combined phacovitrectomy for ERM with at least 6 months of follow-up and exclusion criteria were as follows; patients with missing data, previous history of intraocular or refractive surgery, presence of corneal disease such as pteyrigum, intraoperative events including posterior capsule rupture or zonular dialysis, and loss to follow-up within 6 months after surgery.

Examinations

Preoperative clinical data such as age, sex, ophthalmologic history, preoperative visual acuity, refractive error (RE) measured in spherical equivalent form with an autorefractor keratometer (RKT-7700, Nidek), underlying disease including diabetes or hypertension, axial length (AL) and anterior chamber depth (ACD) measured by partial interferometry (IOL Master, Carl Zeiss Meditec), ERM etiology (idiopathic or secondary), central macular thickness (CMT) measured with spectral domain optical coherence tomography (Spectralis OCT, Heidelberg Engineering), and target RE based on SRK/T, Haigis, and SRK II formulae were acquired from medical charts. Patients were divided into two groups according to preoperative CMT cutoff value of 500 μm and comparative analyses within the two groups were also done.

Intraoperative data including whether intraoperative procedures such as tamponade, laser photocoagulation, inner limiting membrane (ILM) peeling, and intravitreal or subtenon steroid injections were performed, and the type of implanted intraocular lens (IOL) were collected.

Observed RE and CMT at postoperative 1, 3, and 6 months were reviewed. The predictive refraction error (PE), defined as difference between observed refraction error and target refraction error, was calculated using SRK/T, Haigis, and SRK II formulae.

Surgical methods

Cataract extraction with phacoemulsification (2.8-mm clear corneal incision) and posterior capsular IOL implantation with an acrylic foldable IOL were performed in all patients. Following cataract surgery, three 23G trocars were inserted, and pars plana vitrectomy (PPV) was performed. Epiretinal membranes were peeled using end-grip forceps with or without additional ILM peeling. When ILM peeling was done, the ILM was stained with indocyanine green dye (Diagnogreen, Daiichi Sankyo) and removed with ILM forceps. Laser photocoagulation was done in the presence of any retinal tears, breaks, or degenerative lesions. Gas or air tamponade, intravitreal or subtenon steroid injections were done according to the surgeons' discretion. At the end of the surgery, trocars were removed, sclerotomy sites were checked for leakage, and transconjunctival 8-0 absorbable suture were placed if any leakages were detected. All patients were treated by three retina surgeons (JA, TWK, JYS).

Statistics

IBM SPSS ver. 21.0 (IBM Corp) was used for statistical analysis. A p-value of <0.05 was considered statistically significant. Unpaired *t*-test, Mann-Whitney test, chi-square test, and Fisher exact test were used to assess intergroup differences. One-way repeated measures analysis of variance and Friedman test were used to determine the presence of significant differences among the three IOL formulae. The results are presented as mean ± standard deviation unless otherwise indicated. Simple linear regression analysis and stepwise multiple linear regression analysis were used to investigate factors associated with PE.

Results

A total of 195 eyes of 195 patients who underwent com-

Table 1. Patient demographics

Characteristic	All patients (n = 53)	CMT ≥500 µm (n = 25)	CMT <500 µm (n = 26)	*p*-value
Age (yr)	68.5 ± 7.4	67.6 ± 7.6	69.1 ± 7.6	0.502*
Sex				0.313†
Male	22 (41.5)	9 (36.0)	13 (50.0)	
Female	31 (58.5)	16 (64.0)	13 (50.0)	
Laterality				0.688†
Right	31 (58.5)	14 (56.0)	16 (61.5)	
Left	22 (41.5)	11 (44.0)	10 (38.5)	
Diabetes mellitus	14 (26.4)	6 (24.0)	8 (30.8)	0.588†
Hypertension	28 (52.8)	12 (48.0)	15 (57.7)	0.488†
Cause of epiretinal membrane				0.703‡
Idiopathic	44 (83.0)	22 (88.0)	21 (80.8)	
Secondary	9 (17.0)	3 (12.0)	5 (19.2)	
Preoperative characteristic				
BCVA (logMAR)	0.58 ± 0.32	0.71 ± 0.39	0.47 ± 0.19	0.020§
Axial length (mm)	23.51 ± 0.81	23.40 ± 0.81	23.58 ± 0.85	0.440*
Spherical equivalent (D)	–0.12 ± 1.88	–0.09 ± 1.66	–0.12 ± 2.16	0.560§
CMT (µm)	498.29 ± 96.14	575.36 ± 62.54	424.19 ± 55.50	<0.001§
Anterior chamber depth (mm)	3.13 ± 0.39	3.11 ± 0.34	3.14 ± 0.45	0.759*
K1 (D)	43.85 ± 1.43	44.12 ± 1.25	43.66 ± 1.60	0.258*
K2 (D)	44.74 ± 1.50	45.07 ± 1.44	44.48 ± 1.57	0.173*
Intraoperative procedure				
Endolaser	11 (20.8)	6 (24.0)	5 (19.2)	0.679†
ILM peeling	21 (39.6)	13 (52.0)	8 (30.8)	0.124†
Steroid injection	8 (15.1)	7 (28.0)	1 (3.8)	0.024‡
Tamponade	5 (9.4)	3 (12.0)	2 (7.7)	0.668‡
Type of intraocular lens				0.405‡
Akreos AO	39 (73.6)	18 (72.0)	19 (73.1)	
Hoya iSert 250	2 (3.8)	2 (8.0)	0 (0)	
Hoya PC-60AD	2 (3.8)	0 (0)	2 (7.7)	
Tecnis ZCB00	10 (18.9)	5 (20.0)	5 (19.2)	

Values are presented as mean ± standard deviation or number of eyes (%). Two eyes did not have preoperative CMT data.
CMT = central macular thickness; BCVA = best-corrected visual acuity; logMAR = logarithm of the minimum angle of resolution; D = diopters; K = keratometry; ILM = internal limiting membrane.
*Unpaired *t*-test; †Chi-square test; ‡Fisher exact test; §Mann-Whitney test.

bined phacovitrectomy between March 2013 and January 2020 were initially reviewed and 142 cases were excluded leaving 53 eyes available for analysis. According to preoperative CMT, there were 25 eyes for CMT ≥500 µm, 26 eyes for CMT <500 µm, and two eyes without preoperative CMT data. Table 1 summarizes the patients' baseline clinical and demographic data.

The mean patient age was 68.5 ± 7.4 years and the mean CMT was 482.29 ± 96.14 µm. When demographics were compared between two groups divided according to CMT, preoperative best-corrected visual acuity was significantly worse and the number of eyes receiving intraoperative steroid injection was significantly higher in patients with CMT ≥500 µm (0.71 ± 0.39 logarithm of the minimum angle of resolution [logMAR] vs. 0.47 ± 0.19 logMAR, $p = 0.020$; 28% vs. 3.8%, $p = 0.024$). There were no significant differences regarding age, sex, laterality, underlying disease such as diabetes mellitus or hypertension, cause of ERM, AL, preoperative RE, ACD, intraoperative endolaser, ILM peeling, tamponade, and type of IOL used in surgery between the two groups.

Table 2 shows PEs calculated with the SRK/T, Haigis,

Table 2. PE and absolute PE (n = 53)

Variable	SRK/T	Haigis	SRK II	*p*-value
Mean PE (D)				
Postoperative 1 mon	–0.54 ± 0.71	–0.40 ± 0.73	–0.60 ± 0.71	0.001*
Postoperative 3 mon	–0.47 ± 0.75	–0.33 ± 0.78	–0.53 ± 0.73	0.001*
Postoperative 6 mon	–0.42 ± 0.81	–0.28 ± 0.82	–0.48 ± 0.79	0.001†
p-value	0.099†	0.359*	0.099†	-
Mean absolute PE (D)				
Postoperative 1 mon	0.71 ± 0.55	0.62 ± 0.55	0.74 ± 0.56	0.019*
Postoperative 3 mon	0.66 ± 0.59	0.60 ± 0.60	0.70 ± 0.57	0.040*
Postoperative 6 mon	0.68 ± 0.59	0.61 ± 0.61	0.71 ± 0.59	0.045*
p-value	0.686*	0.897*	0.826*	-

PE = predictive refraction error; D = diopters.
*Friedman test; †One-way repeated measures analysis of variance.

Table 3. Comparison of mean PE according to preoperative CMT

Formula	Preoperative CMT ≥500 µm (n = 25)	Preoperative CMT <500 µm (n = 26)	*p*-value
SRK/T mean PE (D)			
1 mon	–0.70 ± 0.62	–0.42 ± 0.80	0.158*
3 mon	–0.59 ± 0.65	–0.33 ± 0.83	0.205*
6 mon	–0.61 ± 0.70	–0.31 ± 0.79	0.097†
Haigis mean PE (D)			
1 mon	–0.53 ± 0.73	–0.29 ± 0.74	0.261*
3 mon	–0.42 ± 0.81	–0.21 ± 0.76	0.187†
6 mon	–0.44 ± 0.81	–0.19 ± 0.75	0.221†
SRK II mean PE (D)			
1 mon	–0.71 ± 0.63	–0.52 ± 0.79	0.335*
3 mon	–0.60 ± 0.62	–0.43 ± 0.81	0.389*
6 mon	–0.62 ± 0.70	–0.41 ± 0.79	0.316*

PE = predictive refraction error; CMT = central macular thickness; D = diopters.
*Unpaired *t*-test; †Mann-Whitney test.

and SRK II formulae. Regardless of the formula used and timepoint of examination, all mean PEs had negative values, indicating an overall myopic shift. The Haigis formula showed the least myopic shift among the three formulae (Friedman test, $p = 0.001$). Mean PEs using the Haigis formula were –0.40 ± 0.73, –0.33 ± 0.78, and –0.28 ± 0.82 diopters (D) at postoperative 1, 3, and 6 months. In addition, the Haigis formula showed the smallest mean absolute PE among three formulae ($p = 0.019$, $p = 0.040$, and $p = 0.045$ at postoperative 1, 3, and 6 months, respectively; Friedman test). Considering all eyes, target refractions were calculated on average most precisely with the Haigis formula. There was no significant difference in PEs or absolute PEs according to the timepoint of examination in all formulae.

Table 3 shows PEs of the two groups divided according to CMT at postoperative 1, 3 and 6 months. There were no significant differences in PEs between the two groups at all visits, regardless of the IOL formulae.

Table 4 shows simple and multiple linear regression analyses between selected variables and PE at postoperative 6 months. On multiple linear regression analysis, cause of ERM was significantly associated with postoperative PE for all the three IOL formulae (SRK/T: β = 0.759, $p = 0.004$; Haigis: β = 0.733, $p = 0.008$; SRK II: β = 0.933, $p < 0.001$). CMT difference between preoperative and postoperative 6 months was a significant factor for the SRK/T formula (β = –0.003; $p = 0.025$), and preoperative ACD was significantly associated with postoperative PE for the Haigis (β = –0.662, $p = 0.013$) and SRK II formulae (β = –0.747, $p = 0.003$). In summary, patients with idiopathic ERM, greater reduction in CMT, and deeper ACD had significantly larger myopic shift.

Discussion

Simultaneous phacovitrectomy has been widely accepted as a standard procedure for patients with macular disease and cataract because it enables visual rehabilitation while also saving time and cost [17]. However, there have been concerns regarding refractive outcome after combined surgery and previous studies have reported varying

Table 4. Simple and multiple linear regression analyses between selected variables and predictive refraction error at postoperative 6 months

Variable	Linear regression analysis				
	Simple			Multiple	
	R^2	β	*p*-value	β	*p*-value
SRK/T					
Target refraction calculated by SRK/T (D)	0.091	0.505	0.028	-	-
Type of IOL*	0.114	–0.225	0.014	-	-
Cause of ERM†	0.167	0.869	0.002	0.759	0.004
CMT difference at postoperative 6 mon (μm)	0.009	–0.003	0.037	–0.003	0.025
Preoperative mean keratometry (D)	0.081	–0.160	0.039	-	-
Haigis					
Type of IOL*	0.124	–0.239	0.010	-	-
Cause of ERM†	0.103	0.692	0.019	0.733	0.008
Preoperative ACD (mm)	0.093	–0.633	0.027	–0.662	0.013
SRK II					
Type of IOL*	0.109	–0.217	0.016	-	-
Cause of ERM†	0.168	0.855	0.002	0.933	<0.001
Presence of hypertension	0.094	0.483	0.025	-	-
Preoperative refraction (D)	0.114	0.143	0.014	-	-
Preoperative ACD (mm)	0.106	–0.653	0.018	–0.747	0.003

D = diopters; IOL = intraocular lens; ERM = epiretinal membrane; CMT = central macular thickness; ACD = anterior chamber depth.
*Akreos AO = 1, Hoya iSert250 = 2, Hoya PC-60AD = 3, Tenics ZCB00 = 4; †Idiopathic = 0, secondary = 1.

results. Shi et al. [18] demonstrated no significant differences in the predicted and postoperative RE for combined phacovitrectomy and cataract surgery only groups. On the other hand, Falkner-Radler et al. [12] found significantly induced myopia of approximately –0.4 D in patients who underwent combined surgery. Hamoudi et al. [9] also showed myopic shift of –0.31 D 1 month after surgery, decreasing to –0.15 D after 12 months in the phacovitrectomy group. In addition, Kim et al. [13] showed combined phacovitrectomy for ERM resulted in significant myopic shift of postoperative refraction compared to the cataract surgery only group, for both A-scan and IOL Master, with a mean PE of –0.305 and –0.356 D, respectively, compared to +0.215 and +0.077 D in the cataract surgery only group. Kang et al. [14] also showed the mean postoperative prediction error of –0.37 D in the phacovitrectomy group. Our results were consistent with previous studies reporting myopic shifts after combined phacovitrectomy, with a mean PE of –0.54, –0.40, and –0.60 D for SRK/T, Haigis, and SRK II formulae, respectively, at postoperative 1 month, decreasing to –0.42, –0.28, and –0.48 D, respectively, at postoperative 6 months. Among the three IOL formulae, Haigis performed the best with the least myopic shift (–0.40 ± 0.73 and –0.28 ± 0.82 D at postoperative 1 and 6 months, respectively).

There are many possible causes for the myopic shift in phacovitrectomy. Frings et al. [19] suggested that underestimation of the actual AL due to increased preoperative macula thickness associated with concomitant macular pathologies such as epiretinal membranes may result in myopic shift. An AL measurement error of 0.1 mm may cause an error of 0.28 D [20]. IOL Master is based on partial coherence interferometry and measures AL from the corneal epithelium to the retinal pigment epithelium (RPE) using an interference signal that is reflected on the RPE [19]. Even though the distance between ILM and external limiting membrane (ELM) is variable according to macular pathology [21], the distance between the ELM and the RPE is negligible [19]. Therefore, AL measured by IOL Master is not expected to be influenced by retinal thickening or macular edema due to the presence of ERM [19]. However, tractions induced by ERM may alter the RPE/ELM anatomical structure [19]. In such cases, underestimation of the AL can occur. On the other hand, Kojima et al. [22] suggested that in some macular disease cases, a double peak was observed by IOL Master in AL measurements, with the posterior peak representing RPE and the anterior peak representing the retina surface, such as an ERM, an ILM, or a posterior vitreous membrane. If the anterior peak is selected for IOL calculation, AL may be falsely underestimated and cause severe myopic shift [22]. In our study, CMT difference at postoperative 6 months was significantly associated with PE using the SRK/T formula ($\beta = -0.003$, $p = 0.025$). This implies possible underestimation of AL associated with ERM-induced macular edema or erroneously selected anterior peak for AL measurement.

On the other hand, Falkner-Radler et al. [12] suggested that myopic shift may be the result of postoperative AL increase caused by sclera thinning or stretching in or around the sclerotomy sites after vitrectomy. Kim et al. [13] suggested that myopic shift might result from a significantly higher postoperative keratometry value, which implies corneal steepening after surgery. However, due to the retrospective design, it was not possible to obtain postoperative AL and keratometry measurements and further studies are warranted to investigate whether underestimation of preoperative AL, postoperative AL elongation, or changes in keratometry truly occur.

Jeoung et al. [11] suggested myopic eyes with preoperative AL of more than 24.5 mm developed significant myopic shifts, with mean PE –1.24 ± 0.79 D after phacovitrectomy. In the present study, no significant association was found between AL and PE.

Schweitzer and Garcia [23] have reported that postoperative myopic shift occurs after phacovitrectomy due to the forward movement in IOL position caused by gas tamponade. They explained that gas can force the IOL to move forward and reduce the ACD, resulting in significant myopic shift. However, in our study, gas or air tamponade was not significantly associated with PE for all IOL formulae (SRK/T, $p = 0.189$; Haigis, $p = 0.302$; SRK II, $p = 0.202$).

Kang et al. [14] suggested effective lens position (ELP) shift as another possible cause. ELP is defined as the distance between the cornea apex and the IOL, and a 0.25 mm shorter ELP causes myopia of 0.5D [24]. According to Kang et al. [14], thicker lenses and shallower ACDs were associated with significant postoperative PEs resulting in myopia after phacovitrectomy. In addition, there was a significant correlation between ACD change and PEs since vitreous and posterior lens capsule interactions disappear after vitrectomy, resulting in a shift in the IOL position [14]. Although it was not possible to obtain data on the absolute change of preoperative and postoperative ACD in this study, we found a significant association between preoperative ACD and PE at postoperative 6 months with Haigis ($\beta = -0.662$, $p = 0.013$) and SRK II ($\beta = -0.747$, $p = 0.003$), which may indicate a possible contribution of ACD in the observed myopic shift.

The novelty of our study is that ERM etiology, whether idiopathic or secondary, has a significant association with PE at postoperative 6 months for all IOL formulae (SRK/T: $\beta = 0.759$, $p = 0.004$; Haigis: $\beta = 0.733$, $p = 0.008$; SRK II: $\beta = 0.933$, $p \leq 0.001$). We defined secondary ERM as ERM caused by diabetic retinopathy, retinal vein occlusion, or uveitis. All other ERM with unknown etiology were considered as idiopathic ERM. Our results show that there was less myopic shift in patients with secondary ERM. This may be explained by the fact that RPE/ELM alteration is not reversed even after surgery in secondary ERM. Although partial coherence interferometry is not influenced by changes in the overlying retinal layers for case with macular edema, epiretinal tractions may have an impact since it alters the RPE/ELM anatomical structure [19,25]. A previous study by Kang et al. [26] examined ERM recurrence following PPV with membrane peel and found that secondary ERMs have higher rates of recurrence than primary ERMs (20% vs. 4.88%, $p = 0.03$). They explained the higher chance of ERM recurrence as a result of the involvement of retinal pigment epithelial or glial cells during retinal damage and tissue recovery secondary to a preceding ophthalmologic disorder, even after PPV and membranectomy [26]. Furthermore, Yazici et al. [27] showed vitreomacular traction rates to be slightly higher in secondary ERM groups than idiopathic ERM groups, even though the difference was not statistically significant (10% vs. 4%, $p = 0.071$). These results imply that there may be more recurrent and persistent traction for secondary ERM, even after surgery, and as a result, it may be difficult for the altered RPE/ELM structure to be reversed. This may lead to more precise measurement of AL by IOL Master in secondary ERM, as the ELM configuration is not much altered after surgery. Further studies are needed to prove this finding.

Another strength of this study is the fact that we examined PE using three different formulae (SRK/T, Haigis, and SRK II) rather than using only one formula as in other previous studies [11–16]. We also analyzed PE at different timepoints of postoperative 1, 3, and 6 months to identify any time-related changes. Regardless of the formula used and timepoint of examination, myopic shifts were observed. The Haigis formula showed the least myopic shift among the three formulae and on average calculated target refractions most precisely. There was no significant difference in PEs or absolute PEs according to the timepoint of examination for all formulae.

There are some limitations to this study. First, the study population was relatively moderately sized, which may not be sufficient to represent a general population of patients with cataract and ERM. Second, due to the inherent limitation of the cross-sectional, retrospective, and nonrandomized study design, a cause-and-effect relationship cannot be proven, and only association between factors may be observed. Third, owing to the lack of longitudinal postoperative data such as AL or keratometry, specific evidence for any possible association between these values and the myopic shift could not be provided. In addition, this study was conducted at a single center, which may affect the generalizability of the results. Furthermore, because three different surgeons performed surgeries in this study, heterogenous surgeon factors might play a role. Therefore, a prospective study with larger number of patients, longitudinal data collection, conducted by a single surgeon, is warranted.

In conclusion, regardless of the IOL formula, myopic shift was observed after phacovitrectomy for ERM. There was no significant difference in PE between patients divided according to a preoperative CMT value of 500 µm. Factors significantly associated with myopic shift on multiple regression analysis were ERM etiology, preoperative ACD, and reduction in CMT.

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