

Usefulness of the Components of Full-Field Electroretinography to Predict Postoperative Visual Outcomes in Patients With Epiretinal Membranes

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Purpose: To confirm the predictors of postoperative visual outcomes by performing full-field electroretinography (ffERG) before surgery in patients with epiretinal membranes (ERMs).

Methods: Sixty-one eyes of patients with ERMs who underwent pars plana vitrectomy with membrane peeling were prospectively reviewed. Correlations between preoperative data (ffERG and optical coherence tomography) and postoperative best-corrected visual acuity (BCVA) were investigated. Receiver operating characteristic (ROC) curve analysis was performed to obtain cutoff values of the ffERG parameters predicting good visual outcome (final BCVA $\geq$ 20/30).

Results: Postoperative BCVA was significantly correlated with the implicit time and amplitude of the b-wave in light-adapted (LA) 3.0 electroretinography (ERG), with the amplitude difference between N1 and P1 in the LA 30-Hz flicker ERG, and with the sum of the amplitudes of OS1, OS2, and OS3 in dark-adapted (DA) oscillatory potential (OP) ERG ($P < 0.01$). The area under the ROC curve to predict good visual outcome was statistically significant for the four parameters (0.787, 0.815, 0.757, and 0.792, respectively).

Conclusions: The postoperative BCVA in patients with ERM was significantly correlated with the implicit time and amplitude of the b-wave in the LA 3.0 ERG, the amplitude difference between N1 and P1 in the LA 30-Hz flicker ERG, and the sum of the amplitudes of OS1, OS2, and OS3 in DA OP ERG of ffERG. It is thought that ffERG before surgery may help predict visual outcomes after surgery.

Translational Relevance: It was confirmed that the degree of retinal function in the ERM can predict BCVA after treatment.

Introduction

Epiretinal membrane (ERM) is a macular disease that is relatively common among elderly individuals; it is characterized by the formation of a fibrocellular membrane along the surface of the internal limiting membrane (ILM) of the retina. Although individuals with thin and transparent ERMs may not present with visual symptoms, a thicker and more opaque membrane causes profound symptoms, such as decreased visual acuity and metamorphopsia. In addition, membrane contraction, which progresses to fibrotic remodeling, is a severe sight-threatening event.¹ Pars plana vitrectomy with ERM peeling is considered

the standard treatment for ERM; however, in some cases, vision recovery after surgery is limited.²

Many studies found that better preoperative best-corrected visual acuity (BCVA) was associated with better postoperative BCVA.^{3–6} However, Koutsandrea et al.⁷ did not find a statistically significant relation between pre- and postoperative BCVA. Additionally, because the presence and degree of cataracts before surgery differ, the prognosis cannot be accurately predicted from preoperative visual acuity alone.

Several studies have been conducted to determine what preoperative tests can predict postoperative vision. Among these studies, several have investigated the macular function of individuals with ERMs using multifocal electroretinography (ERG) and

pattern ERG.^{8–10} In multifocal ERG, P1 response amplitude densities in rings 1 and 2 and P1 implicit time in ring 1 were significantly changed in eyes with ERMs compared with controls,⁸ and final BCVA was significantly correlated with preoperative P1 implicit time.⁹ In pattern ERG, the preoperative N95 amplitude ratio was significantly correlated with visual acuity at 6 months after ERM removal.¹⁰

However, these tests are not perfect for measuring postoperative prognosis. In multifocal ERG, several artifacts can make interpretation difficult. One result of this configuration is that relatively low levels of noise can cause larger disturbances centrally than peripherally because they are averaged out over a smaller area in the center than in the periphery.¹¹ Small noise levels often create artificially high central peaks on the topographic map. Therefore, in the presence of ERMs, when the function of the center of the retina has to be confirmed, there is a possibility that an error in measurement of visual prognosis after surgery may occur due to noise. In pattern ERG, the actual recording is difficult and inaccurate, the signal is very small (0.5–8 μ V), and the procedure is technically more demanding.¹² Because of these problems, we questioned whether these tests provide accurate prognoses after surgery.

Full-field electroretinography (ffERG) is an electrophysiologic test widely used for the assessment of complete retinal function. Previous studies have evaluated the function of the macula using multifocal ERG and pattern ERG but not full-field ERG in patients with ERMs. Macular ERG techniques such as multifocal ERG and pattern ERG have the aforementioned drawbacks. Additionally, previous studies of ERMs were limited to the idiopathic type. Secondary ERMs due to different ocular conditions are often found among patients undergoing ERM surgery; therefore, previous studies have had limited ability to confirm prognoses after surgery for all ERM patients, including secondary ERM patients.

The purpose of the current study was to confirm the prediction of postoperative visual outcome through ffERG before surgery in patients with ERMs.

Methods

Patients

The current research followed the tenets of the Declaration of Helsinki, and all patients provided informed consent after explanation of the study protocol. The Institutional Review Board at Kyung Hee

University Hospital (KHNMC-2016-12-035) approved this prospective study. This prospective study involved a series of 61 eyes with epiretinal membranes; the patients came to the Department of Ophthalmology at Kyung Hee University Hospital at Gangdong from March 2016 to July 2019.

The following inclusion criteria were used: (1) pars plana vitrectomy with ERM peeling and (2) a minimum follow-up period of 6 months. Exclusion criteria included the following: (1) bilateral ERMs, (2) macular or lamellar hole, (3) glaucoma, or (4) other ocular pathology that could interfere with visual function.

All patients underwent a complete ophthalmologic examination, including an assessment of BCVA, slit-lamp examination, pupil-dilated fundus examination, color fundus photography, optical coherence tomography (OCT), and ffERG before surgery. Fluorescein angiography (FA) was performed when secondary ERMs could not be excluded. Snellen BCVA was recorded before and 6 months after surgery and was converted to logMAR BCVA for analysis. The OCT images were obtained using Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) before and 6 months after surgery, and the central macular thickness (CMT) was assessed and recorded. The FA images were obtained using a Heidelberg Retinal Angiograph 2 (HRA2).

In total, 21 patients with newly formed secondary ERMs had a previous history of diabetic retinopathy, retinal vascular disease, vascular occlusion, or intraocular inflammation and had a history of treatment (e.g., laser, injection, surgery).¹³ To confirm the distinction between idiopathic and secondary ERMs, we performed FA in 40 patients. Of these patients, four had confirmed vascular abnormalities and were diagnosed with secondary ERMs. The remaining 36 patients who did not present with any abnormalities on FA were diagnosed with idiopathic ERMs. The proportions of patients with secondary ERMs were as follows: diabetic retinopathy, 16 eyes (64.0%); branch retinal vascular occlusion, three eyes (12.0%); other retinal vascular disease, four eyes (16%), including macular telangiectasia (two eyes), retinal macroaneurysm (one eye), and radiation retinopathy (one eye); and intraocular inflammation, two eyes (8.0%).

Full-Field Electroretinography

According to the standard guidelines of the International Society for Clinical Electrophysiology of Vision (ISCEV, 2015 update), the ffERG values of all patients with ERMs were recorded with the RETI-port

system before surgery (Roland Consult, Brandenburg, Germany).¹⁴

Normal patient preparation before the examination is as follows: After the pupils are maximally dilated, the recording conditions outlined below specify 20 minutes of dark adaptation before recording dark-adapted (DA) ERGs and 10 minutes of light adaptation before recording light-adapted (LA) ERGs. Because we used contact lens electrodes, dark adaptation was performed first to minimize the wearing time. The patient is then instructed to look at a fixation point incorporated into the stimulus Ganzfeld dome. Stable gaze is very important; therefore, we used a weak red light-emitting diode fixation point that does not interfere with dark adaptation.

The ISCEV standard ERG series includes six protocols. These are named according to the stimulus (flash strength in $\text{cd} \cdot \text{s} \cdot \text{m}^{-2}$) and the state of adaptation:

1. DA 0.01 ERG (rod-driven response of bipolar cells)
2. DA 3.0 ERG (combined responses arising from photoreceptors and bipolar cells of both the rod and cone systems; rod dominated)
3. DA 10.0 ERG (combined response with enhanced a-waves reflecting photoreceptor function)
4. DA oscillatory potentials (responses primarily from amacrine cells)
5. LA 3.0 ERG (responses of the cone system; a-waves arise from cone photoreceptors and OFF cone bipolar cells; the b-wave comes from ON and OFF cone bipolar cells)
6. LA 30-Hz flicker ERG (sensitive cone-pathway-driven response)

Statistical Methods

Statistical analysis was performed using SPSS Statistics 25.0 (IBM, Armonk, New York). Data were compared using unpaired and paired *t*-tests. The Kruskal–Wallis test and the Mann–Whitney *U* test were used for subgroup analysis based on visual acuity after surgery. Correlations among variables were analyzed using Pearson's correlation analysis. A receiver operating characteristic (ROC) curve was constructed to obtain cutoff values of ffERG for the prediction of visual prognosis. A good visual outcome was defined as a BCVA of 20/30 or better. To predict good visual acuity after surgery, the likelihood ratio test was used to determine whether there was a difference due to changing the number of parameters. $P < 0.05$ was considered statistically significant.

Results

In total, 61 eyes of 61 patients were enrolled (27 men, 44.26%; 34 women, 55.74%). The average age of the participants was 66.74 ± 8.92 years (range, 38–84). Of the 61 eyes, 55 (90.16%) were phakic and six (9.84%) were pseudophakic at the time of surgery. Fifty-three patients (86.89%) underwent combined cataract surgery and later presented with pseudophakia. Thirty-one eyes (50.82%) underwent ERM peeling, and 30 eyes (49.18%) underwent ERM peeling with ILM peeling. The mean preoperative BCVA was 0.59 ± 0.33 logMar, and the mean postoperative BCVA was 0.19 ± 0.21 logMar. The mean preoperative CMT measured using OCT were $478.72 \pm 97.92 \mu\text{m}$, and the postoperative CMT was $367.18 \pm 66.57 \mu\text{m}$. After performing pars plana vitrectomy with ERM peeling, there was a significant improvement in BCVA values and a reduction in CMT values (paired *t*-test, $P < 0.01$) (Table 1).

Correlation of Preoperative ffERG Parameters with Pre- and Postoperative Visual Acuity

The correlation between pre- and postoperative BCVA and the preoperative parameters of ffERG was confirmed (Table 2). In the LA 3.0 ERG, the implicit times of both a- and b-waves were statistically significantly correlated with postoperative BCVA ($P < 0.01$). These parameters were also observed in the case of preoperative BCVA ($P = 0.017$ and $P < 0.01$). In the case of amplitude, b-waves showed a statistically significant correlation with both pre- and postoperative BCVA ($P = 0.021$ and $P < 0.01$, respectively). The amplitude of a-waves showed a statistically significant correlation with only postoperative BCVA ($P < 0.01$), not preoperative BCVA ($P = 0.061$). In the LA 30-Hz flicker ERG, the amplitude parameters—the difference in amplitude of N1 and P1 ($N1 - P1$) and the 30-Hz amplitude—showed a statistically significant correlation with both pre- and postoperative BCVA (both, $P < 0.01$). In DA oscillatory potentials (OPs), the amplitudes of OS1, OS2, and OS3 had a statistically significant correlation ($P < 0.05$) with postoperative BCVA. The sum of the amplitudes of OS1, OS2, and OS3 ($OS1 + OS2 + OS3$) in DA OP ERG was significantly correlated with postoperative BCVA ($P < 0.01$). Interestingly, the amplitudes of OPs were not correlated with preoperative BCVA. In the DA 10.0 ERG, the implicit time of the b-wave and the amplitudes of the a- and b-waves were similar in postoperative BCVA ($P < 0.05$) but not in preoperative BCVA. In the case of parameters with statistically significant correlation, it was confirmed that Pearson's correlation coefficient

Table 1. Demographic and Clinical Characteristics of ERM Patients (61 Patients, 61 Eyes)

Characteristic	Value	P
Age (y)	66.74 ± 8.92	
Sex (male:female)	27:34	
Phakic eyes, <i>n</i> (%)	55 (90.16)	
Combined cataract surgery and ERM peeling, <i>n</i> (%)	53 (86.89)	
Combined ILM peeling, <i>n</i> (%)	30 (49.18)	
BCVA (logMAR)		
Preoperative	0.59 ± 0.33	<0.01*
Postoperative	0.19 ± 0.21	
CMT (μm)		
Preoperative	478.72 ± 97.92	<0.01*
Postoperative	367.18 ± 66.57	

*Statistically significant by paired *t*-test ($P < 0.05$).

(*r*) was greater in all postoperative BCVA than preoperative BCVA.

In order to improve the accuracy of the predictor of postoperative visual outcome, four parameters with $r > 0.45$ and $P < 0.01$ were selected (only between postoperative BCVA and the parameters of ERG): the implicit time and amplitude of b-wave in the LA 3.0 ERG, the amplitude difference between N1 and P1 ($N1 - P1$) in the LA 30-Hz flicker ERG, and the sum of the amplitudes of OS1, OS2, and OS3 ($OS1 + OS2 + OS3$) in DA OP ERG. Figure 1 shows the correlations among the above four parameters and the postoperative BCVA (Figs. 1A–1D).

Subgroup Analysis According to Postoperative Visual Acuity

The mean postoperative BCVA value was significantly correlated with the mean preoperative BCVA ($r = 0.642$, $P < 0.01$) (Fig. 2). We performed a comparative analysis by dividing the patients into three subgroups according to the postoperative BCVA to confirm that it is more accurate to predict postoperative visual acuity through the four parameters of the full-field ERG. After 6 months of surgery, patients with BCVA less than 20/50 were classified as group 1 (poor), 20/50 to 20/30 as group 2 (intermediate), and 20/30 or higher as group 3 (good). As a result of subgrouping according to the BCVA after surgery, group 1 included 10 patients; group 2, 19 patients; and group 3, 32 patients (Fig. 2).

In group 1 (poor visual outcomes), the implicit time of the b-wave in the LA 3.0 ERG was longer than for groups 2 and 3, and the amplitudes of the b-wave in the LA 3.0 ERG, the amplitude of the LA 30-Hz flicker ERG, and the sum of the amplitudes of OS1, OS2, and

OS3 in DA OP ERG were smaller than those of groups 2 and 3. The results for group 2 (intermediate visual outcome) were better than those of group 1 but worse than those of group 3. By comparing the ffERG parameters of the three groups using the Kruskal–Wallis test, we confirmed that the values of the three groups were different ($P < 0.001$); however, there were no differences in pre- or postoperative CMT values among the three groups ($P = 0.205$ and $P = 0.422$, respectively) (Table 3).

The Mann–Whitney *U* test was used for post hoc testing of each group; the results are shown in Figure 3. It was confirmed that there were differences among the three groups in all four parameters ($P < 0.05$), except for the implicit time of the b-wave in the LA 3.0 ERG when comparing group 1 with group 2; however, the *P* value between the two groups was 0.056.

Correlation with CMT

We measured CMT before and 6 months after surgery using OCT; the average CMT before surgery was 478.72 ± 97.92 μm, and the average CMT after surgery was 367.18 ± 66.57 μm, which was significantly reduced (paired *t*-test, $P < 0.01$) (Table 1). The correlation between pre- and postoperative CMT values and postoperative BCVA was confirmed, but both CMT values did not correlate ($P = 0.140$ and $P = 0.598$, respectively). A statistically significant correlation was observed between preoperative BCVA and preoperative CMT ($r = 0.338$, $P = 0.008$). In the correlation between full-field ERG and CMT, no parameter could be correlated. In a further analysis classified into three subgroups according to postoperative visual acuity, the preoperative CMT value of group 1 (531.40 ± 105.61 μm) was greater than that of group

Table 2. Correlation of Preoperative and Postoperative BCVA With the Preoperative Parameters of ffERG in 61 Eyes With ERMs

Preoperative ffERG	BCVA (logMar)			
	Preoperative		Postoperative	
	Pearson's Coefficient (r) [†]	P [‡]	Pearson's Coefficient (r) [†]	P [‡]
LA 3.0 ERG				
a-Wave implicit time (ms)	0.304	0.017*	0.427	<0.01*
b-Wave implicit time (ms)	0.386	<0.01*	0.539	<0.01*
a-Wave amplitude (μ V)	-0.242	0.061	-0.357	<0.01*
b-Wave amplitude (μ V)	-0.295	0.021*	-0.456	<0.01*
b-Wave/a-wave	-0.094	0.471	-0.134	0.272
LA 30-Hz flicker ERG				
P1 time (ms)	0.050	0.701	0.116	0.344
N1 – P1 (μ V)	-0.335	<0.01*	-0.511	<0.01*
30-Hz amplitude (μ V)	-0.332	<0.01*	-0.492	<0.01*
DA oscillatory potentials				
OS1 (μ V)	-0.239	0.064	-0.364	<0.01*
OS2 (μ V)	-0.203	0.116	-0.317	0.013*
OS3 (μ V)	-0.097	0.459	-0.252	0.050*
OS4 (μ V)	0.023	0.861	-0.132	0.310
OS1 + OS2 + OS3 (μ V)	-0.203	0.117	-0.483	<0.01*
DA 10.0 ERG				
a-Wave implicit time (ms)	0.197	0.135	0.211	0.109
b-Wave implicit time (ms)	0.101	0.448	0.287	0.028*
a-Wave amplitude (μ V)	-0.175	0.186	-0.382	<0.01*
b-Wave amplitude (μ V)	-0.220	0.094	-0.386	<0.01*
b-Wave/a-wave	-0.123	0.353	0.054	0.685

*Statistically significant by paired t -test ($P < 0.05$).

[†]Because postoperative BCVA was expressed in logMAR, it showed a positive correlation with the implicit time of ERG and a negative correlation with the amplitude of ERG.

[‡]Pearson correlation analysis.

2 ($476.05 \pm 92.64 \mu\text{m}$) and that of group 3 ($480.68 \pm 98.21 \mu\text{m}$), and the values did not show a difference among groups (Table 3).

ROC Curves As Predictors of a Good Vision Prognosis

Figure 4 shows the ROC curve for the parameters of ffERG used as prognostic factors for good visual outcome (group 3, postoperative BCVA of 20/30 or better). In the ROC curve predicting good vision prognoses, the area under the ROC curve (AUROC) for the implicit time of the b-wave was 0.787, and the amplitude of the b-wave was 0.815 in the LA 3.0 ERG. The AUROC for the amplitude difference between N1 and P1 (N1 – P1) in the LA 30-Hz flicker ERG was 0.757. The AUROC for the sum of the amplitudes of

OS1, OS2, and OS3 (OS1 + OS2 + OS3) in DA OP was 0.792. The cutoff value for a good visual prognosis is 33.25 ms (sensitivity, 68.4%; specificity, 78.3%) in the implicit time of the b-wave, 70.8 μV (sensitivity, 94.7%; specificity, 60.9%) in the amplitude of the b-wave, 59.7 μV (sensitivity, 86.8%; specificity, 60.9%) in the amplitude difference between N1 and P1 in the LA 30-Hz flicker ERG, and 44.1 μV (sensitivity, 81.6%; specificity, 69.6%) in the sum of the amplitudes of OS1, OS2, and OS3 in DA OPs.

Discussion

The results of our study can be summarized as follows: (1) Predicting postoperative visual outcome could be improved through the use of four ERG

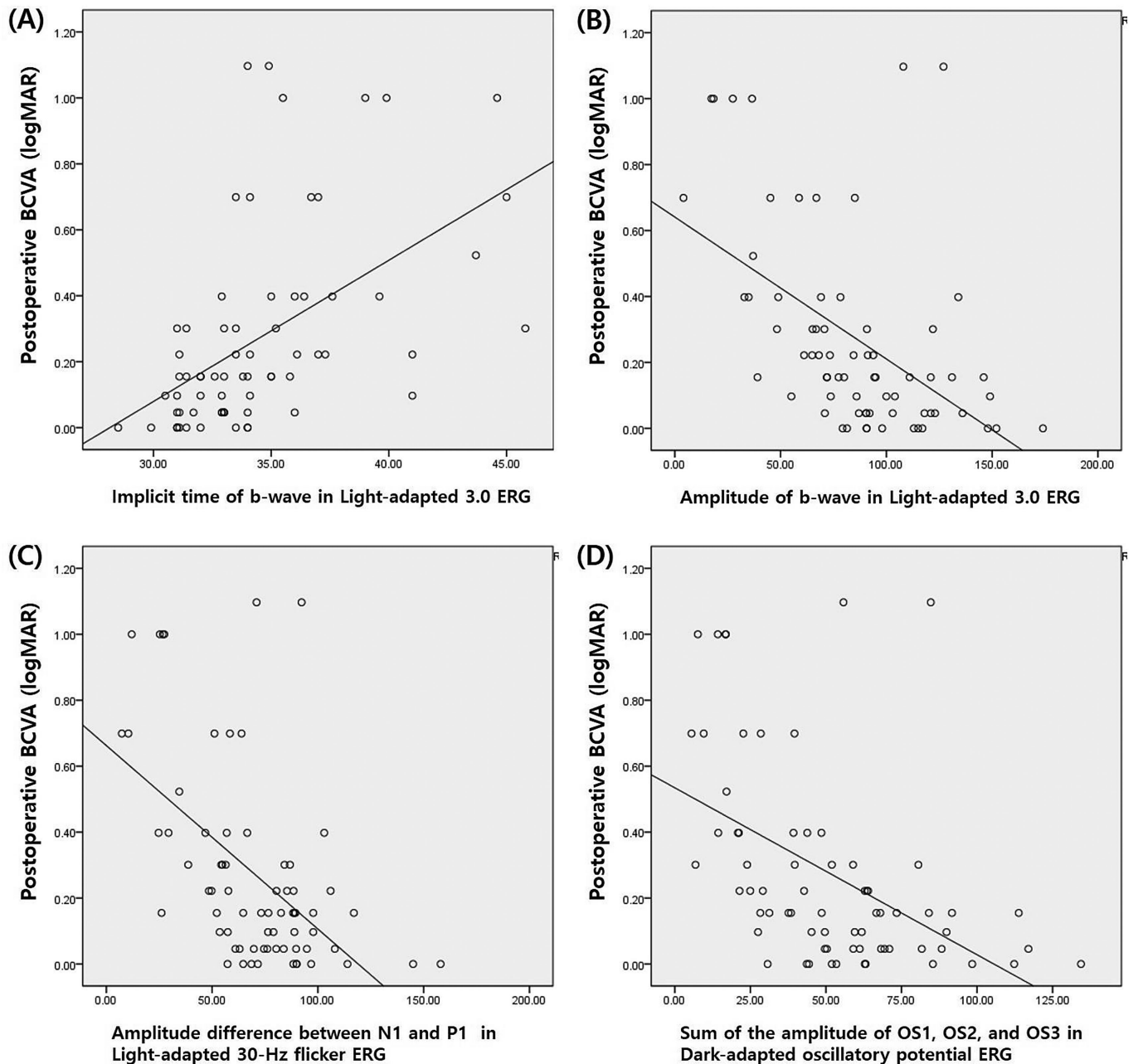


Figure 1. Graph showing the correlation between the four preoperative parameters of ffERG and postoperative BCVA (logMAR) in all patients with ERM ($N = 61$). (A) Implicit time of b-wave in LA 3.0 ERG ($r = 0.539$, $P < 0.01$). (B) Amplitude of b-wave in LA 3.0 ERG ($r = -0.456$, $P < 0.01$). (C) Amplitude difference between N1 and P1 in LA 30-Hz flicker ERG ($r = -0.511$, $P < 0.01$). (D) Sum of amplitudes of OS1, OS2, and OS3 in three DA oscillatory potentials ($r = -0.483$, $P < 0.01$).

parameters: the implicit time and the amplitude of the b-wave in the LA 3.0 ERG, the amplitude difference between N1 and P1 (N1 – P1) in the LA 30-Hz flicker ERG, and the sum of the amplitudes of OS1, OS2, and OS3 (OS1 + OS2 + OS3) in DA OP ERG. (2) There were differences among the four parameters when compared among the three subgroups according to the postoperative BCVA. (3) Among the full-field

ERG parameters before surgery, no factor was associated with CMT.

Some preoperative parameters of ffERG were significantly correlated with pre- and postoperative BCVA, suggesting that postoperative BCVA tends to be more correlated with ERG parameters than is preoperative BCVA. Among them, the implicit time and amplitude of the b-wave in the LA 3.0 ERG, the

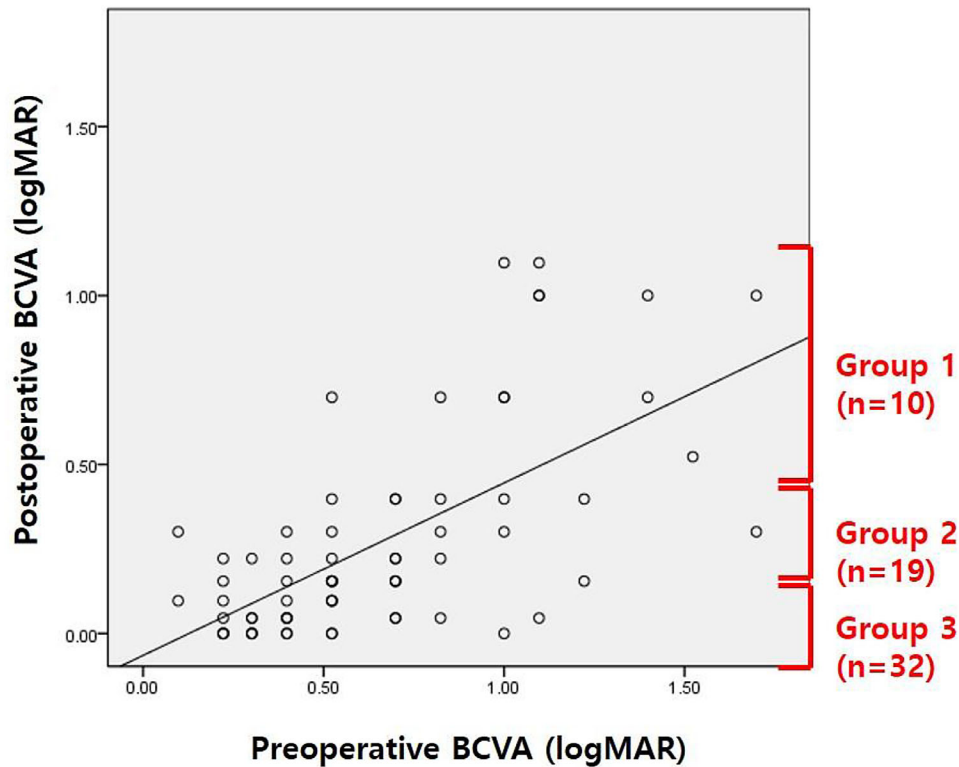


Figure 2. Graph showing correlation between preoperative and postoperative BCVA ($r = 0.642$, $P < 0.01$) and three subgroups classified by postoperative BCVA.

Table 3. Mean Values of the Four ffERG Parameters and CMT of Three Subgroups Classified According to Postoperative Visual Acuity

Parameter	Group			$P^{\dagger}$
	1 ($n = 10$)	2 ($n = 19$)	3 ($n = 32$)	
LA 3.0 ERG				
Implicit time of b-wave (ms)	38.90 ± 4.29	35.68 ± 3.68	32.72 ± 2.14	$<0.001^*$
Amplitude of b-wave (μV)	39.65 ± 24.92	73.62 ± 25.78	102.56 ± 28.92	$<0.001^*$
LA 30-Hz flicker ERG (μV)				
Amplitude difference (N1 – P1)	31.70 ± 20.15	64.15 ± 23.56	83.02 ± 24.41	$<0.001^*$
DA 3.0 oscillatory potentials (μV)				
Sum of amplitudes (OS1 + OS2 + OS3)	17.84 ± 10.27	39.93 ± 20.17	66.11 ± 26.22	$<0.001^*$
CMT (μm)				
Preoperative	531.40 ± 105.61	476.05 ± 92.64	480.68 ± 98.21	0.205
Postoperative	355.20 ± 87.69	352.47 ± 80.02	375.71 ± 45.90	0.422

*Statistically significant ($P < 0.05$).

† Kruskal–Wallis test.

amplitude difference between N1 and P1 (N1 – P1) in the LA 30-Hz flicker ERG, and the sum of the amplitudes of OS1, OS2, and OS3 (OS1 + OS2 + OS3) in DA OP ERG with postoperative BCVA had higher r values than other parameters (Table 2, Fig. 1). In the ROC curve, it was confirmed that the following parameters showed a good AUROC value (Fig. 4).

The assessment of these factors before surgery may help predict postoperative visual outcomes. We also tried to calculate the cutoff value for the prediction of good visual outcome. These values may be useful for predicting the visual outcome after surgery and to determine the appropriate surgery timing. As shown in Table 2, the mentioned ERG parameters showed

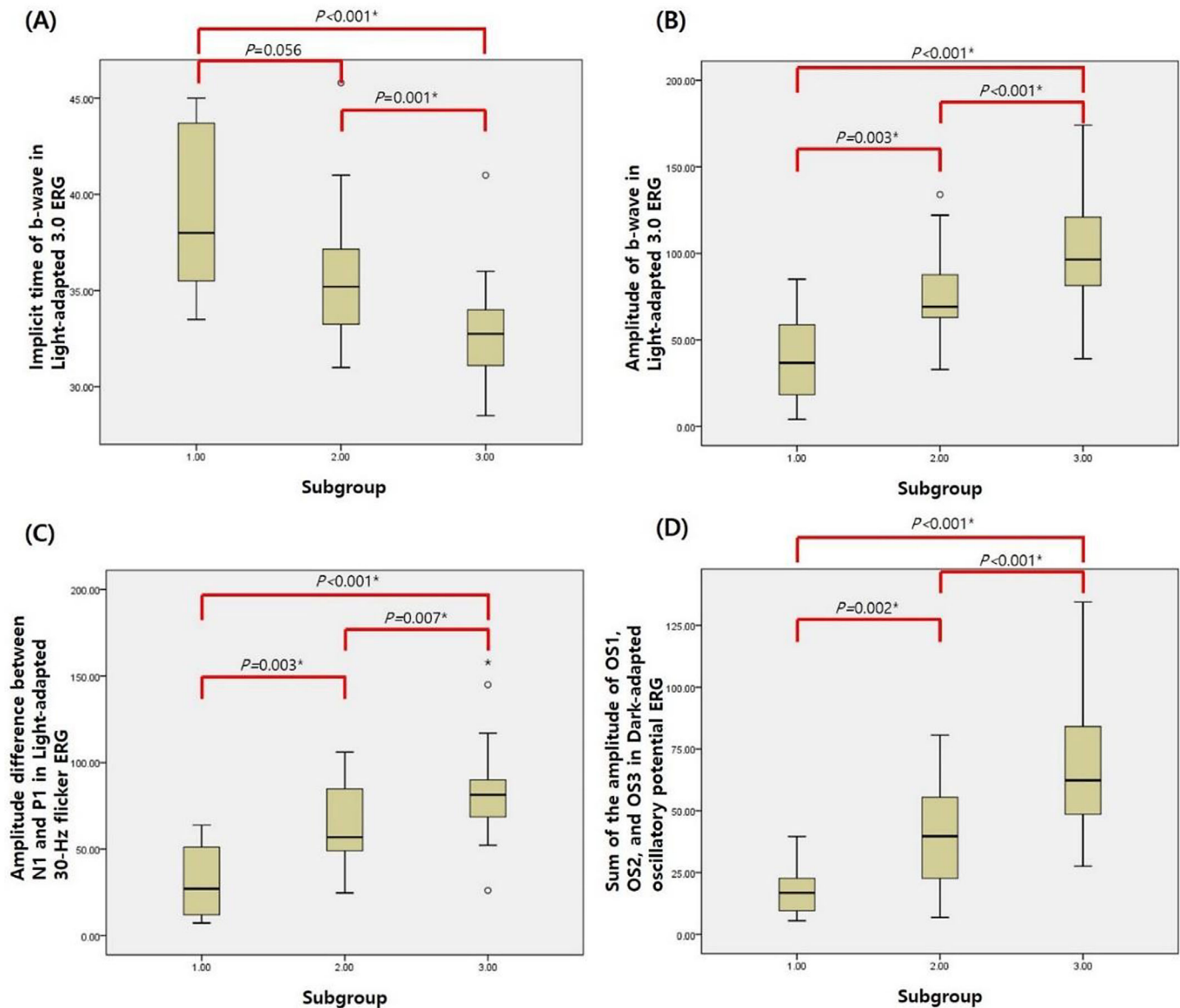


Figure 3. Graph showing differences among four parameters of fERG for each of the three subgroups classified according to postoperative visual acuity: BCVA < 20/50 (group 1, poor), 20/50 to 20/30 (group 2, intermediate), and >20/30 (group 3, good). * $P < 0.05$, Mann–Whitney test.

a tendency for greater correction with postoperative BCVA than preoperative BCVA, thus indicating the potential usefulness of fERG in predicting postoperative visual outcomes for ERM surgery.

The LA 3.0 ERG measures the responses of the cone system; a-waves arise from cone photoreceptors and OFF cone bipolar cells; the b-wave comes from ON and OFF cone bipolar cells. The LA 30-Hz flicker ERG is a sensitive cone-pathway-driven response.¹⁴ Cone cells are most concentrated in the fovea, where they are densely packed in a hexagonal pattern that accounts for the high visual acuity capability of the fovea. The cone system has high spatial resolution but

is relatively insensitive to light; thus, it is specialized for visual acuity at the expense of sensitivity, unlike the rod system.¹⁵ For this reason, we believed that the implicit time and amplitude of the b-wave in the LA 3.0 ERG and the amplitude difference between N1 and P1 (N1 – P1) in the LA 30-Hz flicker ERG would accurately evaluate the function of the macula of an ERM patient, which mainly contains cone cells, and these values showed a strong correlation with postoperative BCVA.

ERMs can cause distortion and disorganization of all inner retinal layers.¹⁶ Some studies have analyzed the predictive values of outer retinal integrity, such

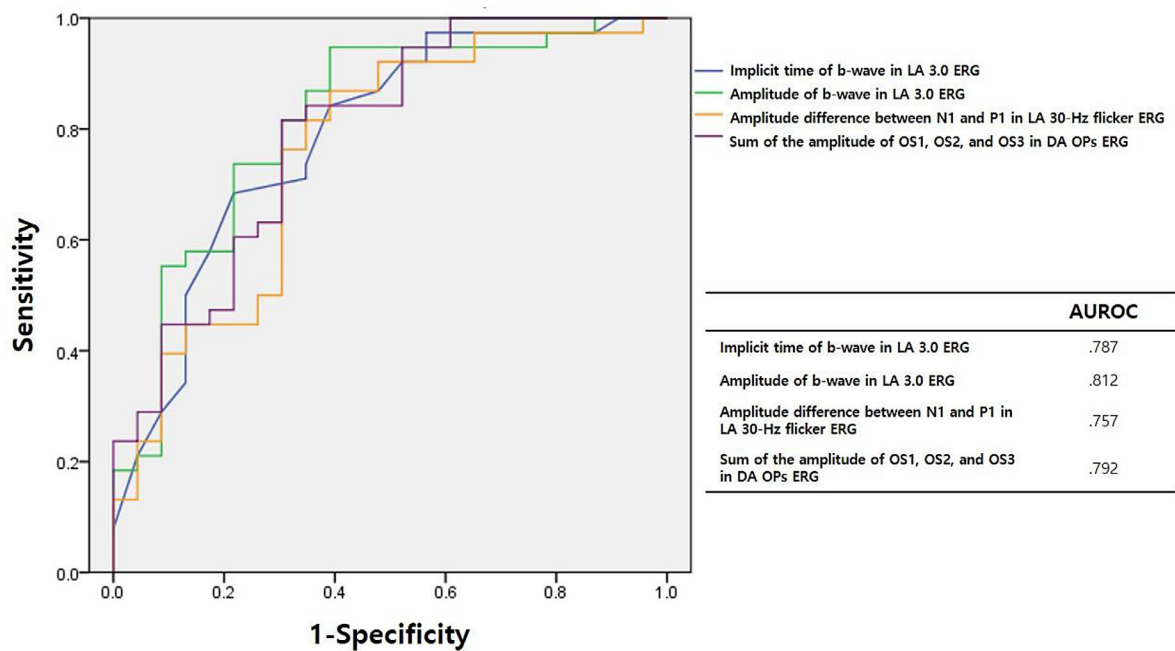


Figure 4. ROC curves obtained for preoperative parameters of ffERG as predictors of a good vision prognosis (postoperative BCVA ≥ 20/30).

as foveal photoreceptors for the prognostic factor of postoperative visual outcome in ERMs,^{17,18} and other studies have reported that the inner retinal irregularity index was significantly correlated with visual outcomes before and after ERM surgery. This inner retinal irregularity was found to correlate with outer retinal changes before and after ERM surgery,^{19,20} suggesting an important role for inner retinal changes in visual recovery after pars plana vitrectomy with ERM peeling. Distortion of the inner retina was caused by the tractional membrane of the ERM, and as a result permanent functional impairment of the fovea decreased visual acuity after surgery. In the case of the LA 3.0 ERG, it was confirmed that b-waves were statistically significant with postoperative visual acuity, which was thought to be related to inner retina function and visual outcome. When functional impairment of the fovea occurs due to distortion, the bipolar cells in the inner retina are damaged, and the ERG value decreases, which results in low visual acuity after surgery. DA OP measure the responses primarily from amacrine cells.¹⁴ Amacrine cells are also located in the inner retina, and, if they are damaged by distortion of the retina due to ERMs, it is thought that there is a great correlation between visual outcomes and DA OP. Based on such findings, anatomical evaluation of the inner retina by OCT is able to accurately evaluate the degree of functional damage using ffERG.²¹ We suggest that the b-wave of the LA 3.0 ERG and the amplitude of DA OP changes observed in this study may reflect

the inner retina layer damage induced by ERMs, which seems to play an important role in vision loss. After classifying three subgroups according to postoperative BCVA, further analysis (Fig. 2) confirmed that it was significantly lower in the poor result group (less than 20/50) and significantly higher in the good result group (more than 20/30) (Fig. 3, Table 3). This analysis gave us confidence that the above four parameters play an important role in predicting postoperative BCVA. A statistically significant correlation was observed in BCVA before and 6 months after surgery (Fig. 2). This result is consistent with that of previous studies; that is, the preoperative BCVA value can be a predictive factor of visual outcome after surgery.^{3–6} Maintaining good vision before surgery in ERM patients indirectly indicates good retinal function, but not in all of the cases. One patient in this study had a visual acuity of 20/60 before surgery, but it decreased further to 20/80 after surgery (implicit time of b-wave, 33.5 ms; amplitude of b-wave, 58.7 μV; OS1 + OS2 + OS3, 28.4 μV; N1 – P1, 51.1 μV). The overall value decreased compared with the cutoff value of the ROC curve. Preoperative BCVA may be accurate in predicting postoperative visual outcome; however, there was a case where it was not. Two patients had the same preoperative BCVA of 20/50, but their postoperative BCVA was 20/40 and 20/22, respectively. The ERG parameter value also showed a significant difference (implicit time of b-wave, 33.5/33.0 ms; amplitude of b-wave,

66.8/123.0 μ V; OS1 + OS2 + OS3, 39.7/61.2 μ V; N1 – P1, 54.9/80.3 μ V). If lens opacity affects preoperative BCVA, then preoperative BCVA is likely to be less accurate than ERG parameters in predicting the visual outcome after surgery. For patients whose visual acuity cannot be measured, ERG measurement may be helpful. Visual acuity can be a subjective measure, but ERG can obtain more objective results. Therefore, to predict postoperative visual outcome, we found that it is more accurate to predict retinal function through fERG. The evaluation of retinal function with fERG allows operators to determine the proper timing for surgery; for example, even in the absence of ERM symptoms or when there is no decrease in vision, surgery could be considered when the values of regular fERG parameters decrease. This result may also support previous studies showing that performing surgery at a relatively early stage results in good visual outcomes.^{22–24}

CMT was not found to be associated with any other preoperative fERG parameters. There was no correlation between CMT and postoperative BCVA. Even in the subgroup analysis classified according to the postoperative BCVA, the preoperative CMT was larger in the poor visual outcome group (group 1) but was not statistically significant. Because only the central thickness of the retina was analyzed, it can be assumed that there was no significant difference between CMT and fERG. Also, because changes in the b-wave of the LA 3.0 ERG and DA OP of fERG parameters are thought to be related to the inner retina, further studies, such as evaluating the inner retina parameters of OCT, are necessary.

In studies that have tried to predict the postoperative visual outcome of ERMs using multifocal ERG, the P1 amplitude value of multifocal ERG played an important role in macular function.^{8,9} The P1 value of multifocal ERG originates from the inner retina, and it is used to determine the function of Müller/bipolar cells such as the b-wave of the LA 3.0 ERG. In this study, we discovered that the b-wave of the LA 3.0 ERG plays a role similar to that of P1 of the multifocal ERG. If the b-wave of fERG is associated with postoperative BCVA, then the results of this study support those of previous studies. Pattern ERG is derived from retinal ganglion cells and the neighboring inner retinal structure. Results of studies evaluating macular function in ERM patients who underwent pattern ERG were similar to those of the current study.^{10,25} They confirmed that the P50 and N95 values of pattern ERG were low in ERM patients. Moreover, these values can be used to predict postoperative BCVA, thereby indicating a correlation between these studies.

Finally, we introduce a method to further increase efficiency by reducing the time of fERG. DA ERG is not very effective in evaluating the prognosis after surgery for ERMs; therefore, time can be saved by excluding it. It was confirmed through statistical analysis that even when only 10 minutes of LA, without 20 minutes of DA, was performed and three parameters (the implicit time and amplitude of b-wave in the LA 3.0 ERG and N1 – P1 in the LA 30-Hz flicker ERG) were measured, that was equivalent to confirming a prognosis of good visual outcome by measuring all four parameters (likelihood ratio test, $P = 0.5163$; AUROC = 0.856 for three parameters and 0.865 for four parameters) (see Supplementary Fig. S1 for a list of mutations).

The current study had limitations. Multifocal ERG and pattern ERG tests are also required to better support the evaluation of retinal function; therefore, further study must be conducted to supplement these test results. Additionally, it is necessary to further analyze the inner retinal compartment by OCT to accurately understand the relationship between the anatomical structure of the inner retina and the functional evaluation of fERG. Despite these limitations, our study predicted postoperative visual outcome for the first time, to the best of our knowledge, using preoperative fERG in patients with ERMs, including secondary.

In summary, ERM is a relatively common macular disease and is usually treated via pars plana vitrectomy with ERM peeling. Although this surgery is the treatment of choice, some cases show no improvement or even regression in vision postoperatively. Therefore, in order to predict postoperative visual acuity, full-field ERG is performed to objectively evaluate retinal function before surgery. In ERM patients, the preoperative BCVA and full-field ERG values can predict the degree of vision recovery after surgery and can determine the appropriate time for surgery.

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