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VISUAL ACUITY AND MULTIFOCAL ELECTRORETINOGRAPHIC CHANGES AFTER ARTERIOVENOUS CROSSING SHEATHOTOMY FOR MACULAR EDEMA ASSOCIATED WITH BRANCH RETINAL VEIN OCCLUSION

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Abstract

Purpose—To evaluate the influence of arteriovenous (AV) sheathotomy on retinal function with central multifocal electroretinography (mfERG) in eyes with macular edema secondary to branch retinal vein occlusion (BRVO).

Methods—Fifteen patients (15 eyes) who underwent AV sheathotomy for macular edema secondary to BRVO were included in the study. Best-corrected visual acuity and mfERG responses from the most central seven hexagons were analyzed before and 6 months after the operation.

Results—The mean preoperative Early Treatment Diabetic Retinopathy Study (ETDRS) score ± SD was 34.1 ± 12.7 letters (Snellen equivalent, 20/50) and significantly improved up to 40.5 ± 10.9 letters (Snellen equivalent, 20/40) at 6 months after AV sheathotomy ($P = 0.027$, Wilcoxon signed rank test). The mean preoperative P1 amplitude ± SD of the most central 7 hexagons was 39.30 ± 10.86 nV/deg^2 for the affected eye versus 47.72 ± 6.67 nV/deg^2 for the normal fellow (control) eye ($P = 0.013$, Mann–Whitney U test) and significantly increased up to 50.71 ± 15.58 nV/deg^2 at 6 months after the operation ($P = 0.014$, Wilcoxon signed rank test). Significant correlations between preoperative and postoperative ETDRS score and preoperative P1 amplitude were present ($r = 0.929$, $P < 0.001$; $r = 0.768$, $P = 0.001$; respectively [Spearman correlation]).

Conclusions—AV sheathotomy improved macular function and anatomical outcome as measured by ETDRS score and mfERG responses in patients with macular edema due to BRVO.

Keywords

arteriovenous sheathotomy; branch retinal vein occlusion; multifocal electroretinography

Branch retinal vein occlusion (BRVO) is a common retinal vascular disease occurring in a significant number of individuals older than 50 years of age.[1,2] The most common cause of visual disturbance in BRVO patients is macular edema, which has been described in 60% of patients.[3] Arteriovenous (AV) sheathotomy is one of the surgical methods proposed to treat

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macular edema in BRVO and has been reported efficacious in cases refractory to conventional focal or grid laser macular photocoagulation.[4–12] The surgery has been reported to be associated with reduction in central macular thickness and improved visual acuities.[4–11]

Multifocal electroretinography (mfERG) has been used for objective functional assessment of many retinal diseases since Sutter and Tran[13] first introduced the method in 1992. Unlike full-field ERG, mfERG allows simultaneous measurements of multiple retinal responses at different locations, enabling topographic mapping of the retinal function in the central retina. Previous studies have described the changes in mfERG recordings of eyes with retinal vein occlusion and showed that mfERG could be a more sensitive indicator of underlying disease affecting the layers of the retina in eyes with vein occlusion.[14–20]

In this study, we investigated the changes in best-corrected visual acuities and mfERG responses in macular edema due to BRVO before and after AV sheathotomy and evaluated the influence of the surgery on central retinal functions.

Materials and Methods

Patients

Fifteen consecutive patients with macular edema secondary to BRVO underwent AV sheathotomy at Yonsei University Eye & ENT Hospital Vitreoretinal Service (Seoul, Korea) from June 2005 to August 2006. The study followed the tenets of the Declaration of Helsinki and was approved by the local institutional review board. Informed consent was obtained from every patient after explanation of the nature and possible consequences of the study.

The patients were included in the study if they had macular edema due to BRVO documented by retinal thickening at 90+ diopter noncontact lens biomicroscopy and diffuse fluorescein leakage at angiography. The exclusion criteria were as follows: intraocular surgery including cataract extraction within the last 6 months of enrollment; laser treatments including panretinal photocoagulation, posterior capsulotomy, and focal/grid macular photocoagulation within the last 6 months; and presence of comorbid ocular conditions that may affect visual acuity and mfERG responses.

The patients were examined at baseline and 1 month, 3 months, and 6 months after the operation. Slit-lamp biomicroscopy using a 90+ diopter noncontact lens, fluorescein angiography, color fundus photography, and mfERG were performed at baseline and 6 months after the operation. Best-corrected visual acuity was determined with the Early Treatment Diabetic Retinopathy Study (ETDRS) chart.[21] mfERG responses were recorded using the RETI scan multifocal system (Roland Consult, Brandenburg, Germany).

Surgical Methods

After the patients were fully informed of all relevant aspects of the procedure, the same surgeon (H.J.K.) performed all of the procedures. Fluorescein angiography with a scanning laser ophthalmoscope (Heidelberg Retinal Angiograph; Heidelberg Engineering, Carlsbad, CA) was performed on every patient to document the responsible AV crossing site preoperatively. Standard pars plana vitrectomy was performed, followed by surgical separation of the posterior cortical vitreous from the optic nerve and posterior retina. After the responsible AV crossing site was identified, a specially designed BRVO knife (Synergetics, Inc., O'Fallon, MO) was used to open the internal limiting membrane and the nerve fiber layer over the artery, starting between 100 μm and 200 μm proximal to the AV crossing. The incision was continued parallel to and under the retinal arteriole, with a gentle lifting motion, until the common AV crossing sheath was encountered and incised in a side-to-side manner. Completion of AV dissection was confirmed by elevation of the overlying artery.

mfERG Settings

Stimulation and recording of mfERG responses were performed using the m-sequence technique according to the ISCEV guidelines.[22] After full dilation of the pupil, contact lens ERG-JET electrodes were applied on the topically anesthetized cornea with one ground electrode in the center of the forehead, and two temporal reference electrodes were positioned. The stimulus, consisting of 103 hexagons covering a visual field of 30°, was presented on a monitor (Samsung 21-in VGA monitor) with a frame rate of 75 Hz at a distance of 24 cm from the patient's eye. Each element alternated between black and white (97% contrast; mean luminance, 61.8 cd/m^2). The patient was instructed to maintain fixation on longitudinal axes intersecting one focal point. The amplifier was set with a gain of 100,000; the lower cutoff frequency was 5 Hz, and the upper, 100 Hz. The first-order response components of mfERG were analyzed, regarding the mean response density of the P1 amplitude (amplitude per unit of retinal area [nV/deg^2]) and mean latency (milliseconds). We selected the most central seven hexagons to collect the central mfERG responses, which were averaged for the analysis.

The main outcome measures included changes in ETDRS visual acuity score and mean mfERG response density between baseline and the end point (6 months after the operation) of the study. Normal fellow eyes served as controls.

Statistical analyses utilized SPSS 12.0.1 (SPSS, Inc., Chicago, IL) for Windows (Microsoft). The analysis was performed using the nonparametric Mann–Whitney *U*/Wilcoxon signed rank test and Spearman correlation test as appropriate. The level of statistical significance was set at $P < 0.05$.

Results

A total of 15 eyes of 15 patients (6 males and 9 females) were included in the study. Normal fellow eyes (15 eyes) served as controls. Fifteen eyes with macular edema secondary to BRVO were treated with pars plana vitrectomy with complete posterior hyaloid membrane detachment and AV crossing sheathotomy. AV crossing sheathotomy was successfully performed without any intraoperative complications on all 15 patients. No serious perioperative or postoperative complications were observed. Demographic data for the patients are shown in Table 1.

The preoperative and postoperative ETDRS scores are shown in Table 2. The average ETDRS score showed significant improvement at the end of 6 months compared with the baseline score ($P = 0.027$, Wilcoxon signed rank test).

Mean preoperative P1 amplitude ± SD of the most central 7 hexagons was 39.3 ± 10.86 nV/deg^2 for the affected eye and showed significant decrease when compared with the control (normal fellow eye, 47.72 ± 6.67 nV/deg^2; $P = 0.013$, Mann–Whitney *U* test). After the operation, the P1 amplitude significantly improved ($P = 0.014$, Wilcoxon signed rank test). Preoperative and postoperative changes in amplitudes and the waveforms of representative mfERG responses are shown in Table 2 and Figure 1, respectively. The difference between the affected eye and the control was no longer significant at the end point because the amplitude ± SD for the affected eye increased up to 50.71 ± 15.58 nV/deg^2 while that for the control was 55.24 ± 12.69 ($P = 0.418$, Mann–Whitney *U* test).

No significant changes were observed regarding implicit times: the mean preoperative implicit time ± SD was 37.2 ± 1.43 milliseconds for the affected eye versus 35.3 ± 2.58 milliseconds for the control ($P = 0.902$, Mann–Whitney *U* test).

The preoperative ETDRS score correlated with the preoperative P1 amplitude of the mfERG response ($r = 0.929$, $P < 0.001$, Spearman correlation) (Fig. 2). There was also a positive

correlation between preoperative mfERG amplitudes and postoperative ETDRS scores (r = 0.768, P = 0.001, Spearman correlation) (Fig. 3).

Discussion

BRVO is the second most commonly occurring retinal vascular abnormality after diabetic retinopathy.[1,2] Several medical and surgical strategies have been undertaken to manage macular edema associated with BRVO because in a study by the Branch Vein Occlusion Study Group[2] the natural history of the disease showed only a 0.23-line gain in visual improvement and 17% of patients lost ≥2 lines during 3 years of follow-up.

AV sheathotomy to decompress a common adventitial sheath at the AV crossing has been proposed to be efficacious in the treatment of macular edema secondary to BRVO.[6–9] The surgical outcomes have been evaluated by various methods such as visual acuity measurement, central macular thickness documented by optical coherence tomography, and venous perfusion by fluorescein angiography.[4–9,23–25] Fluorescein angiography mainly evaluates the vascular status, distinguishing ischemic from nonischemic findings and showing retinal vascular leakage nonquantitatively. Optical coherence tomography measures thickness and morphologic changes of the retina. However, in some clinical settings, macular thickness decreased without any improvement in vision, showing a discrepancy between optical coherence tomography findings and visual function.[11,26]

mfERG is a functional method that reflects the actual function of the retinal neurons in a quantitative manner. It simultaneously measures the multiple retinal responses at different locations, enabling objective functional assessment of retinal diseases. Mester and Dillinger[27] previously used mfERG to assess macular function before and after AV sheathotomy but did not demonstrate the details of mfERG response amplitudes and implicit time findings.

In the present study, we showed the changes in mfERG response with P1 amplitudes and implicit times before and after AV sheathotomy and measured best-corrected visual acuity with a standardized ETDRS chart. Significant improvement in ETDRS score was observed after AV sheathotomy, and these functional outcomes were analyzed along with changes in mfERG responses. We preoperatively analyzed the most central seven hexagons (representing the central 5° of the retina) and observed a significant decrease in P1 amplitudes in eyes with macular edema due to BRVO. This finding is consistent with findings from a previous study in which the main mfERG abnormality at the central macula was reduction of the response amplitude, whereas delay in implicit time was the main abnormality in the quadrant affected by BRVO.[18] After AV sheathotomy was performed, the P1 amplitude significantly increased along with significant improvement in visual acuity. A positive correlation was observed between both preoperative and postoperative ETDRS scores and preoperative mfERG amplitudes, implying that the mfERG response can be a useful indicator to assess objective functional surgical outcomes for patients. A correlation between the mfERG amplitude and visual acuity has also been reported in previous studies regarding maculopathies, such as Best macular dystrophy, Stargardt disease, and retinal vein occlusion.[20,28,29] We observed no significant changes in implicit times compared with control eyes in the current study; other studies reported that implicit times were in many cases just moderately increased or were even within normal values despite severe visual loss and reduced amplitudes, implying that a visual acuity change is not necessarily associated with implicit time changes.[28,29]

This study was limited by the small sample size, short-term follow-up, lack of a control group, and uncontrolled confounding factors that might have influenced the mfERG responses (such as age, sex, cataract grade, refractive errors, etc). However, our results were analyzed

comparing the affected eyes with the normal fellow eyes to minimize bias by these factors and because mfERG is not reliable for comparing the amplitudes of responses from one individual with those from another because of interindividual variation.[13,30,31] Because we included patients who had relatively recent onset of disease (average symptom duration, 2.9 months), we cannot completely exclude the possibility that some of the patients might have had spontaneous resolution of macular edema. However, as the Branch Vein Occlusion Study Group indicated,[2] the natural course of BRVO is relatively static, with only a 0.23-line improvement on average during 3 years of follow-up and 17% of patients lost ≥2 lines among 35 control eyes without treatment. An earlier study that followed up 40 untreated eyes with BRVO for at least 1 year also found that all patients with macular edema had no improvement in vision.[32] In the current study, we observed >1 line of improvement (6.4 letters) on average, and none of the patients lost ≥2 lines by the end of the study, suggesting superior visual outcomes compared with the previously reported natural history. On the other hand, because pars plana vitrectomy without sheathotomy has been successful in the resolution of macular edema due to venous occlusions in previous reports, a group treated with pars plana vitrectomy without sheathotomy may have been a better control group in this study, for which our study could also be criticized. [9,11] However, some studies have reported that sheathotomy without vitrectomy is also effective in the treatment of macular edema due to BRVO, suggesting the beneficial effect of sheathotomy as sole treatment.[33,34] It is still beyond the scope of our study to determine if observation alone or vitrectomy without sheathotomy would have resulted in comparable improvement in vision and mfERG responses in this study. Further investigations involving a larger population with an appropriate control group will be necessary to establish the optimal treatment option for BRVO and demonstrate a prognostic value of mfERG in the selection of patients, who will most likely benefit from the future treatment.

In conclusion, the current study showed that electrophysiological function in the central retina was deteriorated in patients with macular edema secondary to BRVO, with significant improvement of the retinal function after AV sheathotomy as measured by ETDRS score and mfERG response. Because preoperative mfERG amplitudes were well correlated with preoperative and postoperative visual acuities, mfERG may be a suitable tool to evaluate central retinal function and predict visual outcomes after AV sheathotomy in the treatment of macular edema due to BRVO.

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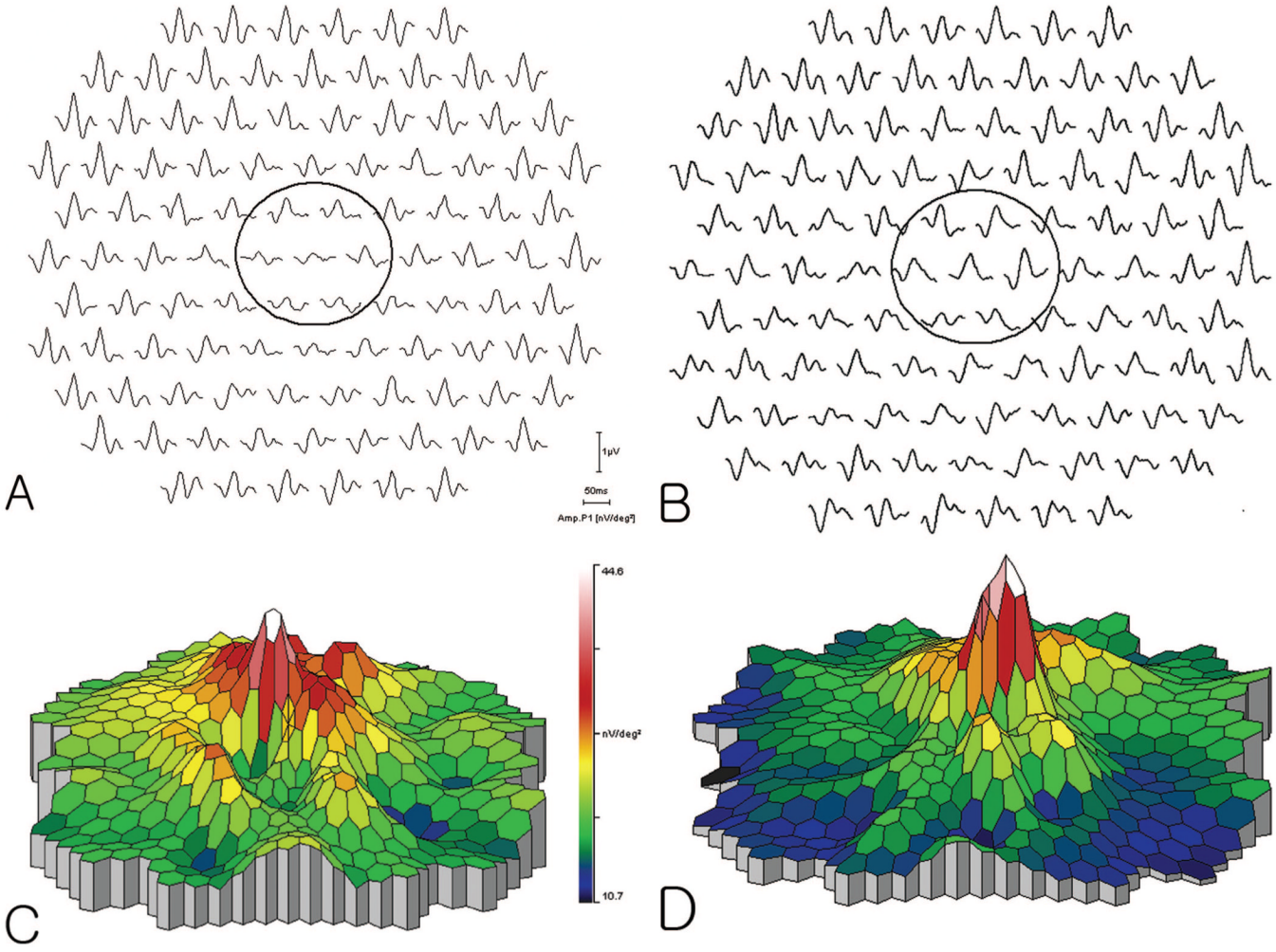

Fig. 1.

Trace arrays and topographic representations before (**A** and **C,** respectively) and 6 months after (**B** and **D,** respectively) surgery. Note the increase in P1 amplitudes of the central area. The Early Treatment Diabetic Retinopathy Study score for the patient improved from 14 letters to 38 letters.

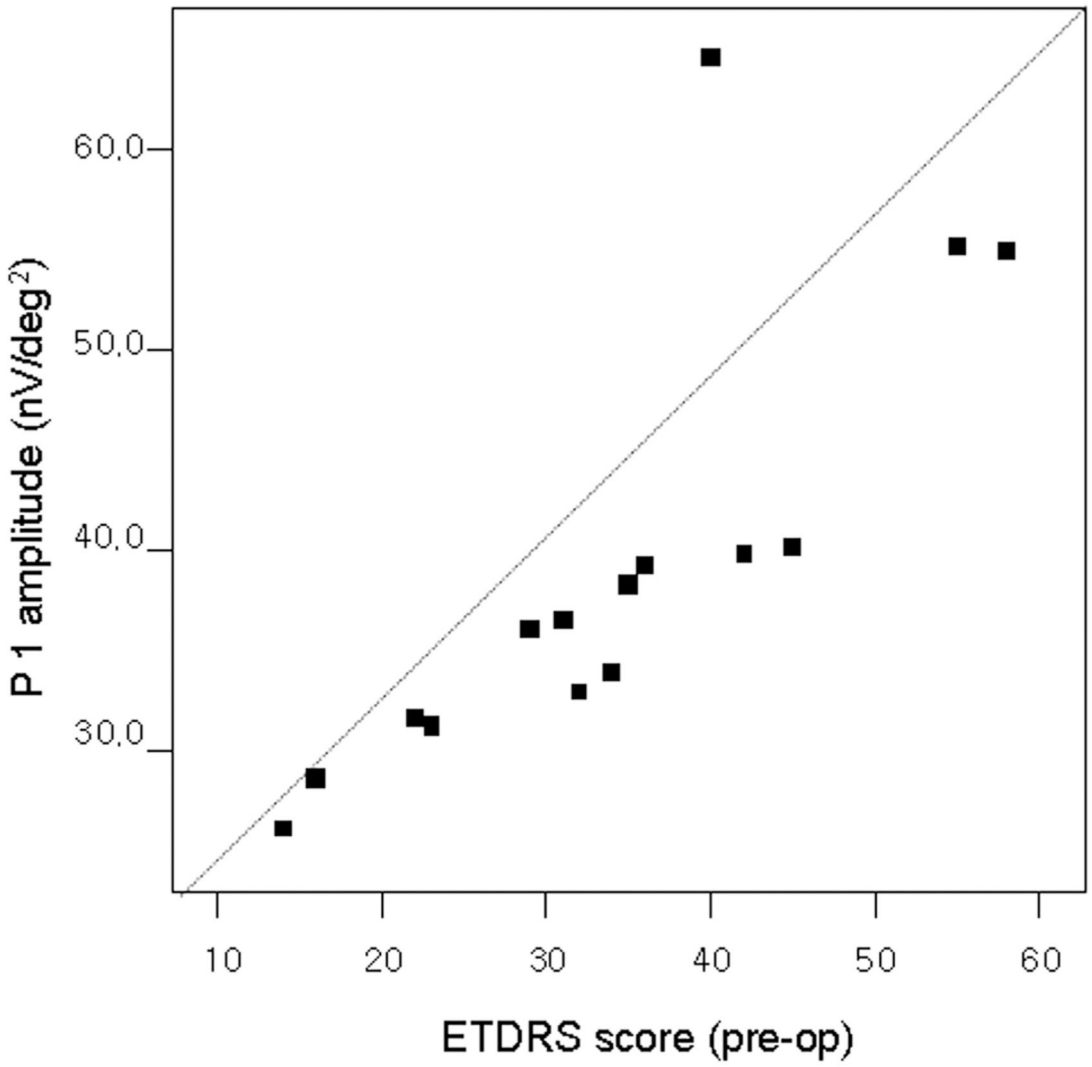

Fig. 2.

Scattergram demonstrating the relation between preoperative Early Treatment Diabetic Retinopathy Study (ETDRS) scores and preoperative multifocal electroretinography P1 amplitudes ($r = 0.929$, $P < 0.001$, Spearman correlation). The Spearman correlation value shows that the preoperative ETDRS scores significantly related to the P1 amplitudes.

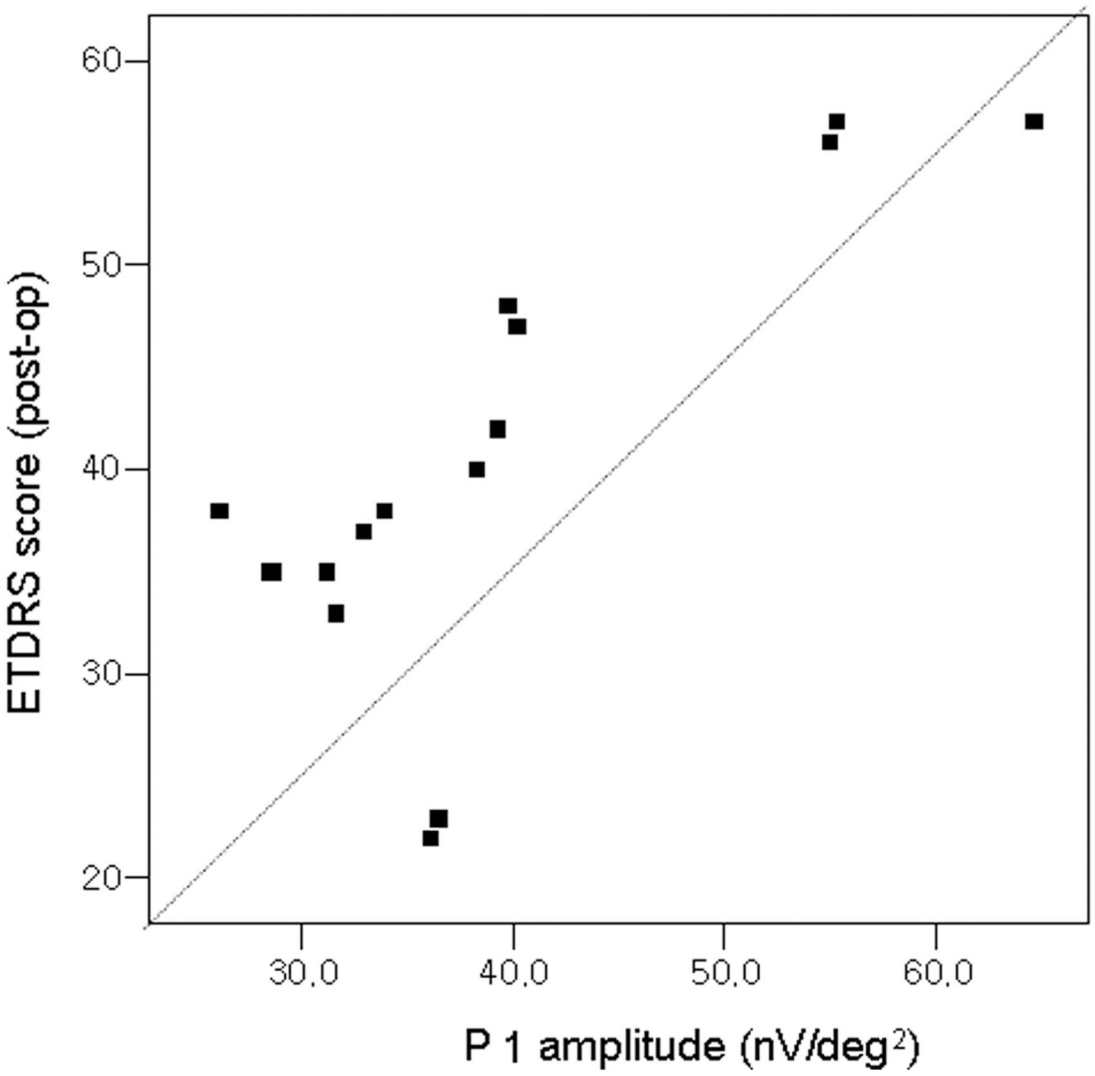

Fig. 3.

Scattergram demonstrating the relation between preoperative multifocal electroretinography P1 amplitudes and end point Early Treatment Diabetic Retinopathy Study (ETDRS) scores ($r = 0.768$, $P = 0.001$, Spearman correlation). The Spearman correlation value shows that the preoperative P1 amplitudes significantly related to the postoperative ETDRS scores.

Table 1

Summary of Preoperative Clinical Characteristics for 15 Patients With Macular Edema Secondary to Branch Retinal Vein Occlusion

Characteristic and Value	
Mean age ± SD (y)	58.1 ± 8.5
Males/females (no.)	6/9
Mean duration of symptoms ± SD (mo)	2.9 ± 2.0
HTN/DM (no. of patients)	2/2
Occluded ST/IT vein (no. of patients)	9/6
Mean preoperative BCVA ETDRS score ± SD (Snellen equivalent)	34.1 ± 12.7 (20/50)

HTN, hypertension; DM, diabetes mellitus; ST, superotemporal; IT, inferotemporal; BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study.

Table 2

Preoperative and Postoperative ETDRS Scores and mfERG Responses

Finding	Baseline	End Point	*P*
Mean ETDRS score ± SD (Snellen equivalent)	34.1 ± 12.7 (20/50)	40.5 ± 10.9 (20/40)	0.027*
Mean P1 amplitude ± SD, nV/deg^2	39.3 ± 10.9	50.7 ± 15.6	0.014*

* Wilcoxon signed rank test.

ETDRS, Early Treatment Diabetic Retinopathy Study; mfERG, multifocal electroretinography.