Clinical analysis of persistent subretinal fluid after pars plana vitrectomy in macular involving diabetic tractional retinal detachment

Yong Koo Kang
Kyungpook National University
Jae Pil Shin (jps11@hanmail.net)
Kyungpook National University

Research Article

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Abstract

The purpose of this study was to analyze the duration of persistent subretinal fluid (PSF) and contributing factors after pars plana vitrectomy in patients accompanying macular involving diabetic tractional retinal detachment (TRD). We included 33 eyes of 33 patients diagnosed macular involving diabetic TRD and received pars plana vitrectomy between 2014 and 2019 were reviewed retrospectively. PSF was confirmed on optical coherence tomography. The duration of PSF after surgery and relevant ocular and systemic factors according to the duration of PSF were analyzed. The prevalence of PSF was 81.8% a 1 month, 54.5% at 3 months, 36.4% at 6 months and 12.1% at 12 months after surgery and mean duration of PSF was 5.2 ± 4.9 months. The mean best corrected visual acuity was significantly improved after 1 year and the final visit than baseline. Blood urine nitrogen, creatinine, and estimated glomerular filtration rate (eGFR) were significantly associated with duration of PSF in univariate analysis, but only eGFR was significantly associated in the multivariate analysis. Therefore, patients with impaired kidney function tend to have delayed subretinal fluid absorption and it would be necessary to explain in advance that PSF could be long-lasting in patient with impaired kidney function.

Introduction

The prognosis of proliferative diabetic retinopathy (PDR) has been greatly improved in the era of panretinal photocoagulation and anti-vascular endothelial growth factor (VEGF) intravitreal injection[1,2]. However, tractional retinal detachment (TRD) is one of the most feared complications of PDR and indications of pars plana vitrectomy in PDR.

Pars plana vitrectomy for TRD still may be one of the most complex vitreoretinal procedures. The goals of surgery are to remove vitreous hemorrhage, reduce anterior to posterior vitreous traction on the retina, and to relieve epiretinal tangential traction on which proliferative tissue grows. However, iatrogenic retinal breaks are the main complication of surgery and intraocular tamponade is used to repair retinal breaks.

Persistent subretinal fluid (PSF) was detected by optical coherence tomography (OCT) after repair of rhegmatogenous retinal detachment[3–5], and it was associated the chronic nature of fluid with higher viscosity, protein composition and cellularity[6]. Recently, clinical cases of PSF were reported after vitrectomy for diabetic TRD[7]. Karimov et al.[8] analyzed the prevalence of PSF in macular involving diabetic TRD after vitrectomy. However, all of cases received pars plana vitrectomy with intraocular tamponade, and there was no published report to our knowledge to find out the effect of intraocular tamponade on PSF in diabetic TRD surgery.

The purpose of this study is to report the prevalence of PSF and to analyze ocular and systemic factors contributing to duration of PSF in patients with PDR accompanying macular involving TRD after pars plana vitrectomy.

Results

Demographics of patients

Ninety patients were initially included; however, 57 patients were excluded according to the exclusion criteria. Thus, a total of 33 patients (33 eyes) were enrolled in this study. The demographic and clinical characteristics for enrolled patients are presented in Table 1.

Table 1
Demographic and clinical characteristics of enrolled patients

Characteristics	**Value**
Number of eyes, n (%)	
OD	11 (33.3%)
OS	22 (66.7%)
Sex, n (%)	
Male	20 (60.6%)
Female	13 (39.4%)
Mean age, years	49.9 ± 12.2
Mean follow up periods, months	30.0 ± 18.8
Duration of PSF, months	5.2 ± 4.9
Systemic characteristics	
Duration of diabetes mellitus, years	10.0 ± 6.4
HbA1c, %	9.5 ± 2.3
Hypertension, n (%)	13 (39.4%)
Chronic kidney disease, n (%)	8 (24.2%)
BUN, mg/dL	24.9 ± 11.6
Creatinine, mg/dL	1.4 ± 0.9
eGFR, mL/min/1.73m^2	64.2 ± 30.0
Ocular characteristics	
Panretinal photocoagulation prior to vitrectomy, n (%)	27 (81.8%)
Anti-VEGF therapy prior to vitrectomy, n (%)	7 (21.2%)

Values are presented as the mean ± standard deviations.BUN: blood urine nitgogen; eGFR:estimated glomerular filtration rate; HbA1c: Hemoglobin A1c; ILM: internal limitingmembrane; PSF: persistent subretinal fluid; SO: silicone oil; VEGF: vascular endothelialgrowth factor

Characteristics	Value
Axial length, mm	23.3 ± 0.78
Preoperative intravitreal bevacizumab injection, n (%)	26 (81.8%)
Combine surgery of phacoemulsification, n (%)	24 (72.8%)
Internal subretinal fluid drainage during vitrectomy, n (%)	20 (60.6%)
ILM peeling during vitrectomy, n (%)	6 (18.2%)
Intraocular SO tamponade, n (%)	25 (75.6%)
Values are presented as the mean ± standard deviations.BUN: blood urine nitgogen; eGFR:estimated glomerular filtration rate; HbA1c: Hemoglobin A1c; ILM: internal limitingmembrane; PSF: persistent subretinal fluid; SO: silicone oil; VEGF: vascular endothelialgrowth factor	

Among the 33 patients, 20 were male, and 13 were female. The mean age of all patients was 49.9 ± 12.2 years and mean follow up duration was 30.0 ± 18.8 months. The duration of diabetes mellitus was 10.0 ± 6.4 years, 13 patients had hypertension, and 8 patients had chronic kidney disease on hemodialysis. HbA1c was 9.5 ± 2.3, blood urine nitrogen (BUN) was 24.9 ± 11.6 mg/dL, creatinine was 1.4 ± 0.9 mg/dL, and estimated glomerular filtration rate (eGFR) was 64.2 ± 30.0 mL/min/1.73m^2 at preoperative laboratory results. 27 eyes had received previous panretinal photocoagulation and 7 eyes received anti-VEGF treatment prior to surgery. 26 eyes were underwent preoperative intravitreal bevacizumab injection in a day before vitrectomy and 24 eyes received combine surgery of phacoemulsification. During pars plana vitrectomy, ILM peeling procedure was performed in 6 eyes. 25 eyes had preexisting or iatrogenic retinal break during vitrectomy and SO tamponade was carried out after fluid-air exchange. Among the 25 eyes, intraoperative SRF drainage was conducted from a retinotomy site in 20 eyes by active aspiration. SO-filled eyes were underwent secondary SO removal surgery at 10.2 ± 5.5 months (range, 3.4 to 22.8 months) after primary surgery.

The duration of PSF

The mean duration of PSF was 5.2 ± 4.9 months (range, 0.2 to 20.5 months). The prevalence of PSF was 81.8% at 1 month, 54.5% at 3 months, 36.4% at 6 months and 12.1% at 12 months on the macula OCT scans after surgery. Figure 1 was shown a representative case of PSF on the OCT scans. A Kaplan-Meier graph was used to display the estimated survival probability of PSF for patients, as shown Fig. 2.

Best corrected visual acuity

The change in mean BCVA was logMAR 1.320 ± 0.690 in baseline, 1.746 ± 0.470 after postoperative day (POD) 2 weeks (P = 0.267), 1.565 ± 0.513 after 1 month (P = 1.0), 1.159 ± 0.551 after 6 months (P = 0.876), 0.981 ± 0.540 after 1 year (P = 0.013), and 0.957 ± 0.731 at the final visit (P = 0.041) (Fig. 3). The mean BCVA was significantly improved 1 year after surgery. The mean BCVA at the final visit was not significantly correlated with the duration of PSF (r = -0.049, P = 0.788).

Clinical factors associated with the duration of PSF

Univariate and multivariate linear regression analyses of associations between clinical factors and the duration of PSF was presented in Table 2. BUN (β = 0.158, 95% confidence interval [CI] = 0.015 to 0.302, P = 0.032), creatinine (β = 2.147, 95% confidence interval [CI] = 0.409 to 3.885, P = 0.017), and eGFR (β = -0.088, 95% confidence interval [CI] = -0.138 to -0.038, P = 0.001) were significantly associated with the duration of PSF in the univariate analysis. In multivariate analysis, however, only eGFR was significantly associated with the duration of PSF (β = -0.100, 95% confidence interval [CI] = -0.122 to -0.011, P = 0.031). However, there was not significantly associated between the duration of PSF and surgical factors, such as internal SRF drainage (β = -1.445, 95% confidence interval [CI] = -5.020 to 2.219, P = 0.416) or intraocular SO tamponade (β = -2.591, 95% confidence interval [CI] = -6.600 to 1.418, P = 0.197).

Table 2
Univariate and multivariate analyses of clinical factors associated with the duration of persistent subretinal fluid.

Parameters	Univariate			Multivariate		
	β coefficient	CI (95%)	*P*-value	*β* coefficient	CI (95%)	*P*-value
Male sex	0.742	-2.895 to 4.379	0.680			
Age	-0.024	-0.170 to 0.122	0.739			
Duration of DM	-0.126	-0.404 to 0.152	0.361			
Hemoglobin A1c	-0.324	-1.206 to 0.559	0.458			
BUN	0.158	0.015 to 0.302	0.032	-0.043	-0.350 to 0.263	0.774
Creatinine	2.147	0.409 to 3.885	0.017	0.022	-4.126 to 4.170	0.992
eGFR	-0.088	-0.138 to -0.038	0.001	-0.100	-0.122 to -0.011	0.031
Axial length	-1.100	-3.411 to 1.211	0.339			
PRP prior to vitrectomy	-1.648	-6.186 to 2.890	0.464			
Anti-VEGF therapy prior to vitrectomy	-1.083	-5.384 to 3.217	0.611			
Preoperative intravitreal bevacizumab injection	1.905	-2.358 to 6.167	0.369			
Combine surgery of phacoemulsification	-2.474	-6.334 to 1.385	0.201			
Internal subretinal fluid drainage	-1.445	-5.020 to 2.129	0.416			
ILM peeling during vitrectomy	1.776	-2.755 to 6.308	0.430			
Intraocular SO tamponade	-2.591	-6.600 to 1.418	0.197			

Parameters	Univariate			Multivariate		
	β coefficient	CI (95%)	P-value	β coefficient	CI (95%)	P-value
BUN: blood urine nitgogen; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; ILM: internal limiting membrane; PRP: panretinal photocoagulation; SO: silicone oil; TRD: tractional retinal detachment; VEGF: vascular endothelial growth factor						

Discussion

The surgical repair of TRD in patients with PDR is among the most technically challenging and iatrogenic retinal breaks are likely to occur because of the friable nature of the ischemic retina being handled, propensity of extensive overlying fibrovascular membrane to induce bleeding intraoperatively[9]. Theoretically, intraocular tamponade was not necessary in TRD surgery if the traction is relieved surgically without creating retinal breaks[10]. Recently, Tao et al.[11] reported successful clinical results of vitrectomy for TRD in PDR without intraocular tamponade and suggested that intraocular tamponade may not be essential for the treatment of TRD in eyes with PDR.

There is controversy over intraoperative procedures such as internal drainage or intraocular tamponade during pars plana vitrectomy in TRD. Meredith et al.[10] proposed the technique of membrane segmentation in TRD surgery and stated that there is no need to drain the SRF because relief of traction is sufficient to allow reattachment of the retina and intraocular tamponade is not necessary if the traction is surgically released without creating retinal breaks. But, in fact, intraocular silicone oil or gas was frequently used after pars plana vitrectomy for severe TRD cases[10,12–14].

The authors focused on whether intraocular tamponade or SRF drainage procedure affects the duration of PSF. Karimov et al.[8] reported the duration of PSF in diabetic TRD after vitrectomy that eyes with SO tamponade showed significantly faster SRF absorption and intraoperative drainage showed also faster SRF absorption, but not statistical significant. As a result, they suggested that SO was a favorable option of tamponade in cases with intraoperative breaks and internal drainage. However, our result shows that intraocular SO tamponade and drainage of SRF during surgery are not related to the duration of PSF (Table 2).

In addition, we found that lower eGFR level is a significant risk factor of long-standing PSF. Basically, absorption of SRF depends on passive diffuse and active pumping by retinal pigment epithelium (RPE)[15]. However, in diabetic retinopathy, presence of SRF may be caused by impaired RPE pumping and disruption of external limiting membrane, which serves as a barrier to subretinal space and contributes fluid shifting from intraretinal space to outer retina[16]. In addition, diabetic retinopathy with chronic kidney disease, decreased serum albumin may lower the intravascular osmotic pressure and increase hydrostatic pressure in outer retina or choroid that could leads to fluid retention and flow into the subretinal space[17,18]. Therefore, decreased kidney function could be contributed to delayed absorption of SRF.

The present study has some limitations. This is retrospective study on a relatively small sample size. Further researches on a greater number of cases with evaluation of characteristics of the PSF after TRD surgery will be necessary. Nevertheless, this study has significance in analyzing the risk factors of PSF in diabetic TRD patients after surgery.

In conclusion, we have shown that PSF is detected by OCT after successful diabetic TRD surgery. In addition, patients with impaired kidney function due to diabetic nephropathy tend to have delayed SRF absorption. Therefore, the investigation of preoperative systemic conditions on PDR patients should be considered before TRD surgery and it would be necessary to explain before surgery that PSF could be long-lasting in patient with impaired kidney function.

Methods

Medical records were reviewed after approval of the Institutional Review Board of Kyungpook National University Hospital (IRB No. 2021-02-009) and waived the requirement for informed consent because of the retrospective nature of the study. The research was conducted in accordance with the tenets of the Declaration of Helsinki.

Patients

We included patients who was diagnosed PDR with macular involving TRD and received pars plana vitrectomy from January 2014 to December 2019. The study included only the eye that had PDR with macular involving TRD and showed subretinal fluid (SRF) on preoperative OCT. If the patient who had macular involving TRD in both eyes, we included only one eye with more poor visual acuity. All patients showed successful anatomical results after vitrectomy and completed at least 3 months follow up period with OCT examinations. Patients were excluded according to the following criteria: (1) diabetic TRD without macular involving; (2) diabetic TRD without SRF on preoperative OCT scan of the macula; (3) the presence of vitreous haze or hemorrhage that are not suitable for OCT imaging.

Ophthalmic examinations were performed including best corrected visual acuity (BCVA) using a Snellen chart, intraocular pressure (IOP) measurement, slit lamp examination, fundus examination, and OCT examination. All examinations were repeated at baseline and at every follow up periods after vitrectomy. BCVA were converted to the logMAR (logarithm of the minimum angle of resolution) for statistical analyses. The detachment of macula was confirmed by a preoperative macular OCT scan. The volume mode scan of 6 × 6 mm area was performed using the spectral-domain OCT (Spectralis®, Heidelberg Engineering, Heidelberg, Germany). The presence of SRF was defined on OCT image as a hyporeflective space between the photoreceptor layer and the retinal pigment epithelium. PSF defined as SRF present within any area on 6 × 6 mm OCT scans that persists after vitrectomy.

The surgical technique

A microinvasive pars plana vitrectomy was conducted using 23 or 25 gauge instrument. When a combined surgery was planned, phacoemulsification of the cataract with the implantation of the intraocular lens was conducted at the beginning of the surgery. Vitrectomy was performed using the Constellation surgical system (Alcon, Forth Worth, Texas, USA) and included removal of the posterior vitreous and shaving of peripheral vitreous body, peeling of the posterior hyaloid, neovascular, and fibrous epiretinal membranes from the retinal surface, and endolaser photocoagulation. Internal limiting membrane (ILM) peeling was carried out after staining with indocyanine green (ICG) dye using membrane forceps, if epiretinal membranes with a risk of postoperative re-proliferation was presented. Internal drainage of SRF was carried out if a preexisting or iatrogenic retinal break was observed intraoperatively. For silicone oil (SO) tamponade, if necessary, 5700 centistokes silicone oil (Oxane®, Bausch and Lomb, USA) was injected to the posterior surface of the pupil after fluid-air exchange.

Statistical methods

Statistical analyses were performed using the Statistical Package for the Social Science software 20 (IBM Corp., Armonk, NY, USA). A plot of Kaplan-Meier graph was showed survival time of PSF. Repeated measures analysis of variance corrected by the Bonferroni method was performed to compare the mean BCVA for the follow-up periods. The Pearson correlation coefficient was calculated the mean BCVA at the final visit and the duration of PSF. Ocular and systemic factors associated with the duration of PSF were analyzed using univariate and multivariate linear regression analyses. P value < 0.05 was considered significant for all statistical tests.

Declarations

Author Information

Affliations

Department of Ophthalmology, School of Medicine, Kyungpook National University, 130 Dongdeok-ro, Jung-gu, Daegu, 41944, Korea

Yong Koo Kang & Jae Pil Shin

Contributions

All authors who contributed to research study design are as follows, YKK and JPS. YKK drafted the manuscript and analyzed the data. JPS contributed to the interpretation of the results. All authors contributed to writing and editing of the manuscript.

Corresponding author

Correspondence to Jae Pil Shin

Ethics declarations

Conflict of interest

The authors declare no competing interests.

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Figures

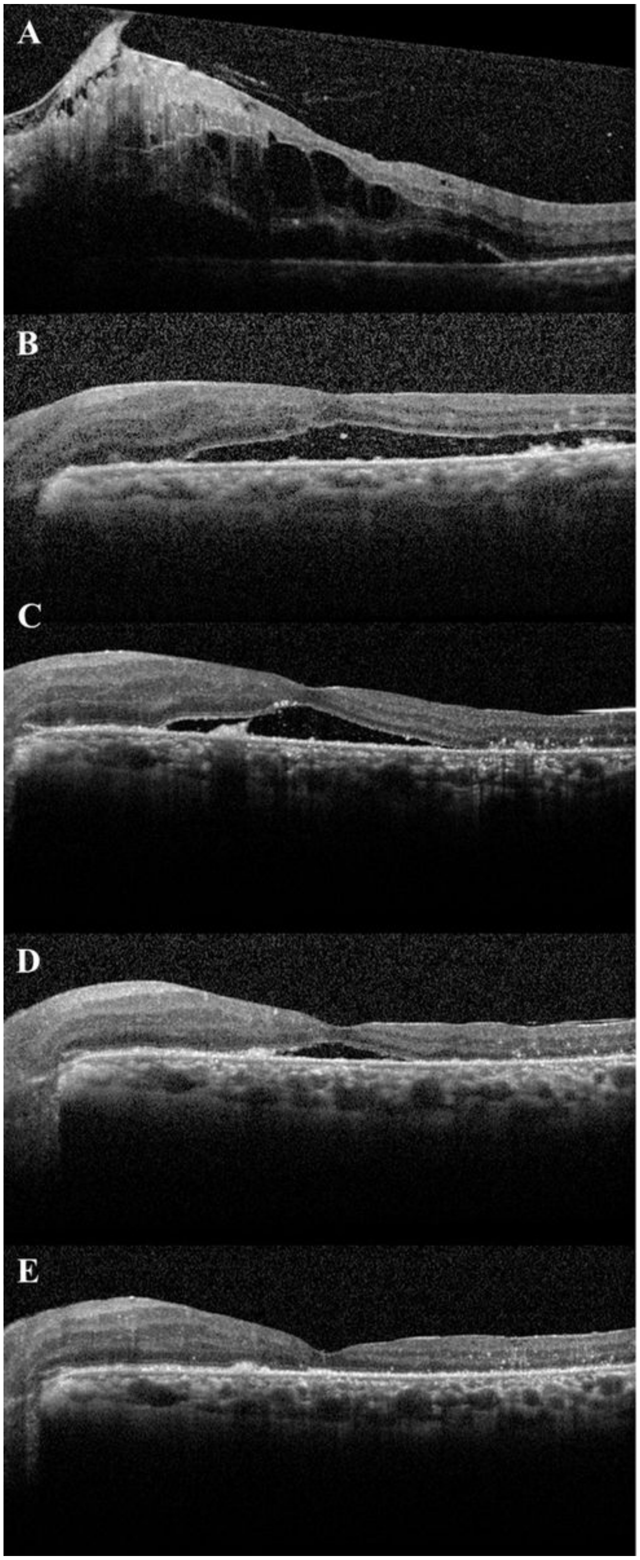

Figure 1

Optical coherence tomography (OCT) scans of diabetic tractional retinal detachment with chronic macular detachment in a 51-year-old male. OCT scans (A) preoperatively, (B) at 1 month, (C) 3 month, (D) 6 month, and (E) 7 month after vitrectomy with silicone oil injection. Persistent subretinal fluid was gradually absorbed after surgery.

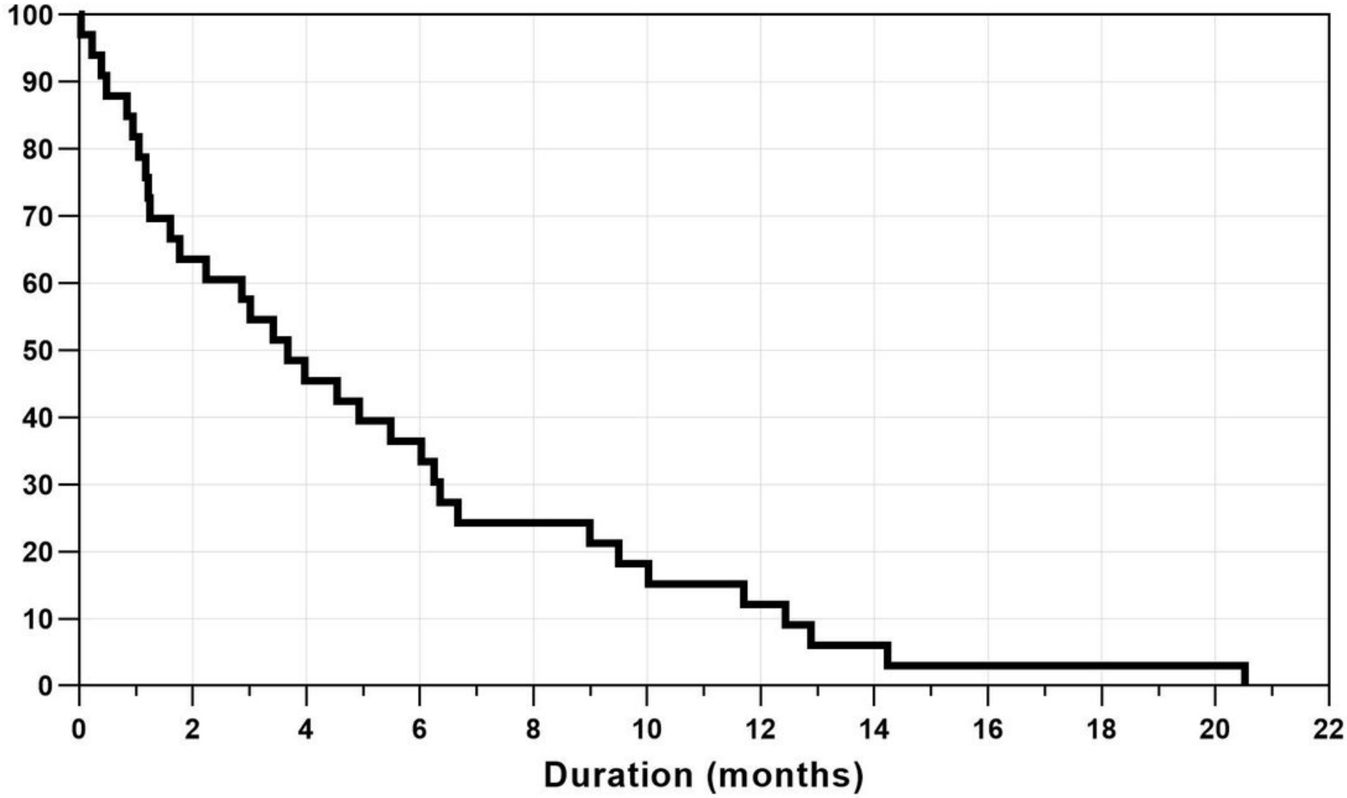

Figure 2

Kaplan-Meier graph illustrating the survival probability of persistent subretinal fluid for patients.

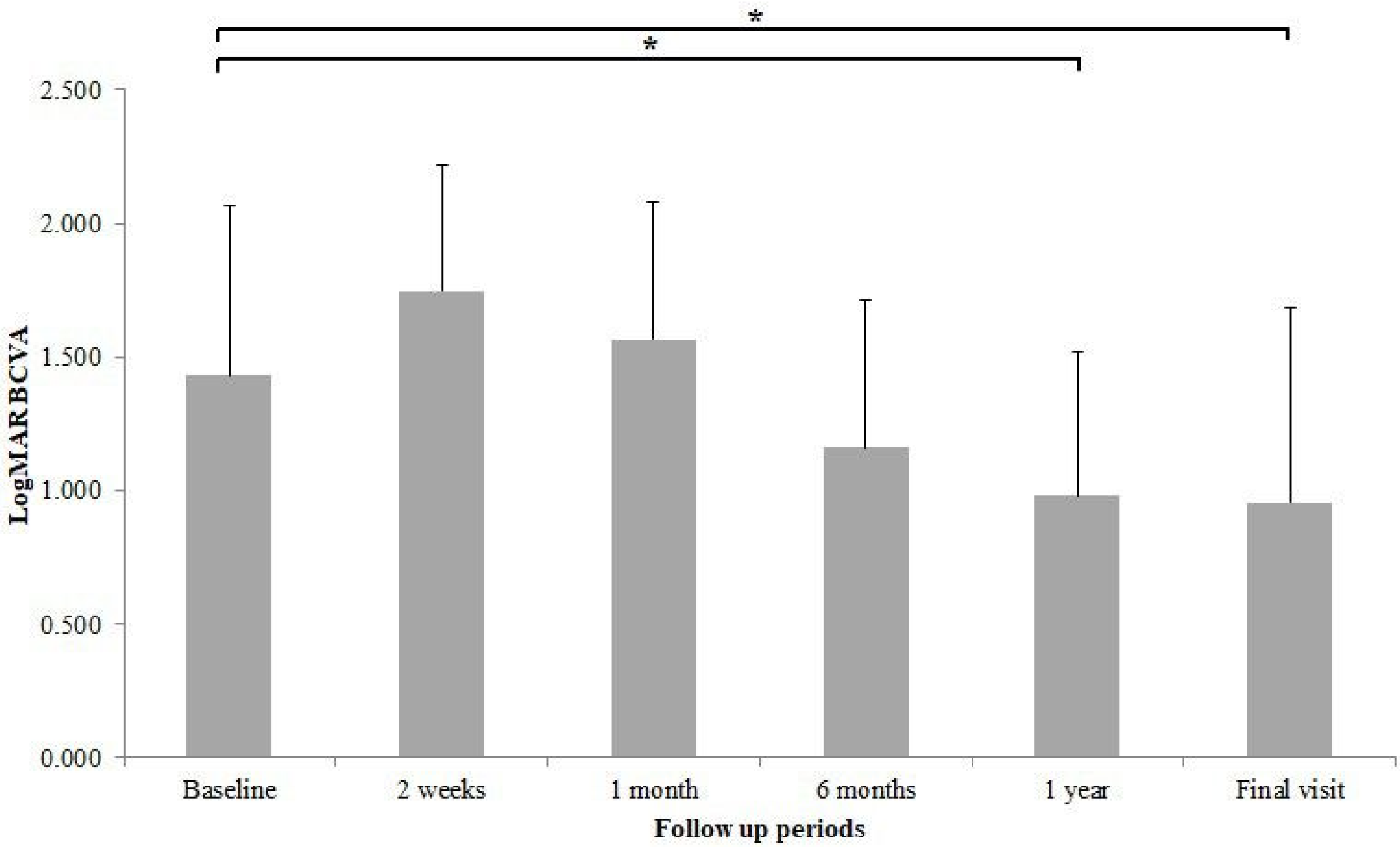

Figure 3

Mean logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) changes during follow-up. Mean BCVA was significantly improved 1 year after surgery than baseline ($P < 0.05$, respectively). * $P < 0.05$ by repeated measures analysis of variance corrected by the Bonferroni method.