The Effect of Ranibizumab and Dexamethasone Implant Treatment on Retinal Nerve Fiber Layer Thickness in Eyes with Branch Retinal Vein Occlusion

Hasan Basri Arifoğlu[1], Orhan Altunel[2], Burhan Başkan[3], Necati Duru[4], Bedirhan Alabay[4], Mustafa Ataş[4]

ABSTRACT

Purpose: To investigate the effects of intravitreal ranibizumab and dexamethasone implant treatments on the retinal nerve fiber layer (RNFL) thickness in patients with branch retinal vein occlusion (BRVO).

Materials and Methods: Fifty-three patients with macular edema secondary to BRVO were enrolled in this retrospective study. These study-group patients were divided into two groups. Group 1 consisted of 29 patients treated with intravitreal ranibizumab, and Group 2 consisted of 24 patients treated with intravitreal dexamethasone implants. The control group was the 53 normal fellow eyes of these patients. Peripapillary RNFL thickness was evaluated by using optical coherence tomography at baseline and during 12 months after treatment in both groups. Also, the RNFL thickness of the affected area in eyes with BRVO was compared with those of the normal fellow eyes.

Results: The average, superior-temporal and inferior-temporal quadrant peripapillary RNFL thicknesses in eyes with BRVO were significantly decreased at 12 months after treatment in two groups. The RNFL thicknesses in the affected areas in Group 1 and Group 2 were significantly thinner than that of the control fellow eyes at 12 months (p=0.04 and p=0.02, respectively). Also, there was no significant difference in terms of RNFL thickness in the affected area between the groups at six and 12 months (p=0.808, p=0.356, respectively).

Conclusion: Our study revealed that the average, superior-temporal and inferior-temporal RNFL thickness in the eyes of BRVO was reduced at 12 months. We suggest that RNFL thinning is due to the natural course of the disease in BRVO.

Key words: Ranibizumab, branch retinal vein occlusion, Dexamethasone implant**,** retinal nerve fiber layer.

INTRODUCTION

Retinal occlusive disorders are second in prevalence among the retinal vascular diseases, after diabetic retinopathy[1]. The reported risk factors for retinal vein occlusion (RVO) include hypertension, arteriosclerosis, diabetes, insulin-resistance, smoking, hyperlipidemia, inflammatory disease, and hypercoagulable states[2,3]. Macular edema (ME) is the most common cause of decreased visual acuity in BRVO patients.[4] The standard of care for ME in BRVO has been grid laser photocoagulation[1,5]. Recently, however, intravitreal injections of anti-vascular endothelial growth factor (VEGF) and dexamethasone implants have shown promising results in the treatment of ME following BRVO[6-8].

Optical coherence tomography (OCT) is a reproducible and non-invasive technique for cross-sectional imaging of the retinal microstructure and has enabled high-resolution quantification of the retinal nerve fiber layer (RNFL) thickness. OCT is widely used to evaluate of RNFL thickness for diagnosis and follow-up of glaucoma treatment. Many studies have reported the peripapillary RNFL thickness changes in eyes with BRVO after various treatment[9-12]. Among them, Kim et al. investigated the natural course of the RNFL thickness without treatment and reported that there is a significant decrease in RNFL thickness in BRVO over time and a significant thinning at 6 months compared with the normal fellow eye[11]. In addition, recent studies have shown structural peripapillary

1- MD, Okan University, Department of Ophthalmology, Istanbul, Turkey

2- MD, Kutahya Health Sciences University School of Medicine, Department of Ophthalmology, Kütahya, Turkey

3- MD, Diyarbakır State Hospital, Department of Ophthalmology, Diyarbakır, Turkey

4- MD, Kayseri City Hospital, Department of Ophthalmology, Kayseri, Turkey

Received: 13.12.2020
Accepted: 21.01.2021

Ret-Vit 2021; 30:265-270

DOİ: 10.37845/ret.vit.2021.30.46

Correspondence Adress:
Orhan Altunel
Kutahya Health Sciences University School of Medicine, Department of Ophthalmology, Kütahya, Turkey

Phone: +90 507 756 3574
E-mail: orhan_altunel@hotmail.com

RNFL changes in the fellow eyes of unilateral RVO patients[13,14]. VEGF is an important factor for neuronal cells as a growth factor, which is secreted by neuronal and glial cells. Intravitreal ranibizumab and dexamethasone implant may lead to neural damage by decreasing VEGF levels. However, there are no studies in the literature comparing the long term effects of ranibizumab and dexamethasone implant on RNFL thickness in the affected eyes of BRVO patients. Therefore, in this study, we investigated the RNFL thickness in affected eyes and fellow eyes of BRVO patients after ranibizumab injection and dexamethasone implant injection treatment.

METHODS

Study Population and Design

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the local ethics committee. All participants received both oral and written information about the study, and each participant provided written informed consent. It included a total of 53 eyes with treatment naive BRVO and 53 fellow eyes of these patients. The patients were divided into two groups: twenty-nine subjects in the ranibizumab injection group (Group 1) and 24 subjects in the dexamethasone implant injection group (Group 2).

Exclusion criteria

The exclusion criteria were subjects with low vision (BCVA<10/200, Snellen acuity), high intraocular pressure (IOP) (≥ 22 mmHg); high cup-to-disc ratio (≥ 0.5), a history of glaucoma, uveitis, or other retinal diseases; refractive error exceeding ± 6 D, a history of intraocular surgery, such as cataract surgery or vitrectomy, a history of intraocular laser treatment, macular edema persisting for 12 months (central macular thickness ≥ 300 μm), and a history of cerebrovascular disease, ocular trauma, or any other condition that could affect RNFL. Subjects who displayed poor cooperation during scanning, which reduced the reliability of the examination, who had low signal strength on scanning, and who were lost to follow-up were also excluded. One month after the last injection subjects who had central macular thickness ≥ 300 μm were also excluded.

Examination Protocol and Study Measurements

All participants in both groups underwent a complete examination that included a Snellen best-corrected visual acuity (BCVA) test, an IOP measured by Goldmann applanation tonometry, biomicroscopy, a dilated fundus examination, fundus photography, a fluorescein angiography (FA), and OCT measurements. For the OCT assessments, the fourth-generation Spectralis OCT device (Spectralis OCT, Heidelberg Engineering, Dossenheim, Germany) was used. OCT measurements were performed on both the fellow eyes and BRVO-affected eyes several times from the initial examination to the twelfth month and during the follow-up period.

The eyes with BRVO underwent either intravitreal ranibizumab treatment or intravitreal dexamethasone implant treatment. If the central macular thickness was ≥ 300 μm during the follow-up period, one more intravitreal injection was administered. Mean number of injections was 6.1 in ranibizumab group and 3.2 in dexamethasone implant group in the 12 months follow-up period. We used the contralateral eye in the BRVO patients as a control for the BRVO-affected eyes. The ocular exclusion criteria were the same for the control eyes as for those with BRVO. Only BCVA ≥ 20/20 (Snellen) was accepted.

OCT Measurements

RNFL thickness and macular thickness were measured by SD-OCT (Spectralis SD-OCT, Heidelberg Engineering, Heidelberg, Germany). Measurements were made by a well-trained technician who was not given information about the eyes.

Following pupil dilatation, the RNFL thickness measurements (diameter 3.5 mm, 768 A-scans) were obtained. The device's eye tracking system compensated for eye movement. The auto re-scan function, which uses a reference point, was activated to minimize variation in allocating the acquisition protocols to the follow-up sessions. The RNFL thickness from the inner margin of the internal limiting membrane to the outer margin of the RNFL layer was automatically segmented using SD-OCT software (version 5.6.3.0, Heidelberg Engineering). Images with non-centered scans, inaccurate segmentation of the RNFL, or quality scores of ≤15 dB were excluded from the analysis. Peripapillary RNFL thickness and central macular thickness (CMT) were evaluated by using OCT at baseline and during 12 months after treatment. Also, peripapillary RNFL thickness measurements of the superotemporal (TS) area and inferotemporal (TI) area were analyzed in eyes with BRVO. If BRVO occurred in the superotemporal area, the RNFL thickness was measured in the superotemporal area of the control eyes. The RNFL thicknesses of the same sectors of both eyes were compared.

Statistical Analyses

All statistical analyses were performed by using SPSS for Windows version 21.0 software (SPSS, Inc, Chicago,

IL, USA). Continuous variables were presented as mean ± standard deviation. For each continuous variable, normality was checked by the Kolmogorov-Smirnov test. The chi-square test was used to evaluate qualitative variables. BCVA values were converted into the logarithms of the minimum angle of resolution (logMAR) to perform a statistical analysis. The change in parameters before and after the injection in the groups was analyzed with Paired-samples t test. Differences in measured parameters between the two groups were analyzed with independent samples t-test. P values of less than 0.05 was considered statistically significant.

RESULTS

The mean values of age, sex distribution, and the BRVO-affected areas in Groups 1 and 2 are summarized in Table 1. The mean ages of Groups 1 and 2 were 65.6±11.7 years and 63.4±9.5 years, respectively. There was no significant difference in terms of age, sex distribution, and the BRVO-affected areas between the groups (Table 1).

The mean BCVA, CMT and peripapillary RNFL thicknesses of the groups at baseline, six and 12 months after treatment are shown in Table 2. The average, superior-temporal and inferior-temporal quadrant peripapillary RNFL thicknesses

Table 1: *Patient demographics and baseline characteristics.*

	Group 1	Group 2	*P*
Number of eyes	29	24	
Male/Female	15/14	12/12	0.797
Age (years)	65.6±11.7	63.4±9.5	0.451
Affected area TS/TI	18/11	14/10	0.660

Group 1: ranibizumab injection group, **Group 2:** dexamethasone intravitreal implant injection group, **TS:** superotemporal region, **TI:** inferotemporal region, **Mean ± SD:** Standard deviation

Table 2: *The mean BCVA, CMT and peripapillary RNFL thicknesses of the groups at baseline and after treatment.*

	Group 1					Group 2				
	Baseline	**6 Months**	***p****	**12 Months**	***p****	**Baseline**	**6 Months**	***p****	**12 Months**	***p****
BCVA (logMAR)	0.76±0.21	0.24±0.18	**<0.001**	0.23±0.19	0.352	0.78±0.22	0.24±0.15	**<0.001**	0.26±0.17	0.219
CMT	641.2±198.7	263.1±54.9	**<0.001**	247.5±49.2	0.112	652±201.3	258.7±48.6	**<0.001**	239.1±46.2	0.215
Eyes with BRVO										
Average	125.4±32.8	108.3±19.6	**0.03**	99.7±16.3	**0.041**	129.1±29.6	107.5±20.6	**0.02**	100.1±19.3	**0.05**
TS	-	112.3±25.9	-	102.2±21.4	**0.03**	-	115.7±23.1	-	102.6±24.7	**0.04**
NS	101.5±28.4	99.6±23.9	0.101	97.1±22.3	0.221	105.7±26.5	98.3±20.6	0.09	96.8±22.4	0.07
TI	-	110.6±35.5	-	100.7±31.7	**0.02**	-	113.5±32.9	-	101.4±30.6	**0.03**
NI	115.6±29.3	113.4±26.4	0.09	112.8±30.4	0.235	118.9±27.4	115.4±29.5	0.09	113.4±25.7	0.102
T	118.5±31.7	108.4±27.6	**0.05**	106.6±26.5	0.07	115.9±30.5	106.1±25.4	**0.04**	103.5±24.7	0.08
N	89.4±19.8	85.6±17.6	0.06	84.9±18.7	0.09	83.9±26.4	82.9±18.4	0.115	82.5±18.3	0.243
Fellow eyes										
Average	107.1±21.6	106.6±23.8	0.108	105.5±24.3	0.102	108.5±25.7	106.2±23.9	0.09	103.4±24.7	0.09
TS	120.6±33.7	119.2±35.4	0.865	120.1±32.4	0.412	128.5±31.4	128.3±34.6	0.321	127.8±30.7	0.352
NS	96.1±21.6	95.4±22.4	0.314	95.6±20.9	0.363	94.5±25.4	95.2±23.6	0.471	94.7±22.3	0.368
TI	123.5±33.4	121.7±30.7	0.102	117.3±32.6	0.06	129.3±30.9	130.4±31.6	0.832	126.8±32.4	0.07
NI	112.5±24.6	111.9±23.1	0.705	110.6±25.4	0.671	115.4±25.4	114.1±23.9	0.506	113.5±24.6	0.349
T	109±28.3	107.6±29.2	0.234	107.5±26.7	0.482	110.3±31.4	110.4±32.6	0.371	109.4±31.9	0.285
N	90.6±16.4	89.2±17.3	0.501	87.6±19.4	0.214	83.9±15.7	84.1±19.6	0.614	82.7±16.2	0.296

Group 1: ranibizumab injection group, Group 2: dexamethasone intravitreal implant injection group, **Mean ± SD:** Standard deviation (µm)
* Paired-samples t test, between the baseline and 6 months
** Paired-samples t test, between 6 month and 12 months

in eyes with BRVO were significantly decreased 12 months after treatment compared to six months values in two groups. Also, the inferior-temporal quadrant RNFL thickness in fellow eyes was decreased 12 months after treatment compared to baseline in two groups, but not significant (Group 1 p=0.06, Group 2 p=0.07).

A comparison of the affected area of RNFL thickness between the eyes with BRVO and the fellow eyes at baseline, six and 12 months after treatment is presented in Table 3. The RNFL thicknesses in the occluded areas before treatment were not significantly different between Group 1 and Group 2 (171.4±81.8 µm and 170.2±56.5 µm, respectively, p=0.970), but the thicknesses in both groups were significantly thicker than in the control fellow eyes (121.7±35.8 µm, p=0.009 and 128.8±27.8, p=0.006, respectively). The RNFL thickness in the affected areas at six months after treatment was significantly thinner than the baseline value in Group 1 (112.8±21.6 µm, *p*=0.001) and Group 2 (114.3±16.3 µm, p<0.001). However, the RNFL thicknesses in the affected areas in Group 1 and Group 2 were thinner than that of the control fellow eyes at six months, but not significant (*p*=0.218 and p=0.076, respectively). The RNFL thickness in the affected areas at 12 months after treatment was significantly thinner compared with six months after treatment values in Group 1 (101.4±26.3 µm, p=0.023) and Group 2 (102.6±26.2 µm, p=0.03). The RNFL thicknesses in the affected areas in Group 1 and Group 2 were significantly thinner than that of the control fellow eyes at 12 months (p=0.04 and p=0.02, respectively). Also, there was no significant difference in terms of RNFL thickness in the affected area between the groups at six and 12 months (p=0.808, p=0.356, respectively).

DISCUSSION

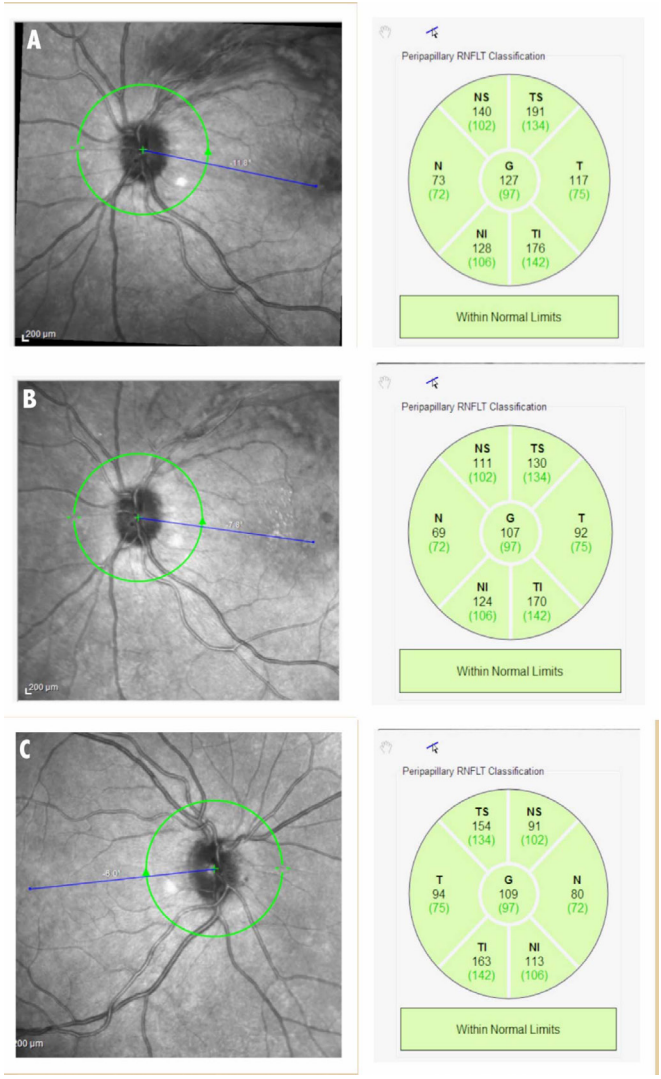
This study showed that the RNFL thickness initially increased because of edema secondary to BRVO. However, subsequent RNFL thinning in the affected areas was observed 12 months after the intravitreal injections in both the ranibizumab and the dexamethasone implant groups. Also, there was no significant difference in terms of RNFL thickness in the affected area between the groups at six and 12 months.

Lim et al. reported that the RNFL thickness was reduced in the affected areas in patients with BRVO during the two-year follow-up period[9]. Also, they reported that the RNFL thickness in ischemic BRVO was significantly reduced compared to than that of the non-ischemic BRVO. If the RNFL thickness is less than 78.00 µm during the follow-up of BRVO patients, the presence of ischemic BRVO should be suspected.[9] We did not include ischemic BRVO patients in this study to avoid the extra impact of the ischemic areas on RNFL thickness. There is inconsistency in the effects of repeated intravitreal injections and of IOP fluctuations on RNFL thickness[9,15-17]. Although the study of Hayreh et al. shows that all patients presented an IOP in the normal range, with no known glaucoma, the researchers reported that the IOP might increase in RVO patients[17]. Lim et al. reported that elevation in the IOP is not correlated with a RNFL defect in BRVO[9]. In addition, Shin et al. reported that IOP-related variables have no association with RNFL change in RVO patients[10]. Bulut et al. evaluated the peripapillary RNFL thicknesses of BRVO patients treated with intravitreal dexamethasone implant[18]. They observed IOP elevations within the first month after the injection and showed the average and inferior quadrant RNFL thinning six months after the injection. Another study was revealed that dexamethasone implant have no adverse effect on RNFL thickness in eyes with BRVO patients in a 6-month period[19]. In our study, none of the patients required anti-glaucomatous medication after the injections, and no instance of sustained IOP increase or inflammatory reaction was observed.

Table 3: *Comparison of retinal nerve fiber layer thickness measurements between the affected area and control area of fellow eye at baseline and after treatment.*

	Group 1					Group 2				
	Baseline	**6 Months**	***p****	**12 Months**	***p****	**Baseline**	**6 Months**	***p****	**12 Months**	***p****
Affected Area	171.4±81.8	112.8±21.6	**0.001**	101.4±26.3	**0.023**	170.2±56.5	114.3±16.3	**<0.001**	102.6±26.2	**0.03**
Control Area	121.7±35.8	121.1±34.9	0.951	119.5±32.9	0.326	128.8±27.8	129.3±28.8	0.721	127.8±24.9	0.215
p*	**0.009**	0.218		**0.04**		**0.006**	0.076		**0.02**	

Group 1: ranibizumab injection group, Group 2: dexamethasone intravitreal implant injection group, Mean ± SD: Standard deviation (µm)
* Paired-samples t test, between the baseline and 6 months
** Paired-samples t test, between 6 month and 12 months
& Independent samples t-test



Shin et al. reported that the RNFL thickness was reduced in RVO patients who were followed up for at least 12 months, in both those treated with bevacizumab injection and those without injection[10]. Also, they reported that a decreased RNFL thickness in the injection group was not statistically different from that in the non-injection group. They suggested that the frequency of the injections and the IOP-related variables had no association with RNFL change. Therefore, the decrease in the RNFL thickness in RVO patients is attributed to the inner retinal ischemia itself, not anti-VEGF therapy[10]. Kim et al. reported that there was a significant decrease in RNFL thickness in the BRVO eyes over time. There was also a significant thinning of the RNFL in the BRVO eyes without treatment compared to the unchanged RNFL thickness in the normal eyes at six months.[11] They suggested that the reduction in the RNFL thickness should be considered part of the natural course of the disease in BRVO. Recent a study was described neuroretinal atrophy following the resolution of macular edema in patients treated with ranibizumab in RVO.[20] They suggested that the neuroretinal atrophy may be caused by the retinal hypoxia due to vascular damage resulting from the occlusion. In this study, we found that the reduction in affected areas of RNFL thickness in the eyes of the BRVO in the treatment groups was not significantly different from the unchanged thickness in the fellow eyes in the control group at six months (p=0.218 and p=0.076, respectively). However, we observed that RNFL thicknesses in the affected areas in both groups were significantly thinner than that of the control fellow eyes at 12 months (p=0.04 and p=0.02, respectively).We postulate that ranibizumab and dexamethasone implant treatments may decelerate the RNFL thinning, which is part of the natural course of the disease in BRVO. We also predict a significant RNFL thinning over time.

In the RAVE study, Brown et al. reported that the risk of neovascular complications in eyes with severe central retinal vein occlusion was not ameliorated by vascular endothelial growth factor blockade, but was merely delayed[22]. Haller et al. reported that dexamethasone implant treatment might have an impact on the development of ischemia and the disease progression[23]. The VEGF play an important role in the trophic maintenance of neural cells as a neuroprotective growth factor. Therefore, inhibition of VEGF may lead to neurodegeneration. Nishijima et al. revealed that inhibition of VEGF may exacerbate ischemia induced neural damage[24]. Considering that intravitreal ranibizumab and dexamethasone implant is frequently used in RVO, blockage of VEGF may lead to neurodegeneration. In this study, in accordance with the literature, the average, superior-temporal and inferior-temporal quadrant peripapillary RNFL thicknesses in eyes with BRVO were significantly decreased 12 months after treatment compared to six months values in two groups. However, there was no significant difference in terms of RNFL thickness in the affected area between the ranibizumab and dexamethasone injections groups at six and 12 months (p=0.808, p=0.356, respectively).

Several recent studies have shown structural peripapillary RNFL changes in the fellow eyes of unilateral RVO patients[13,14,25]. Also, OCTA studies revealed peripapillary microvascular dysfunction in the fellow eyes of patients with unilateral RVO[14]. In our study, the inferior-temporal quadrant RNFL thickness in fellow eyes was decreased 12 months after treatment compared to baseline in two groups, but not significant.

Our study had several limitations. First, this study was conducted with a small number of cases and has a

retrospective design. Second, this study did not include healthy control group.

In conclusion, ranibizumab and dexamethasone implant injections do not lead to a significant change in RNFL thickness in BRVO at six months. The average, superior-temporal and inferior-temporal quadrant peripapillary RNFL thicknesses in eyes with BRVO were significantly decreased 12 months after treatment compared to six months values, which is part of the natural course of the disease in BRVO.

Acknowledgment: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper. No author has a financial or proprietary interest in any material or method mentioned

REFERENCES

1. Rogers S, McIntosh RL, Cheung N, et al. International Eye Disease Consortium. The prevalence of retinal vein occlusion: pooled data from population studies from the United States, Europe, Asia, and Australia. Ophthalmology 2010 Feb;117:313-319.
2. Zhou JQ, Xu L, Wang S, et al. The 10-year incidence and risk factors of retinal vein occlusion: the Beijing eye study. Ophthalmology 2013;120:803-8.
3. Stewart RM, Clearkin LG. Insulin resistance and autoregulatory dysfunction in glaucoma and retinal vein occlusion. Am J Ophthalmol 2008;145:394-6.
4. Mitchell P, Smith W, Chang A. Prevalence and associations of retinal vein occlusion in Australia: the blue mountains eye study. Archives of Ophthalmology. 1996;114:1243-1247.
5. Evaluation of grid pattern photocoagulation for macular edema in central vein occlusion. The Central Vein Occlusion Study Group M report. Ophthalmology 1995;102:1425-33.
6. Gerding H, Monés J, Tadayoni R, et al. Ranibizumab in retinal vein occlusion: treatment recommendations by an expert panel. Br J Ophthalmol. 2015; 99: 297-304.
7. Hoeh AE, Ach T, Schaal KB,et al. Long-term follow-up of OCT-guided bevacizumab treatment of macular edema due to retinal vein occlusion. Graefes Arch Clin Exp Ophthalmol 2009;247:1635-41.
8. Haller JA, Bandello F, Belfort R Jr, et al. Dexamethasone intravitreal implant in patients with macular edema related to branch or central retinal vein occlusion twelve-month study results. Ophthalmology 2011;118:2453-60.
9. Lim HB, Kim MS, Jo YJ, et al. Prediction of retinal ıschemia in branch retinal vein occlusion: Spectral-domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2015; 56: 6622-6629.
10. Shin HJ, Shin KC, Chung H, et al. Change of retinal nerve fiber layer thickness in various retinal diseases treated with multiple intravitreal antivascular endothelial growth factor. Invest Ophthalmol Vis Sci. 2014;55:2403-2411.
11. Kim CS, Shin KS, Lee HJ, et al. Sectoral retinal nerve fiber layer thinning in branch retinal vein occlusion. Retina, 2014, 34: 525-530.
12. Sakimoto S, Gomi F, Sakaguchi H, et al. Analysis of retinal nonperfusion using depth-integrated optical coherence tomography images in eyes with branch retinal vein occlusion. Invest Ophthalmol Vis Sci. 2015;56: 640-646
13. Kim MJ, Woo SJ, Park KH, et al. Retinal nerve fiber layer thickness is decreased in the fellow eyes of patients with unilateral retinal vein occlusion. Ophthalmology. 2011;118: 706-710.
14. Yong-Il Shin, Ki Yup Nam, Seong Eun Lee et al. Changes in Peripapillary Microvasculature and Retinal Thickness in the Fellow Eyes of Patients With Unilateral Retinal Vein Occlusion: An OCTA Study. Invest Ophthalmol Vis Sci. 2019;60:823-829.
15. Horsley MB, Mandava N, Maycotte MA, et al. Retinal nerve fiber layer thickness in patients receiving chronic anti-vascular endothelial growth factor therapy. Am J Ophthalmol. 2010; 150:558-561.
16. Martinez-de-la-Casa JM, Ruiz-Calvo A, Saenz-Frances F, et al. Retinal nerve fiber layer thickness changes in patients with age-related macular degeneration treated with intravitreal ranibizumab. Invest Ophthalmol Vis Sci. 2012;53:6214-6218.
17. Bulut MN, Özertürk Y, Çallı Ü, et al. Evaluation of Peripapillary Nerve Fiber Layer after Dexamethasone Implantation (Ozurdex) in Branch Retinal Vein Occlusions. J Ophthalmol. 2016;2016:2050796.
18. Bulut MN, Özertürk Y, Çallı Ü, et al. Evaluation of Peripapillary Nerve Fiber Layer after Dexamethasone Implantation (Ozurdex) in Branch Retinal Vein Occlusions. J Ophthalmol. 2016;2016:2050796.
19. Ayar O, Alpay A, Koban Y, et al. The Effect of Dexamethasone Intravitreal Implant on Retinal Nerve Fiber Layer in Patients Diagnosed with Branch Retinal Vein Occlusion. Curr Eye Res. 2017;42:1287-1292.
20. Podkowinski D, Philip A, Vogl WD, et al. Neuroretinal atrophy following resolution of macular oedema in retinal vein occlusion. Br J Ophthalmol. 2019;103:36-42.
21. Hayreh SS, Zimmerman MB, Beri M, et al. Intraocular pressure abnormalities associated with central and hemicentral retinal vein occlusion. Ophthalmology. 2004;111:133-141.
22. Brown DM, Wykoff CC, Wong TP, et al. Ranibizumab in preproliferative (ischemic) central retinal vein occlusion: the rubeosis anti-VEGF (RAVE) trial. Retina 2014;34:1728-1735.
23. Haller JA, Bandello F, Belfort R, et al. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology 2010; 117: 1134-1146.
24. Nishijima K, Ng YS, Zhong L, Bradley J, Schubert W, Jo N, et al.Vascular endothelial growth factor-A is a survival factor for retinal neurons and a critical neuroprotectant during the adaptive response to ischemic injury. Am J Pathol 2007;171:53-67.
25. Shin Y, Lim HB, Koo H, et al. Longitudinal changes in the peripapillary retinal nerve fiber layer thickness in the fellow eyes of unilateral retinal vein occlusion. Sci Rep. 2020 7;10:7708.