• Clinical Research •

Dexamethasone intravitreal implant monotherapy in naive patients with macular edema secondary to retinal vein occlusion: long term follow-up retrospective cohort study

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Abstract

● **AIM:** To investigate the efficacy and safety of repeated dexamethasone implants with real-life data in eyes with naive retinal vein occlusion (RVO) with macular edema (ME) at a minimum of 60mo follow-up.

● **METHODS:** In this retrospective cohort study, the data about best corrected visual acuity (BCVA), central macular thickness (CMT), serous macular detachment (SMD), hard exudate, hyperreflective foci (HRF), cystoid degeneration, pearl necklace sign, epiretinal membrane (ERM), disorganization of retinal inner layers (DRIL), ellipsoid zone and external limiting membrane (EZ-ELM) integrity, intraocular pressure (IOP) and lens condition were recorded.

● **RESULTS:** Thirty-eight eyes of 38 patients were included in the study. Thirteen patients presented with central RVO (CRVO) and 25 with branch RVO (BRVO). The mean follow-up time was 69.9±15.8mo, and the mean number of injections was 7.9±4.0. The mean BCVA gain was 25.0±36 letters, and this difference was statistically significant (*P*=0.021). The BCVA gain was 19.4±20.4 letters in the CRVO group, and 26.5±38.6 letters in the BRVO group (*P*=0.763). Besides, 21 (55.2%) of the patients achieved ≥15 letters improvement. At the end of the follow-up period, SMD was not observed in any of the patients (*P*=0.016). Hard exudate, HRF number were decreased; while DRIL, ERM and EZ-ELM defects were increased but not significantly.

● **CONCLUSION:** Intravitreal dexamethasone monotherapy is an effective and safe treatment option for the treatment-naive RVO-ME patients in the long-term follow-up.

● **KEYWORDS:** dexamethasone; intravitreal naïve; retinal vein occlusion; macular edema

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INTRODUCTION

Retinal vein occlusion (RVO) is the most common retinal vascular disease after diabetic retinopathy[1]. The most common cause of RVO is the deterioration of hemodynamics in the veins as a result of compression due to atherosclerosis in the central retinal artery. RVO is a retinal vascular disease characterized by dilatation of retinal veins, retinal and subretinal hemorrhages, macular edema (ME), and varying degrees of retinal ischemia[2]. Central retinal vein occlusion (CRVO) is a condition that develops due to occlusion of the central vein caused by a thrombus formed because of the deterioration of hemodynamics. Occlusion in the branches of the central retinal vein is called branch retinal vein occlusion (BRVO)[3].

One of the most important causes of vision loss in RVO is ME secondary to RVO[4]. High vascular endothelial growth factor (VEGF) levels, inflammatory cells, and cytokines are responsible for the pathogenesis of RVO-ME. Intravitreal anti-VEGF is beneficial in the treatment of ME due to RVO and is used as first-line therapy in patients with RVO-ME. However, the fact that inflammation is also responsible in pathogenesis has made it reasonable to use intravitreal steroid agents. Currently, intravitreal anti-VEGF therapy and intravitreal steroid agents (especially intravitreal dexamethasone implant) are among the most used and effective treatments, either alone or in combination, in the treatment of RVO-ME[5-6].

Dexamethasone intravitreal implant 0.7 mg (DEX; OZURDEX, Allergan, Inc., Dublin, Republic of Ireland) was first approved by the United States Food and Drug Administration for the treatment of ME secondary to central retinal vein and BRVO[7]. As a result of the clinical studies, it has been found to be effective in many diseases, especially diabetic macular edema (DME)[8-10].

In a previous Meta-analysis study, sustained-release corticosteroids (intravitreal DEX implant) were effective in improving vision and reducing central macular thickness (CMT) in the initial (3mo) and long-term (12mo) treatment periods for ME, reducing the need for intravitreal injections[10]. The current study with a much longer follow-up period (60 to 101mo) more strongly demonstrates the effectiveness and safety of intravitreal DEX monotherapy in the treatment of RVO-ME. In today's conditions, where time is valuable, the reduced number of visits and the reduced number of injections provide a cost-effective advantage. However, the risk of developing cataracts and glaucoma should be considered as a disadvantage of this treatment[11].

In our study, we wanted to share the treatment outcomes of our naive RVO-ME patients, whom we followed with only the intravitreal DEX treatment. With this study, we aimed to present the long-term results of the efficacy and safety of the intravitreal DEX implant when used alone. We think that the long-term follow-up results in a single center can make a valuable contribution to the literature.

PARTICIPANTS AND METHODS

Ethical Approval The study was carried out in accordance with the tenets of the Declaration of Helsinki and Good Clinical Practice guidelines. The Institutional Ethical Board of Prof. Dr. Cemil Taşcıoğlu City Hospital in Istanbul, Türkiye approved the study (approval ID: 07.2023.126). Informed consent was obtained from all individual participants included in the study.

Study Participants Forty-five patients with naive RVO-ME who received DEX implant monotherapy between February 2013 and April 2023 in the retina clinic of Prof. Dr. Cemil Taşcıoğlu City Hospital were reviewed. Finally, considering the exclusion criteria, 38 eyes of 38 patients with treatment-naive RVO-ME and a minimum follow-up of 60mo were included in this retrospective cohort study. All patients were divided into two groups as CRVO and BRVO, according to their diagnosis.

The exclusion criteria were as follows: previous treatment with grid laser or other intravitreal anti-VEGF agents, ischemic CRVOs, severe macular ischemia on fluorescein angiography (FA), the presence of vitreomacular adhesion or vitreomacular traction syndrome, history of glaucoma, retinal comorbidities such as diabetic retinopathy or tractional detachment, history of complicated cataract surgery, trauma, having poor quality OCT scans or FA scans and missed data/informed consent form in the medical records.

The patients were followed-up throughout the study period and underwent the following examinations at each visit: best-corrected visual acuity (BCVA), anterior segment biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometer, indirect ophthalmoscopy, and optical coherence tomography (OCT) imaging. FA imaging was performed at the baseline visit and as needed. The history of cerebrovascular/cardiovascular events and other diseases at the baseline and at the last visit was questioned and recorded. The patients who required anti-glaucomatous therapy or trabeculectomy during the follow-up were noted. In addition, the total duration of the follow-up period as well as the total number of injections they had during the follow-up were recorded.

We performed FA-guided focal photocoagulation restricted to ischemia areas (areas of ischemia larger than 10 optic disc diameters) on FA. No patient underwent macular grid photocoagulation or panretinal photocoagulation.

All patients were treated based on the *pro re nata* (PRN) protocol. The criteria for such retreatment were as follows: an increase in retinal thickness in OCT of >100 μm, and/or a loss of BCVA >5 letters in the Early Treatment Diabetic Retinopathy Study (ETDRS) score without cataract progression. If visually significant cataract progression was detected, the patients underwent cataract surgery.

All intravitreal DEX implant injections were performed in an operating room. Informed consent was obtained from all patients before the injection. Under sterile conditions, a sterile lid speculum was used, and a 5% povidone-iodine solution was applied to the ocular surface for a minimum of 5min before the injection after which DEX 0.7 mg (Ozurdex, Allergan) was injected at 3.5- or 4 mm posterior to the corneoscleral limbus. A topical moxifloxacin 0.5% was prescribed four times daily for 5d.

Optical Coherence Tomography Analysis Spectral Domain OCT scans were performed with OCT Spectralis (Spectralis, Heidelberg Engineering, Heidelberg, Germany) at each visit. The device automatically measures the CMT to quantitatively evaluate ME. OCT biomarkers at baseline and last visit were evaluated and recorded by two independent experienced investigators (Karataş G and Çakir A) who were masked to the patients' information. These biomarkers were serous macular detachment (SMD), edema type, hard exudate, hyperreflective foci (HRF), pearl necklace, epiretinal membrane (ERM), disorganization of retinal inner layers (DRIL), Ellipsoid zone-external limiting membrane (EZ-ELM) integrity.

Eyes with cystoid spaces of horizontal diameter ≥600 μm were graded as cystoid degeneration. SMD was considered present if the posterior surface of the retina was elevated over a non-reflective cavity. Eyes with cystoid spaces of horizontal diameter ≥600 μm were graded as cystoid degeneration. EZ and ELM integrity was evaluated together. Eyes with continuous EZ and ELM on OCT sections within 1 mm centrally were classified as EZ-ELM intact. If the EZ-ELM was disrupted, it was classified as an EZ-ELM defect[12]. DRIL was identified when the boundaries of the ganglion cell, inner plexiform layer, inner nuclear layer, and outer plexiform layer could not be identified[13]. The presence of HRF was graded as follows according to the number of HRF counted in the OCT scans: 1-10, 11-20, and ≥21[14]. The combination of HRFs on the inner wall of the cystoid cavities and forming a ring image was called the pearl necklace sign[15].

Outcome Measures The main outcome measures were visual and anatomical changes throughout the follow-up period. Secondary outcome measures were the proportion of eyes with ≥15 letters of vision gain or loss, the change of OCT biomarkers and their effect on the treatment success, the proportion of cataract extraction and IOP-lowering treatment during the study period.

Statistical Analysis Statistical analyses were performed using the IBM SPSS software version 21.00. The variables were investigated using visual (histograms) and analytical methods (Kolmogorov-Smirnov). Descriptive analyses were presented using means and standard deviations for normally distributed variables. Paired Student's *t*-test and Wilcoxon signed rank test were used to compare the measurements at two-time points (baseline and final) where appropriate. The proportions were compared by using the Chi-square test or Fisher's exact test. Spearman and Pearson tests were performed to calculate correlation coefficients. $P<0.05$ was used to determine statistical significance.

RESULTS

In this retrospective, cohort case series, 38 eyes of 38 patients with RVO who had received repeated intravitreal DEX therapy for at least 5y were included. The participants' demographic characteristics are summarized in Table 1.

The minimum follow-up time was 60mo while the maximum follow-up time was 101mo. In addition, 25 (65.7%) of the 38 patients were followed for 6y or more, and 10 (26.3%) of them were followed for 7y or more. Thirteen subjects (34.2%) were followed for a mean of 34.2±15.7mo without treatment. Two (5.2%) of the patients were diagnosed with diabetes mellitus and 28 (73.6%) patients were diagnosed with systemic hypertension. Loss to follow-up ratio was 7/45 (15.5%) due to patient who missed the examinations or has an exclusion criteria.

Table 1 Demographic characteristics of patients

Items	Data
Age, y, mean±SD	67.7±8.1
Sex, female/male, *n*	17/21
CRVO/BRVO, *n*	13/25
Follow-up time, mo, mean±SD	69.9±15.8
Total DEX implants within 60mo, mean±SD	7.9±4.0

BRVO: Branch retinal vein occlusion; CRVO: Central retinal vein occlusion; DEX: Dexamethasone.

Functional Results The mean baseline BCVA was 1.2±0.5 logMAR, and the mean final BCVA was 0.8±0.6 logMAR; the improvement was statistically significant ($P=0.021$). The mean BCVA gain was 25.0±36 letters, and this difference was statistically significant ($P=0.021$). The BCVA gain was 19.4±20.4 letters in the CRVO group, and 26.5±38.6 letters in the BRVO group. There was no statistically significant difference between the two groups ($P=0.763$). Also, 21 (55.2%) of the patients achieved ≥15 letters improvement, of which 8 (38%) were CRVO and 13 (62%) were BRVO. Six (15.7%) patients lost >15 letters, of which 2 (33.3%) were CRVO and 4 (66.6%) were BRVO.

In the CRVO group, the baseline BCVA was 35.2±21.7 letters, and the final BCVA was 55.2±45.8 letters; this difference was statistically significant ($P<0.001$). In the BRVO group, the baseline BCVA was 36.3±34.7 letters, and the final BCVA was 63.7±34.2 letters; this difference was also statistically significant ($P<0.001$). However, there was no statistically significant difference between the two groups ($P=0.734$). Figure 1 shows the distribution of BCVAs overtime according to groups.

Structural Results The mean baseline CMT was 632.2±147.2 μm while the mean final CMT was 372.4±178.2 μm, and the change was statistically significant ($P<0.001$). In the CRVO group, the baseline CMT was 684.6±122.1 μm while the final CMT was 391.2±254.3 μm, and this difference was statistically significant ($P<0.001$). In the BRVO group, the baseline CMT was 603.59±161.47 μm while the final CMT was 359.3±142.8 μm, and this difference was statistically significant ($P<0.001$). However, there was no statistically significant difference between the two groups ($P=0.437$). Figure 2 shows the distribution of CMTs overtime according to groups.

Biomarker Changes There were 14 eyes (36.8%) with SMD at baseline. At the end of the follow-up period, SMD was not observed in any of the patients ($P=0.016$). Hard exudate was present in 12 (31.5%) patients at the beginning, and hard exudate remained still in 9 (23.6%) patients at the end of the study ($P=0.102$). The baseline HRF number decreased, but there was no statistically significant difference when compared to the final visit ($P=0.062$). The pearl necklace sign was

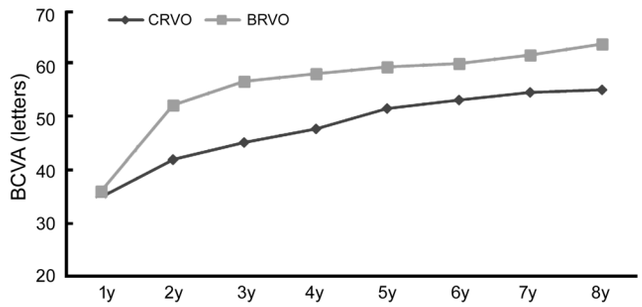

Figure 1 The distribution of BCVAs over time among groups BCVA: Best-corrected visual acuity; BRVO: Branch retinal vein occlusion; CRVO: Central retinal vein occlusion.

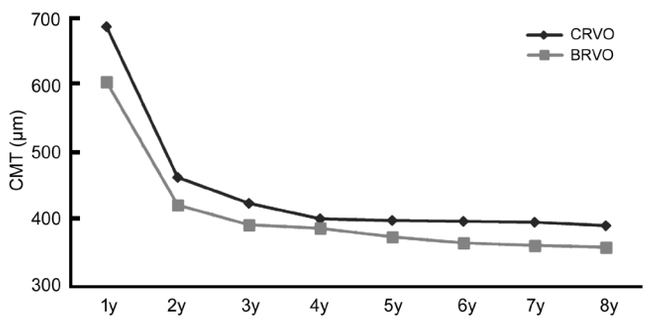

Figure 2 The distribution of CMTs over time among groups CMT: Central macular thickness; BRVO: Branch retinal vein occlusion; CRVO: Central retinal vein occlusion.

Table 2 Baseline-final clinical characteristics of patients *n* (%)

Parameters	Baseline	Final	*P*
BCVA, logMAR, mean±SD	1.2±0.5	0.8±0.6	0.021
CMT, μm, mean±SD	632.2±147.2	372.4±178.2	<0.001
IOP, mm Hg, mean±SD	15.3±3.2	15.6±2.7	0.615
Lens status, pseudophakia	18 (47.3)	36 (94.7)	<0.001
PRP	2 (5.2)	4 (10.5)	0.578
PPV	1 (2.6)	3 (7.8)	0.612
CeVE/CVE	6 (15.7)	6 (15.7)	1
SMD	14 (36.8)	0	0.016
Hard exudate	12 (31.5)	9 (23.6)	0.102
Pearl necklaces	1 (2.6)	1 (2.6)	1
HRF			0.062
Grade 1 (1-10)	18 (47.3)	8 (21)	
Grade 2 (11-20)	5 (13.1)	12 (31.5)	
Grade 3 (≥21)	2 (5.2)	1 (2.6)	
ERM	23 (60.5)	29 (76.3)	0.087
DRIL	18 (47.3)	23 (60.5)	0.358
EZ-ELM	14 (36.8)	19 (50)	0.063

BCVA: Best-corrected visual acuity; CeVE/CVE: Cerebrovascular events/cardiovascular events; CMT: Central macular thickness; DRIL: Disorganization of retinal inner layers; ERM: Epiretinal membrane; EZ-ELM: Ellipsoid zone-external limiting membrane; HRF: Hyperreflective foci; IOP: Intraocular pressure; PPV: Pars plana vitrectomy; PRP: Panretinal photocoagulation; SMD: Serous macular detachment.

detected in 1 eye (2.6%) initially, and there was no change at the end of the study (P=1). The number of eyes with ERM at baseline was 23 (60.5%), and the number of eyes with ERM at the final examination was 29 (76.3%; P=0.087). There were 18 eyes (47.3%) with DRIL at the initial examination, and the number of eyes with DRIL at the final examination was 23 (60.5%; P=0.358). There were 14 (36.8%) eyes with a disrupted EZ-ELM at the beginning, while EZ-ELM defect was detected in 19 (50%) eyes at the end of the follow-up time (P=0.063).

The final BCVA was found to be correlated with age and initial EZ/ELM status. Older age and disrupted EZ/ELM were negatively correlated with final BCVA (r=-0.603, P=0.008, r=-0.617, P=0.006; respectively). The mean BCVA gain was found to be correlated only with baseline EZ/ELM status (correlation coefficient, r=-0.479, P=0.044).

Complications The mean baseline IOP was 15.3±3.2 mm Hg, and the mean final IOP was 15.6±2.7 mm Hg. The change in IOP was not statistically significant (P=0.615). During the study, 28 (73.6%) eyes were followed without any anti-glaucomatous therapy. Two (5.2%) eyes were followed up with a single agent, 4 (10.5%) eyes with two agents, and 4 (10.5%) eyes with three agents of anti-glaucomatous therapy. No patient required glaucoma surgery.

There were 20 phakic eyes at baseline, and 18 (90%) of them underwent phacoemulsification surgery during the follow-up period (P<0.001). Of those who underwent phacoemulsification surgery, 7 were in the CRVO group and 11 were in the BRVO group. Cataract progression throughout the study was 87.5% in the CRVO group and 91.6% in the BRVO group (P=0.857).

At baseline, focal photocoagulation was present in 2 (5.2%) eyes. During the follow-up, focal photocoagulation was performed on 2 (5.2%) eyes (P=0.578). Initially, 1 (2.6%) patient presented with vitreous hemorrhage at baseline, and was diagnosed as CRVO after pars plana vitrectomy (PPV) and underwent treatment. Three (7.8%) patients had PPV during the follow-up period (P=0.612). Two of these 3 patients who underwent PPV were operated on due to ERM, while 1 was operated on due to vitreous hemorrhage. All 3 patients were diagnosed with BRVO.

At the baseline of the study, 6 (15.7%) patients had a history of cerebrovascular/cardiovascular events within previous 6mo. No cerebrovascular/cardiovascular events were observed in any patient during the treatment or the follow-up period. The participants' baseline and final clinical characteristics are summarized in Table 2.

DISCUSSION

This study was conducted in order to investigate the long-term consequences of the therapeutic effect of dexamethasone intravitreal implants in patients with CRVO and BRVO. The current study is a retrospective cohort of naive RVO patients

who were treated only with an intravitreal DEX implant, with the longest follow-up (60-101mo) in the literature. To the best of our knowledge, the closest study to us in the literature is Garay-Aramburu and Gómez-Moreno[16] who shared the results of 5-year intravitreal DEX treatment of 10 RVO-ME patients, but these patients were not treatment-naive. In addition, there is a prospective and non-randomized study in the literature in which only the intravitreal DEX injection was applied for 12mo for the treatment of naive RVO-ME[17]. The fact that the naive RVO patients began the treatment shortly after the diagnosis and received only the intravitreal DEX implant in our study made our results exceptional.

Only 6 (15.7%) of the patients had a history of cerebrovascular and/or cardiovascular events, thus all the remaining patients received intravitreal DEX implant therapy at the clinician's discretion. This study demonstrated that intravitreal DEX implant therapy alone resulted in functional and anatomical improvement in the naive RVO patients at the long-term follow-up. To the best of our knowledge, there is no other study in the literature in which naive RVO patients were followed for such a long period with only intravitreal DEX implants.

In a previous randomized clinical trial, SCORE-2 study, the mean BCVA gain from baseline was +18.6 letters in the bevacizumab group and +18.9 letters in the aflibercept group[18]. In our study, a 19.4±20.4 letters increase of BCVA in the CRVO group, and 26.5±38.6 letters in the BRVO group were achieved within at least 60mo of follow-up. In a multicenter, retrospective study Coscas *et al*[19] reported that 39% of the patients improved ≥15 letters after the first 2 DEX implant injections, of which 48% were CRVO and 16% were BRVO patients. In the SCORE-CRVO study, the percentage of participants who received 1mg intravitreal triamcinolone acetonide (TA) at the end of 12mo with ≥15 letters gain in BCVA was 26.5%[20]. In the SCORE-BRVO study, the percentage of patients with a ≥15 letters increase in BCVA gain at 12mo with 1 mg intravitreal TA was 28.9%[21]. In our study, 21 (55.2%) of the patients achieved ≥15 letters improvement, of which 8 (38%) were CRVO and 13 (62%) were BRVO. Although our follow-up period is considerably longer than these studies, we think that our findings are similar to the literature. In addition, we attribute the high BCVA gain in our study to the fact that those with ischemic CRVO and macular ischemia were not included in the current study, and that the patients were treatment-naive.

In a prospective, nonrandomized case series, Mayer *et al*[22] compared a dexamethasone implant with dexamethasone implant monotherapy after three intravitreal injections of bevacizumab in eyes with ME secondary to RVO. This study found that DEX implant monotherapy was associated with a better functional outcome in BRVO patients, whereas both treatment modalities demonstrated no functional difference in CRVO patients. In our study, long-term intravitreal DEX implant monotherapy demonstrated good anatomical and functional results in both BRVO and CRVO patients. However, the study by Mayer *et al*[22] shares 6-month results, while our study has a median value of 62mo. Therefore, our study provides a more elaborate outcome than short-term monotherapy results as it presents repeated intravitreal DEX implant results in the long term.

In the GENEVA trial, 32.8% of eyes receiving recurrent intravitreal DEX implant treatment had an increase in IOP of at least 10 mm Hg from baseline at 12mo. The IOP elevation was controlled with observation or topical anti-glaucomatous drugs[7]. In our study, 26.3% of the patients required anti-glaucomatous treatment, consistent with the literature.

In the IRGREL-DEX study, 15 (93.7%) of 16 phakic eyes at baseline in the naive DME group receiving intravitreal DEX implant monotherapy underwent cataract surgery during 24-month follow-up period[23]. In the present study, 20 eyes were phakic at baseline, and 18 (90%) of them underwent phacoemulsification surgery during the follow-up period. As it is reported previously for many times, cataract development is a well-known complication of DEX implant treatment and develops in almost all cases in the long term.

We know that BRVO and inflammation increase the incidence of ERM[24]. During the follow-up period, two patients diagnosed with BRVO were operated on because of their decreased visual acuity due to ERM. One patient with BRVO had PPV due to vitreous hemorrhage during the follow-up. In the previous studies, the efficacy of the laser photocoagulation therapy in the treatment of BRVO has not been demonstrated, and the focal photocoagulation therapy has not been recommended[25-26]. However, we performed focal photocoagulation treatment in the ischemic areas as needed in our clinic. Yet vitreous hemorrhage was observed in one of our patients, even though we had performed focal laser photocoagulation in the ischemic areas.

When we evaluated the OCT findings, none of the patients had SMD at the last visit. In a retrospective study, Ding *et al*[27] showed that intravitreal DEX implant therapy was more effective on SMD than the anti-VEGF therapy in the treatment of ME secondary to RVO. Moreover, in another study, Horozoğlu *et al*[28] showed that the intravitreal DEX implant was highly effective on SMD in the short-term results of the intravitreal DEX implant treatment in resistant DME patients. In a retrospective study conducted with resistant and naive RVO-ME patients, a decrease in HRF was observed at the end of 6mo, but it was not statistically significant[29]. In the current study, the baseline HRF number decreased but there

was no statistically significant difference when compared to the final visit. Our results were found to be compatible with the literature. In a retrospective study evaluating OCT biomarkers before and after the intravitreal DEX implantation in the patients with anti-VEGF-resistant ME; the percentage of EZ-ELM defect, DRIL, and ERM significantly worsened at the last visit[28]. In our study, the presence of DRIL, ERM and EZ-ELM defects increased at the last visit compared to the beginning, but it was not statistically significant. We thought that the DRIL, EZ-ELM defects and ERM increase were due to the recurrent ME. Rebound ME occurred in these patients due to the lack of regular show-up of the patients to their visits during the PRN regimen. More reliable results can be obtained by choosing a treat-and-extend regimen instead of PRN in the DEX monotherapy. In that study[28], all anti-VEGF-resistant MEs were included in the study and followed for 3mo, but in our study, naive patients, including only RV-ME patients, were followed for at least 60mo. We think that our results are more reliable in assessing the therapeutic effect of intravitreal DEX implants, since evaluating the results of DME and RVO-ME patients together may affect the outcome. We would also like to point out that although the presence of ERM and EZ-ELM defects increased, the final BCVA was significantly higher when compared to the baseline.

In many studies on RVO in the literature, age and initial BCVA were found to be among the most important factors affecting the prognosis[25-26]. In our study, the final BCVA was negatively correlated with age and EZ-ELM defect. Although our results are consistent with the literature, our study also revealed that the EZ-ELM defect is an important OCT parameter for BCVA prediction.

A total of 13 subjects (34.2%) in our study group have been followed-up without treatment for an average of 34.2±15.7mo, and this period is quite long. This demonstrates that with the DEX treatment, patients need fewer injections after a while and may even end the treatment. This reduction in the frequency of visits and the number of injections can significantly reduce the treatment and cost burden.

The main limitation of this study was its retrospective design. However, we think that we have overcome this limitation with the advantages of a long follow-up period, pure cohort group, and the standardization of our data (same OCT device and evaluation by the same experienced investigators).

In conclusion, the long-term intravitreal DEX monotherapy in the patients with ME secondary to CRVO and BRVO presented a favorable safety and tolerability profile. These results demonstrated that the DEX implant for RVO-ME patients is a reproducible treatment without safety concerns. Complications such as cataract and glaucoma were easily managed. More comprehensive results can be reached with a larger number of patients and prospective randomized studies.

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REFERENCES

1 Romano F, Lamanna F, Gabrielle PH, *et al*. Update on retinal vein occlusion. *Asia Pac J Ophthalmol* (*Phila*) 2023;12(2):196-210.

2 Nicholson L, Talks SJ, Amoaku W, *et al*. Retinal vein occlusion (RVO) guideline: executive summary. *Eye* (*Lond*) 2022;36(5):909-912.

3 Song PG, Xu YH, Zha MM, *et al*. Global epidemiology of retinal vein occlusion: a systematic review and meta-analysis of prevalence, incidence, and risk factors. *J Glob Health* 2019;9(1):010427.

4 Scott IU, Campochiaro PA, Newman NJ, *et al*. Retinal vascular occlusions. *Lancet* 2020;396(10266):1927-1940.

5 Arrigo A, Bandello F. Retinal vein occlusion: drug targets and therapeutic implications. *Expert Opin Ther Targets* 2021;25(10): 847-864.

6 Hu QM, Li HY, Xu WH, *et al*. Comparison between Ozurdex and intravitreal anti-vascular endothelial growth factor treatment for retinal vein occlusion-related macular edema: a systematic review and meta-analysis of randomized controlled trials. *Indian J Ophthalmol* 2019;67(11):1800-1809.

7 Haller JA, Bandello F, Belfort R, *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(12):2453-2460.

8 Neves P, Ornelas M, Matias I, *et al*. Dexamethasone intravitreal implant (Ozurdex) in diabetic macular edema: real-world data versus clinical trials outcomes. *Int J Ophthalmol* 2021;14(10):1571-1580.

9 Karasu B, Kesim E, Celebi ARC. The efficacy of different anti-vascular endothelial growth factor agents, and dexamethasone implant therapy in patients with serous retinal detachment caused by Irvine-Gass syndrome. *Eur J Ophthalmol* 2024;34(2):510-523.

10 Qiu XY, Hu XF, Qin YZ, *et al*. Comparison of intravitreal aflibercept and dexamethasone implant in the treatment of macular edema associated with diabetic retinopathy or retinal vein occlusion: a Meta-analysis and systematic review. *Int J Ophthalmol* 2022;15(9): 1511-1519.

11 Mello Filho P, Andrade G, Maia A, *et al*. Effectiveness and safety of intravitreal dexamethasone implant (ozurdex) in patients with diabetic macular edema: a real-world experience. *Ophthalmologica* 2019;241(1):9-16.

12 Arf S, Sayman Muslubas I, Hocaoglu M, *et al*. Spectral domain optical coherence tomography classification of diabetic macular edema: a new proposal to clinical practice. *Graefes Arch Clin Exp Ophthalmol* 2020;258(6):1165-1172.

13 Sun JK, Lin MM, Lammer J, *et al*. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with center-involved diabetic macular edema. *JAMA Ophthalmol* 2014;132(11): 1309-1316.

14 Zur D, Iglicki M, Busch C, *et al*. OCT biomarkers as functional outcome predictors in diabetic macular edema treated with dexamethasone implant. *Ophthalmology* 2018;125(2):267-275.

15 Ajay K, Mason F, Gonglore B, *et al*. Pearl necklace sign in diabetic macular edema: evaluation and significance. *Indian J Ophthalmol* 2016;64(11):829-834.

16 Garay-Aramburu G, Gómez-Moreno Á. A 5-year follow-up study of the treatment of macular edema due to retinal vein occlusion using dexamethasone intravitreal implants. *J Ocul Pharmacol Ther* 2018;34(6):436-441.

17 Mayer WJ, Wolf A, Kernt M, *et al*. Twelve-month experience with Ozurdex for the treatment of macular edema associated with retinal vein occlusion. *Eye* (*Lond*) 2013;27(7):816-822.

18 Scott IU, VanVeldhuisen PC, Ip MS, *et al*. Effect of bevacizumab vs aflibercept on visual acuity among patients with macular edema due to central retinal vein occlusion: the SCORE2 randomized clinical trial. *JAMA* 2017;317(20):2072-2087.

19 Coscas G, Augustin A, Bandello F, *et al*. Retreatment with Ozurdex for macular edema secondary to retinal vein occlusion. *Eur J Ophthalmol* 2014;24(1):1-9.

20 Ip MS, Scott IU, VanVeldhuisen PC, *et al*. A randomized trial comparing the efficacy and safety of intravitreal triamcinolone with observation to treat vision loss associated with macular edema secondary to central retinal vein occlusion: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) study report 5. *Arch Ophthalmol* 2009;127(9):1101-1114.

21 Scott IU, Ip MS, VanVeldhuisen PC, *et al*. A randomized trial comparing the efficacy and safety of intravitreal triamcinolone with standard care to treat vision loss associated with macular Edema secondary to branch retinal vein occlusion: the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) study report 6. *Arch Ophthalmol* 2009;127(9):1115-1128.

22 Mayer WJ, Remy M, Wolf A, *et al*. Comparison of intravitreal bevacizumab upload followed by a dexamethasone implant versus dexamethasone implant monotherapy for retinal vein occlusion with macular edema. *Ophthalmologica* 2012;228(2):110-116.

23 Iglicki M, Busch C, Zur D, *et al*. Dexamethasone implant for diabetic macular edema in naive compared with refractory eyes: The International Retina Group Real-Life 24-Month Multicenter Study. The irgrel-dex Study. *Retina* 2019;39(1):44-51.

24 Yoshimura T, Sonoda KH, Sugahara M, *et al*. Comprehensive analysis of inflammatory immune mediators in vitreoretinal diseases. *PLoS One* 2009;4(12):e8158.

25 Campochiaro PA, Hafiz G, Mir TA, *et al*. Scatter photocoagulation does not reduce macular edema or treatment burden in patients with retinal vein occlusion: the RELATE trial. *Ophthalmology* 2015;122(7):1426-1437.

26 Wykoff CC, Ou WC, Wang R, *et al*. Peripheral laser for recalcitrant macular edema owing to retinal vein occlusion: the WAVE trial. *Ophthalmology* 2017;124(6):919-921.

27 Ding XF, Hu YJ, Yu HH, *et al*. Changes of optical coherence tomography biomarkers in macular edema secondary to retinal vein occlusion after anti-VEGF and anti-inflammatory therapies. *Drug Des Dev Ther* 2022;16:717-725.

28 Horozoglu F, Sener H, Polat OA, *et al*. Predictive impact of optical coherence tomography biomarkers in anti-vascular endothelial growth factor resistant macular edema treated with dexamethasone implant. *Photodiagnosis Photodyn Ther* 2023;42:103167.

29 Castro-Navarro V, Monferrer-Adsuara C, Navarro-Palop C, *et al*. Optical coherence tomography biomarkers in patients with macular edema secondary to retinal vein occlusion treated with dexamethasone implant. *BMC Ophthalmol* 2022;22(1):191.