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CLINICAL INVESTIGATION

Improved visual outcome with early treatment in macular edema secondary to retinal vein occlusions: 6-month results of a Korean RVO study

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Abstract
Purpose To determine the correlation between the duration of macular edema (ME) and visual outcomes among Korean patients with retinal vein occlusion (RVO).
Methods Multicenter, interventional case series. Treatment-naive patients ($n = 249$) with branch or central RVO (BRVO/CRVO) and ME for <6 months were included. We assessed the correlation between the duration of ME and treatment outcomes including the mean logarithm of the minimum angle of resolution best-corrected visual acuity (logMAR BCVA) improvement, the proportion of patients achieving at least a 3-line gain in BCVA, and the mean reduction in central retinal thickness (CRT) at 6 months.
Results One hundred and fifty-six patients with BRVO and 93 patients with CRVO were divided into five groups based on the duration of ME (<2, 2–4 weeks, 1–2, 2–3, 3–6 months); the mean baseline BCVA and CRT among the groups did not differ significantly. In BRVO, the mean logarithm of the minimum angle of resolution (logMAR) BCVA improvements in the groups were 0.51, 0.32, 0.17, 0.19, and 0.13, respectively ($P = 0.002$). The respective percentages of at least 3-line gains were 64, 53, 39, 38, and 21 % ($P < 0.001$). The BCVA didn't significantly improve in CRVO. The decrease in CRT was not correlated significantly with the duration of ME in either disease.
Conclusions Treatment of BRVO as early as 2 weeks after onset of ME enhanced the visual outcome; there was no correlation in the patients with CRVO. This finding supports the current trend favoring early treatment to obtain better visual outcomes in patients with BRVO.

Keywords Retinal vein occlusion · Macular edema · Duration of symptom · Early treatment · Korean patients

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Introduction

Macular edema (ME) is the most frequent cause of visual loss following branch retinal vein occlusion (BRVO) and central retinal vein occlusion (CRVO). Many studies report the natural course and prognosis of ME [1–4]; however, the results vary because most of these studies used a small number of patients or examined a subgroup of baseline characteristics. Meta-analyses of published data show that visual acuity (VA) generally improves in the eyes of BRVO cases, but clinically significant improvement

beyond 20/40 is uncommon, whereas the majority of studies report a VA decrease over time in the eyes of CRVO cases [3, 4]. Several recent clinical trials report the efficacy and safety of both steroids and anti-vascular endothelial growth factor (VEGF) drugs [5–9]. The results of these studies suggest that patients with shorter duration of ME before treatment had better visual recovery. A post hoc analysis of the Global Evaluation of Implantable Dexamethasone in Retinal Vein Occlusion with Macular Edema (GENEVA) study found that each 1-month increase in ME duration was associated with a significantly lower likelihood of achieving either an improvement in the best-corrected visual acuity (BCVA) of at least 15 letters or a reduction in the central retinal thickness (CRT) of at least 200 μm, when either parameter was evaluated 6 months after treatment [10]. However, in these studies, <20 % of patients received treatment within 3 months after the onset of ME.

In the current study, we investigated whether earlier treatment improved visual outcomes at 6 months after treatment in a Korean retinal vein occlusion (K-RVO) study, where more than 80 % of patients were treated within 3 months after onset.

Methods

Patient population

Patients enrolled in the K-RVO study were treatment-naive patients with RVO with a disease duration of 6 months or shorter. Patients with diabetic retinopathy (except mild nonproliferative diabetic retinopathy), RVO due to other causes (e.g., known uveitis or vasculitis), RVO accompanied by arterial occlusion or ocular ischemic syndrome or a prior history of intraocular injection, laser treatment or vitrectomy for RVO, were excluded from the study population. The study was conducted at 41 sites nationwide and 63 retina specialists participated. Among 557 patients (354 with BRVO; 203 with CRVO), 331 patients (208 with BRVO; 123 with CRVO) were followed at 6 months. The baseline characteristics of the K-RVO study and baseline predictors of the 6-month visual outcome were evaluated previously [1]. Briefly, multivariate regression analysis showed that significant baseline predictors of the 6-month visual outcome were the baseline BCVA, age, and duration of ME among patients with BRVO. Among those with CRVO, only the baseline BCVA was significant. In neither the patients with BRVO nor those with CRVO, was there any significant difference in either the baseline BCVA or baseline CRT between patients evaluated at 6 months and those for whom there was no follow-up evaluation.

Patients selected for this study were limited to those who had ME on optical coherence tomography (OCT) and those who had received a treatment and whose complete data was available at 6 months as well as at baseline. Patients who failed to provide the duration of ME were excluded. This study was approved by the Institutional Review Board and Ethics Committee of Asan Medical Center and conformed to the tenets of the Declaration of Helsinki.

Outcome measures

The duration of ME was defined as the time between the onset of ME (based on patient history, ophthalmologic diagnosis, or both) and the time of the first treatment. The outcome measures included BCVA and CRT. We evaluated the differences in BCVA and CRT between baseline and 6 months. For BCVA, the mean improvement in logMAR VA, the proportion of patients that achieved an improvement in logMAR VA of at least 0.3, and the proportion of patients with loss of logMAR VA of at least 0.3 were analyzed. For CRT, the mean improvement in CRT [in microns (μm)], and the incidence of a 200-μm or more reduction in CRT were compared among the groups. CRT was automatically measured in the central 1-mm-diameter region of the ETDRS circle. Differences in central macular thickness, depending on the OCT machine used, were corrected for as previously described [11, 12].

Data analysis and statistical methods

Data were analyzed using SPSS software (version 18.0, SPSS Inc., Chicago, IL, USA). The baseline characteristics between each group defined by the duration of ME were analyzed using analysis of variance (ANOVA) and chi-square analysis. Continuous variables were expressed as the mean with standard deviation and analyzed using ANOVA. Categorical variables were expressed as a number and a percentage, both of which were analyzed using the chi-square test.

The correlation between the duration of ME and visual improvement was analyzed using Spearman's correlation rank test. Along with this, ANOVA and chi-square analyses were used to assess the relationship between the duration of ME at the time of the first treatment and patient outcomes 6 months after treatment.

Results

Treatment patterns

Among 233 patients with BRVO treated at baseline, 180 (77.3 %) were followed for 6 months and 156 who could

provide the duration of ME (67.0 %) were selected for this analysis. One hundred twenty-six patients were treated with intravitreal bevacizumab (Avastin, Genentech Inc., South San Francisco, CA, USA), 15 were treated with intravitreal triamcinolone, and 15 were treated with focal laser photocoagulation. Among 128 patients with CRVO treated initially, 100 (78.1 %) were followed and 93 (72.7 %) were selected; 11 of these patients were treated with intravitreal triamcinolone or laser, and 82 were treated with intravitreal bevacizumab.

The mean numbers of treatments at 6 months were 2 ± 1.2 (range 1–7) for BRVO and 3 ± 1.6 (range 1–7) for CRVO.

Duration of symptoms

The timing of the first treatment ranged from 1 week to 6 months after the onset of symptoms. Patients were divided into five groups depending on the duration of symptoms: group 1 (<2 weeks), group 2 (2–4 weeks), group 3 (1–2 months), group 4 (2–3 months), and group 5 (3–6 months). The respective numbers of patients in each group were 28, 32, 51, 21, and 24 with BRVO and 21, 17, 27, 7 and 21, with CRVO.

Baseline characteristics of patients classified by ME duration

Tables 1 and 2 show the baseline characteristics of BRVO and CRVO. The selected parameters, including baseline VA and baseline CRT, did not differ among the groups, which were classified according to the duration of ME. BRVO patients were evaluated separately from CRVO patients.

Table 1 Comparison of baseline characteristics among the five BRVO patient groups defined by the duration of ME

Duration of ME						
Baseline characteristic	≤2 weeks	2–4 weeks	1–2 months	2–3 months	3–6 months	*P* value
Age ± SD (years)	54 ± 8.9	56 ± 8.9	54 ± 11.6	57 ± 8.6	62 ± 10.5	0.16[a]
No. men (%)	12 (42.9)	14 (43.8)	17 (33.3)	6 (28.6)	7 (29.2)	0.64[b]
No. smokers (%)	5 (19.2)	5 (15.6)	7 (14.0)	0 (0)	1 (4.5)	0.34[b]
No. with HTN (%)	9 (32.1)	1 (46.9)	29 (56.9)	9 (42.9)	11 (45.8)	0.33[b]
BMI ± SD	24.7 ± 3.7	25.0 ± 3.2	24.8 ± 2.7	23.9 ± 3.0	23.5 ± 2.3	0.33[a]
Baseline BCVA ± SD (decimal)	0.3 ± 0.2	0.3 ± 0.2	0.4 ± 0.3	0.4 ± 0.3	0.4 ± 0.3	0.39[a]
Baseline CRT ± SD (μm)	518 ± 149	493 ± 150	460 ± 164	531 ± 184	420 ± 157	0.10[a]
No. treatments	2 ± 1.0	2 ± 1.5	2 ± 1.0	2 ± 1.2	2 ± 1.4	0.65[a]

BRVO branch retinal vein occlusion, *ME* macular edema, *SD* standard deviation, *HTN* hypertension, *BMI* body mass index, *BCVA* best-corrected visual acuity, *CRT* central retinal thickness

[a] Analysis of variance

[b] Chi-square

Table 2 Comparison of baseline characteristics between the five CRVO patient groups defined by the duration of ME

Duration of ME						
Baseline characteristics	≤2 weeks	2–4 weeks	1–2 months	2–3 months	3–6 months	*P* value
Age ± SD (years)	54 ± 10.8	58 ± 11.7	60 ± 13.0	58 ± 5.8	64 ± 12.3	0.11[a]
No. men (%)	10 (47.6)	7 (41.2)	13 (48.1)	6 (85.7)	12 (57.1)	0.34[b]
No. smokers (%)	2 (11.1)	2 (12.5)	2 (8.7)	3 (42.9)	4 (23.5)	0.62[b]
No. with HTN (%)	5 (23.8)	5 (29.4)	6 (23.1)	4 (57.1)	6 (28.6)	0.49[b]
BMI ± SD	24.6 ± 4.4	23.3 ± 2.3	24.0 ± 2.8	24.6 ± 3.4	23.9 ± 2.6	0.77[a]
Baseline BCVA ± SD (decimal)	0.4 ± 0.3	0.4 ± 0.3	0.3 ± 0.3	0.2 ± 0.2	0.3 ± 0.3	0.69[a]
Baseline CRT ± SD (μm)	533 ± 171	517 ± 156	540 ± 196	662 ± 336	507 ± 246	0.56[a]
No. treatments	3 ± 1.8	3 ± 1.4	3 ± 1.5	3 ± 1.4	3 ± 1.8	0.78[a]

CRVO central retinal vein occlusion, *ME* macular edema, *SD* standard deviation *HTN* hypertension, *BMI* body mass index, *BCVA* best-corrected visual acuity, *CRT* central retinal thickness

[a] Analysis of variance

[b] Chi-square

Table 3 Effects of the duration of ME at the time of first treatment on visual outcomes at 6 months after the treatment of patients with BRVO

Duration of ME						
	≤2 weeks	2–4 weeks	1–2 months	2–3 months	3–6 months	*P* value
LogMAR BCVA improvement, mean ± SD	0.51 ± 0.50	0.32 ± 0.28	0.17 ± 0.32	0.19 ± 0.52	0.13 ± 0.40	0.002[a]
Gain of ≥0.3 (%)	18 (64 %)	17 (53 %)	20 (39 %)	8 (38 %)	5 (21 %)	0.019[b]
Loss of ≥0.3 (%)	1 (4 %)	0 (0 %)	5 (10 %)	1 (5 %)	3 (13 %)	0.275[b]
Post-hoc analysis[c]						
Group	*N*		*a*		*b*	
≤2 weeks	28		−0.514903			
2–4 weeks	32		−0.316130		−0.316130	
1–2 months	21				−0.186215	
2–3 months	51				−0.173807	
3–6 months	24				−0.133063	
Sig.			0.462		0.547	

ME macular edema, *BRVO* branch retinal vein occlusion, *logMAR BCVA* logarithm of the minimum angle of resolution best-corrected visual acuity, *SD* standard deviation

[a] Analysis of variance

[b] Chi-square

[c] Scheffe test

Effect of ME duration on visual outcomes

There was a significant correlation between the duration of ME and visual improvement in BRVO patients ($P < 0.001$, Spearman's correlation coefficient = −0.293). Analysis of patients with BRVO (Table 3; Fig. 1) showed that a shorter duration of ME was associated with a higher likelihood of achieving visual improvement 6 months after treatment. The difference was significant for both the mean BCVA improvement ($P = 0.002$) and the proportion of patients with a gain of 0.3 or more ($P = 0.019$). However, it was not significant for the proportion of patients with a loss of 0.3 or more ($P = 0.275$).

Analysis of the patients with CRVO (Table 4; Fig. 2) showed that the duration of ME was not correlated with the visual outcome 6 months after treatment. This was consistent with all three parameters measured: mean BCVA improvement ($P = 0.194$), the proportion of gain of 0.3 or more ($P = 0.359$), or the proportion of loss of 0.3 or more ($P = 0.760$).

A subgroup analysis of bevacizumab-treated patients also showed a significant correlation between the duration of ME and the mean BCVA improvement among 126 BRVO patients ($P = 0.023$, one-way ANOVA), but not among 82 CRVO patients ($P = 0.236$, one-way ANOVA).

Effect of ME duration on the anatomic outcome

The anatomic outcomes did not differ based on the duration of ME. For the patients with BRVO, the respective values for the mean improvement in CRT [mean ± standard deviation (SD)] in groups 1–5 were −190 ± 208, −179 ± 157, −172 ± 189, −207 ± 221, and −137 ± 152 microns (μm). There was no significant ($P = 0.834$) correlation between the duration of ME and the mean improvement in CRT. Moreover, there was no significant ($P = 0.905$) difference between the percentage of patients who had a reduction in CRT of 200 μm or more in relation to the duration of ME, with values of 48, 44, 41, 44, and 33 % for groups 1–5, respectively (Fig. 3).

A similar trend was seen in the analysis of patients with CRVO. The respective values for the mean improvements in CRT (μm) (mean ± SD) in groups 1–5 were −236 ± 249, −103 ± 186, −149 ± 306, −207 ± 254, and −132 ± 271 μm. The respective percentages of reductions in CRT of 200 μm or more were 65, 36, 48, 50, and 44 %. The duration of ME was not correlated with the anatomic outcome at 6 months after treatment, when the mean CRT improvement ($P = 0.646$) or the proportion of patients with a CRT reduction of 200 μm or more ($P = 0.582$) were assessed (Fig. 4).

Discussion

Previous studies suggest several predictive factors for visual outcomes in BRVO, including baseline VA, CRT, presence of macular ischemia, and integrity of the IS-OS line beneath the fovea [2, 3, 13]. The results of this analysis from the K-RVO study suggest that the duration of ME at

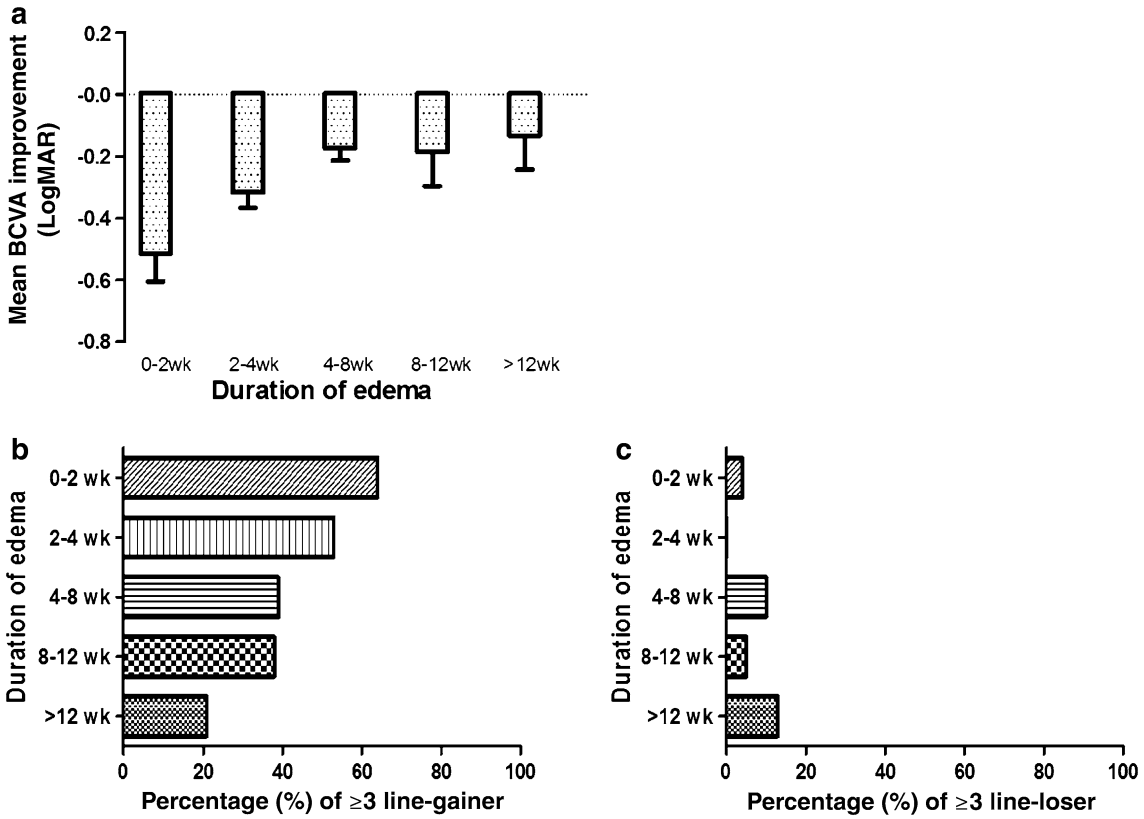

Fig. 1 The effects of the duration of ME on the best-corrected visual acuity (BCVA) outcomes 6 months after treatment of patients with branch retinal vein occlusion (BRVO). **a** The mean improvement in the BCVA. Whereas the baseline VA did not differ among the five groups, the mean BCVA improved significantly as the duration of ME decreased ($P = 0.002$, analysis of variance). **b** The percentage of patients with improved BCVA by at least three lines. An increase in the duration of ME duration is associated with a significantly ($P = 0.019$, chi-square) lower likelihood of improved BCVA by at least three lines. **c** The percentage of patients with worsened BCVA by at least three lines. The likelihood of BCVA worsening by at least three lines is unrelated to the duration of ME ($P = 0.275$, chi-square). *logMAR* logarithm of the minimum angle of resolution

Table 4 Effects of the duration of ME at the time of first treatment on visual outcomes at 6 months after the treatment of patients with CRVO

Duration of ME						
	≤2 weeks	2–4 weeks	1–2 months	2–3 months	3–6 months	*P* value
logMAR BCVA improvement, mean ± SD	−0.30 ± 0.46	+0.05 ± 0.50	−0.33 ± 0.76	−0.27 ± 0.46	−0.19 ± 0.58	0.194[a]
Gain of ≥0.3 (%)	10 (48 %)	4 (24 %)	13 (48 %)	4 (57 %)	7 (33 %)	0.359[b]
Loss of ≥0.3 (%)	2 (10 %)	3 (18 %)	6 (22 %)	1 (14 %)	5 (24 %)	0.760[b]

ME macular edema, *CRVO* central retinal vein occlusion, *logMAR BCVA* logarithm of the minimum angle of resolution best-corrected visual acuity, *SD* standard deviation

[a] ANOVA

[b] Chi-square

the time of the initial treatment is a significant predictor of the visual outcomes of patients with BRVO 6 months after treatment. In contrast, in patients with CRVO there was no significant correlation between the duration of ME and visual outcomes.

This finding is consistent with the results from several previous clinical trials, including the GENEVA, the Ranibizumab for the treatment of ME following BRAVO, and the Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE-BRVO) studies [5–7]. Each trial reports a positive correlation between the duration of ME and visual outcome. However, those studies differed in their final visual outcomes partly because of marked differences in their inclusion criteria for minimal disease duration. Given that the mean duration of ME in the BRAVO study was significantly

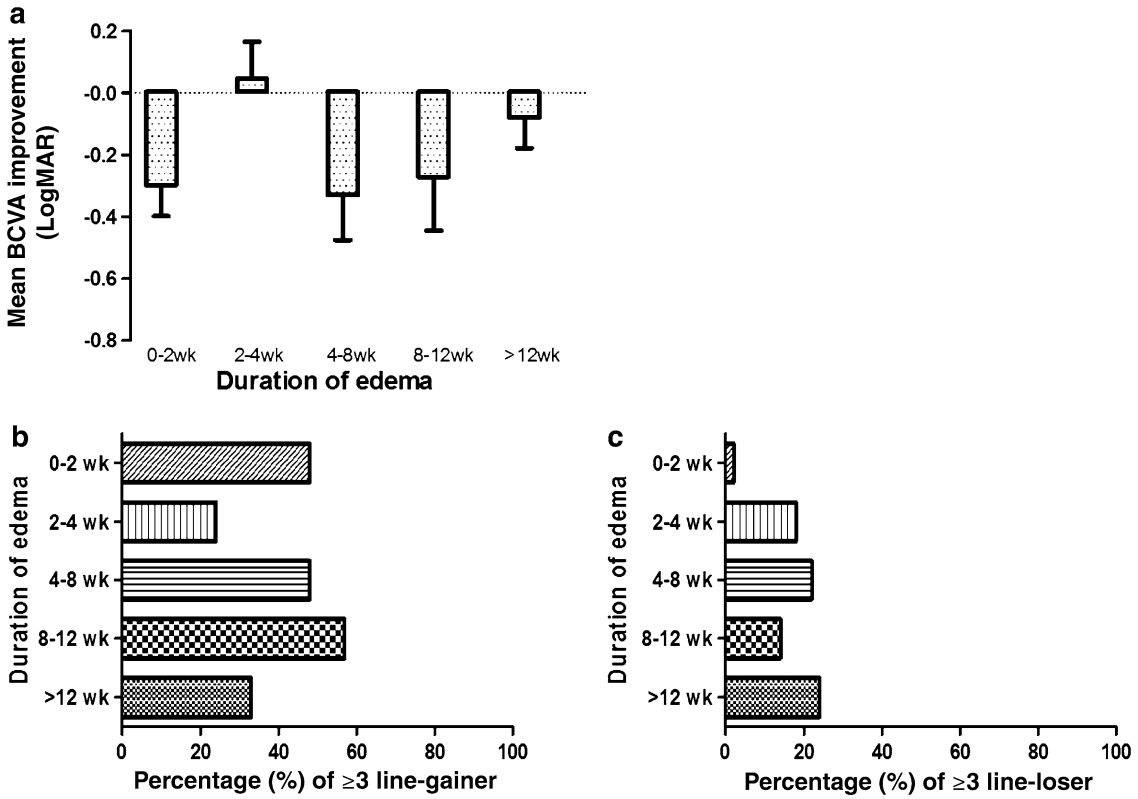

Fig. 2 The effects of the duration of macular edema on best-corrected visual acuity (BCVA) outcomes 6 months after treatment of patients with central retinal vein occlusion. The baseline VA levels do not differ among the five groups. No significant correlation is seen between the visual outcome at 6 months when evaluated as **a** the mean improvement in BCVA ($P = 0.194$, analysis of variance), **b** the percentage of patients with improved BCVA by at least three lines ($P = 0.359$, chi-square) and, **c** the percentage of patients with worsened BCVA by at least three lines ($P = 0.760$, chi-square). *logMAR* logarithm of the minimum angle of resolution

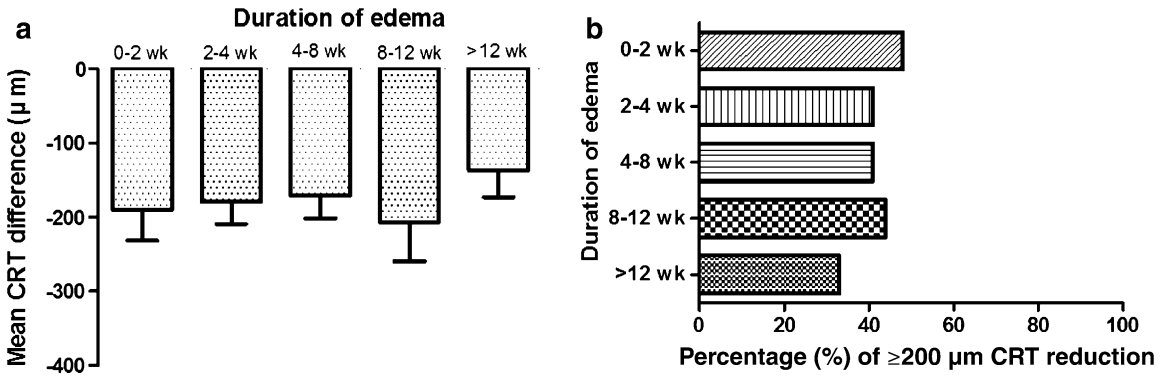

Fig. 3 The effects of the duration of ME on the central retinal thickness (CRT) outcomes 6 months after treatment of patients with branch retinal vein occlusion. The baseline visual acuity levels do not differ among the five groups, but there is no significant correlation between the duration of ME and either the **a** mean reduction in CRT ($P = 0.834$, analysis of variance) or **b** the proportion of patients with a CRT reduction of at least 200 μm ($P = 0.905$, chi-square)

shorter than that in the GENEVA study, the final outcome of the BRAVO study was significantly better. A recent post hoc analysis of the GENEVA trial reports that for every 1-month increase in ME duration, the odds of achieving a 15-letter or better improvement at month 6 decreased by 12 % in the overall population and by 14 % in the subgroup of patients with BRVO [10].

Unlike randomized clinical trials, such as the SCORE, BRAVO/Ranibizumab for the Treatment of Macular Edema after Central Retinal Vein Occlusion Study (CRUISE), and GENEVA studies, where the duration of ME ranged from 6 weeks to 12 months, in the current population, the duration of ME at the time of the first treatment ranged from 1 week to 6 months. Most patients

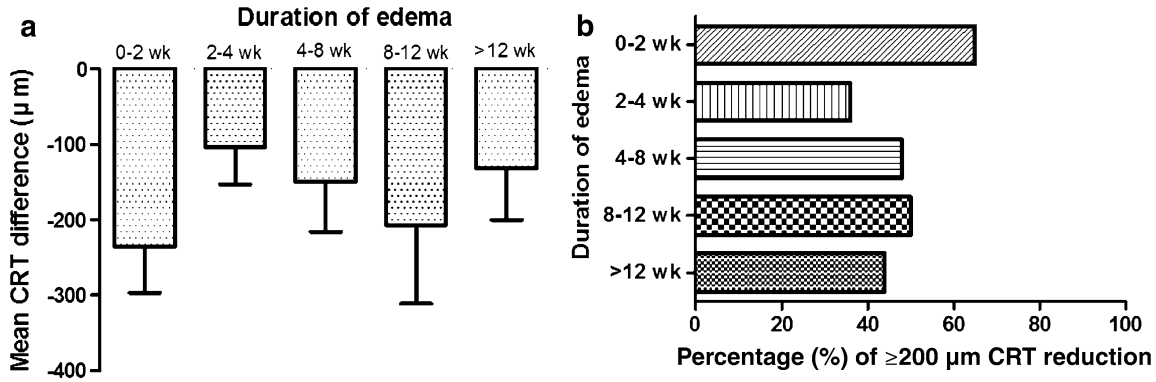

Fig. 4 The effects of the duration of macular edema (ME) on the central retinal thickness (CRT) outcomes 6 months after treatment of patients with central retinal vein occlusion. The baseline visual acuity levels do not differ significantly among the five groups, but there is no significant correlation between the duration of ME and either the **a** mean reduction in CRT ($P = 0.646$, analysis of variance), or **b** the proportion of patients with a CRT reduction of at least 200 μm ($P = 0.582$, chi-square)

(84.6 % of patients with BRVO and 77.4 % of patients with CRVO) were treated within 3 months after disease onset. A substantial number of patients (38.5 % of those with BRVO, 40.9 % of those with CRVO) were treated within 1 month after symptom onset. Therefore, the current study is particularly interesting because it showed that even earlier treatment during the first 3-month period after the onset of disease significantly improved visual outcomes at 6 months.

Interestingly, the anatomic outcomes did not differ between the five groups with different durations of ME. Therefore, earlier treatment did not necessarily enhance anatomic recovery. This discrepancy between visual recovery and anatomic recovery was also seen in the GENEVA study [5]. It is difficult to explain the mechanism of less desirable visual recovery despite the similar anatomic recovery seen in patients that received later treatment. However, one can speculate that retinal tissue, like any other neuronal tissue, failed to gain maximal recovery after exposure to chronic edema.

Several limitations should be considered when interpreting the current results. First, this study was retrospective, and the treatments were not randomized. Because this analysis was based exclusively on treated patients who were successfully followed at 6 months, we failed to include 77 (33.0 %) of the 233 initially treated patients with BRVO and 35 (27.3 %) of the 128 initially treated patients with CRVO in this analysis [13]. In addition, decisions regarding the timing of treatment were left to the discretion of each of the 63 retina specialists.

Despite these limitations, the failure to detect significant differences in terms of the baseline prognostic factors between patients who were followed at 6 months and those who were lost at 6 months suggested the validity of our findings (Kim et al., unpublished data). More importantly, the baseline BCVA, CRT and age, which were the key baseline prognostic factors in the Korean RVO study (Kim et al., unpublished data) and the SCORE study [14], did not differ among the five groups classified according to the duration of ME, among patients with BRVO and CRVO. This finding confirmed that the significantly better visual outcomes in groups of patients that received early treatment did not result from the favorable profile in their baseline characteristics.

The current study clearly showed that the advent of intravitreal steroids and anti-VEGF drugs has changed the preferred practices of Korean retina specialists when treating patients with ME secondary to RVO.

One of the major concerns about anti-VEGF injections as treatment for ME secondary to BRVO is that multiple injections are required. In a previous study, approximately 70 % of BRVO patients required repeat injections after intravitreal anti-VEGF treatment, with a mean of 2.6 injections [15]. In the current study, 81 % of 156 patients with BRVO were treated with intravitreal anti-VEGF injections and these patients had a mean of 1.9 repeat injections within 6 months.

This trend toward increased use of prompt treatments involving anti-VEGF drugs differs from the more conservative approach used in the SCORE study. Until recently, the standard of care for ME secondary to RVO has been either focal laser treatment for BRVO or observation for CRVO [9, 10].

It should be borne in mind that the timing of treatment of patients included in the current study depended solely on physician discretion. Most patients were treated initially within 3 months of symptom onset. Furthermore, 38.5 % of patients with BRVO and 40.9 % of patients with CRVO were treated within 1 month of symptom onset. This survey clearly reflected the current practice of Korean retina specialists. Nonetheless, the possibility of spontaneous recovery can be excluded in the current study.

One can argue that good VA might have been attained without treatment. A systematic review of the natural history of BRVO reports that clinically significant improvement beyond 20/40 is uncommon among untreated symptomatic BRVO patients with poor VA at baseline [3]. In the current study, mean logMAR BCVA at 6 months was 0.18, 0.27, 0.34, 0.51, and 0.40 in groups in which ME duration was <2, 2–4 weeks, 1–2, 2–3, and 3–6 months, respectively. The group in which treatment was delivered earliest (within 2 weeks after the onset of ME) achieved a mean logMAR BCVA of 0.18 (comparable to Snellen VA of 20/30) at 6 months, supporting the idea that early treatment is beneficial for visual outcome up to the 6-month follow-up.

In the HORIZON trial, which was an open-label extension trial of 12-month ranibizumab treatment for ME and followed the BRAVO and CRUISE studies, the sham/0.5 mg group (delayed treatment group) showed improvement of visual outcome comparable to the early treatment groups [16]. However, earlier treatment still seemed to be worthwhile because it provided more rapid visual restoration during the first 12 months as well as better, albeit not remarkably so, visual outcome at the final visit.

In general, the validity of any treatment depends on the ratio of its effectiveness to its safety. Given that several clinical trials and numerous smaller clinical studies have shown that intravitreal injection of anti-VEGF or steroid drugs is safe, more physicians are adopting earlier treatment for patients with ME secondary to BRVO despite the relatively good natural history of patients with BRVO [3]. In the current study, only 15.4 % of patients received treatment more than 3 months after symptom onset, and 38.5 % were treated within 4 weeks of symptom onset.

Unlike BRVO, the visual outcomes in patients with CRVO did not differ based on the duration of ME. This can indicate that earlier treatment is unnecessary for patients with ME secondary to CRVO. Nevertheless, because the clinical records of patients with CRVO show both considerable risk of disease progression if patients are left untreated and a low rate of spontaneous improvement [4], delayed use of safe and effective treatments in these patients should be avoided. The ability to detect a significant association between disease duration and treatment outcomes in the patients with CRVO in the current study might have been affected by the relatively small sample size.

In conclusion, the current results suggest that prompt treatment (even as early as 2 weeks) after diagnosis of ME may increase the chances of favorable visual outcomes in patients with BRVO. Although this analysis did not detect a significant association between disease duration and treatment outcomes in patients with CRVO, these results should not be interpreted as supportive of delayed treatment in those patients. Additional prospective, randomized studies with longer follow-up periods are needed to confirm the current observations.

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