SIN-CHN SCIENTIFIC PRESS PTE.LTD.

Molecular & Cellular Biomechanics 2025, 22(4), 1482.
https://doi.org/10.62617/mcb1482

Article

Observation of the efficacy of ranibizumab combined with dexamethasone intravitreal implant in the treatment of retinal vein occlusion-associated macular edema

Jiao Huang[1,2], Xiaoting Yuan[1,2], Xiaojuan Cheng[1,2], Lishuai Xu[1,2,*]

[1] Department of Ophthalmology, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, China
[2] Medical School of Ophthalmology and Optometry, North Sichuan Medical College, Nanchong 637000, China
*** Corresponding author:** Lishuai Xu, xulishuai12@gmail.com

CITATION

Huang J, Yuan X, Cheng X, Xu L. Observation of the efficacy of ranibizumab combined with dexamethasone intravitreal implant in the treatment of retinal vein occlusion-associated macular edema. Molecular & Cellular Biomechanics. 2025; 22(4): 1482. https://doi.org/10.62617/mcb1482

ARTICLE INFO

Received: 5 February 2025
Accepted: 28 February 2025
Available online: 18 March 2025

Abstract: Purpose: To observe the short-term efficacy and safety of ranibizumab combined with dexamethasone intravitreal implant (DEX) in the treatment of macular edema (ME) secondary to retinal vein occlusion (RVO) (RVO-ME), with a focus on biomechanical changes in retinal vascular and tissue dynamics. **Methods:** A prospective clinical case study was conducted. A total of 88 patients (88 eyes) with RVO-ME were included in the study. According to the treatment strategy, they were divided into the DEX and ranibizumab combination group (combination group), the DEX group, and the ranibizumab group, with 33 eyes, 24 eyes, and 31 eyes, respectively. Patients underwent best-corrected visual acuity (BCVA), spectral domain optical coherence tomography (SD-OCT), optical coherence tomography angiography (OCTA), contrast sensitivity (CS), and visual field testing. The combination group received DEX one week after the first ranibizumab injection, while the other groups followed standard regimens. Follow-up assessments were conducted at 1 week, 2 weeks, and monthly for 6 months. **Results:** All groups showed significant improvements in BCVA, the retinal thickness (CRT), superficial and deep macular vascular density (SVC-MVD) and macular vascular density of deep macular vascular complex (DVC-MVD), mean defect of light sensitivity (MD), contrast sensitivity (CS), compared to baseline ($P < 0.001$). The combination group demonstrated superior vascular microstructure improvement, with better SVC-MVD and DVC-MVD at multiple time points ($P < 0.05$). Biomechanical analysis revealed enhanced vascular compliance and hemodynamic stability in the combination group, contributing to its efficacy. The average injection frequency was lower in the combination group (4.39 ± 0.55) compared to the ranibizumab group (4.65 ± 0.92, $P < 0.05$). Adverse events included subconjunctival hemorrhage and transient intraocular pressure elevation, with no serious complications. **Conclusion:** The combined group had a more significant effect in improving vascular microstructure, good short-term efficacy, could reduce the number of injections, and had better safety. The biomechanical benefits, including improved vascular compliance and hemodynamics, highlight its potential for optimizing retinal microcirculation.

Keywords: ranibizumab; DEX; retinal vein occlusion; macular edema; combined therapy; biomechanics; hemodynamics

1. Introduction

Retinal vein occlusion (RVO) is a common retinal fundus vascular disease, which seriously threatens patients' vision. Macular edema (ME) is one of the most common complications and the main cause of vision decline [1]. According to the location of occlusion, RVO is mainly divided into central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). At present, the methods to treat RVO include

laser photocoagulation, hormone therapy, intravitreal injection of anti-angiogenic factor (VEGF), and vitrectomy [2]. VEGF is a key endogenous factor to promote the growth of vascular endothelial cells. It helps to rebuild endothelial cells under normal physiological conditions and form functional blood vessels without leakage. The increase of VEGF level is closely related to the enhancement of vascular permeability, matrix degradation, migration and proliferation of endothelial cells, and angiogenesis [3,4]. Ranibizumab is a recombinant monoclonal antibody fragment with a similar effect to bevacizumab, and its Fab fragment can specifically bind VEGF, which can inhibit the formation of new blood vessels and reduce ME [5]. Degradable dexamethasone intravitreal implant (DEX) is a compound preparation composed of polylactic acid and polyglycolic acid polymer. With the posterior segment drug delivery system, DEX with a total dose of 0.7 mg is implanted into the vitreous, and powerful hormones can be released in the eye for up to 6 months, which can inhibit the synthesis of prostaglandin and other inflammatory mediators, reduce VEGF expression, reduce vascular leakage, inhibit cellulose deposition, enhance the tight junction of vascular endothelium, and regulate the functions of retinal cells, Müller cells, and microglia [6,7]. In view of the limitation of a single drug, combined drug therapy has a certain prospect, and some clinical studies on combined drugs have been carried out at present. However, the treatment scheme, safety, and effectiveness are still controversial and lack clinical evidence [8,9]. For patients with RVO-ME, the initial sufficient amount and long-term standardized treatment are emphasized, and the combination treatment options need to be explored urgently. Different from the previous combination methods, this study added DEX drugs to the anti-VEGF drug treatment scheme (3+prn) and evaluated the curative effect in multiple dimensions at the same time. By comparing the therapeutic effects of the combination of ranibizumab and DEX with that of a single drug, we explored a better treatment scheme in order to provide new ideas for the treatment of RVO-ME. The results are reported as follows.

2. Objects and methods

Prospective clinical case study. All patients were informed and signed a written informed consent form.From June 2022 to June 2023, RVO-ME was first diagnosed in the Affiliated Hospital of North Sichuan Medical College and was willing to be included in the clinical data of patients in this study. A total of 102 patients were collected, of whom 14 were lost to follow-up. Finally, 88 patients (88 eyes) aged 40–65 years were included in the study according to the standard, and they were followed up for 6 months.

Inclusion criteria: (1) The diagnosis and treatment criteria of RVO-ME were met, and the diagnosis was confirmed as RVO, Evaluation indicators include fundus fluorescein angiography (FFA), optical coherence tomography angiography (OCTA) , optical coherence tomography (OCT) and the central retinal thickness (CRT). (2) First onset and course of disease ≤ 3 months; (3) the age is 40–65 years old, regardless of sex; (4) before treatment, the intraocular pressure (IOP) measured by a non-contact tonometer was 10–21 mmHg; (5) agree to the treatment plan, cooperate to complete the examination during the follow-up, and follow up with the patients for 6 months or more on time after the operation; (6) to minimize confounding factors, we only

included individuals whose systemic conditions (e.g, hypertension, diabetes) were under stable medical control for at least 3 months prior to enrollment, without any history of intravitreal injections or other ocular interventions for RVO or other macular diseases. Exclusion criteria: (1) Patients with unclear refractive medium due to diseases such as corneal opacity, lens opacity or vitreous hemorrhage who cannot complete fundus examination; (2) patients with age-related macular degeneration, epimacular membrane and other fundus diseases; (3) those who were previously diagnosed as glaucoma; (4) the patient currently has acute eye inflammation and other diseases; (5) taking hormonal drugs or using hormones locally (including the history of peribulbar injection around the eye); (6) patients whose eyes have been treated with vitrectomy or retinal photocoagulation before; (7) patients with severe cardiovascular and cerebrovascular diseases, abnormal liver and kidney functions, patients with a history of acute infection, autoimmune diseases or malignant tumors and other serious systemic diseases, or patients with an allergic history to fluorescein sodium and povidone iodine; (8) those with poor follow-up compliance; (9) we additionally excluded patients if their comorbidities (e.g., uncontrolled diabetes) or prior treatments (e.g., previous anti-VEGF injections) could significantly affect the treatment outcomes.

Record all patients' names, gender, age, eyes, hypertension, diabetes, and other basic diseases. Before operation, slit lamp examination, anterior segment photography, intraocular pressure (IOP) measured by Japanese TOPCON and NIDEK non-contact tonometer, best corrected vision (BCVA) examination by international standard visual acuity chart and fundus photography were improved to obtain retinal images. CRT was measured by OCT; OCTA detected the area of the fovea without perfusion (FAZ), obtained the blood flow density (MVD) of the superficial vascular complex (SVC) and the MVD value of the deep vascular complex (DVC) in the macular area, measured the macular contrast sensitivity (CS) by the MARS digital contrast sensitivity test card of TheMars Sensor Company in the United States, and measured the central visual field average defect (MD) and IOP by OCTOPUS101 and 900 automatic perimeters in Switzerland. All patients were examined by the same experienced doctor.

Table 1. Comparison of baseline data of three groups of patients (S) $\chi \pm s$.

	n	**Male/female (example)**	**Age (years old) M(Q1, Q3)**	**BCVA (LogMAR)**	**CRT (μm)**	**IOP (mmHg)**	**RVO type**	
							CRVO	BRVO
Joint group	33	18/15	55(47,60)	0.90 ± 1.34	636.48 ± 19.89	13.85 ± 2.60	16	17
DEX group	24	11/13	56(47,61)	0.90 ± 1.07	627.58 ± 26.48	13.79 ± 2.66	11	13
Ranibizumab group	31	16/15	54(45,60)	0.89 ± 1.09	631.48 ± 22.16	13.58 ± 2.38	14	17
Inspection value		χ^2 = 0.426	χ^2 = 1.273	F = 0.394	F = 0.014	F = 0.105	χ^2 = 0.079	
P value		0.808	0.542	0.956	0.983	0.907	0.961	

Note: BCVA (logMAR): the logarithm of the minimum resolution angle is the best corrected vision; CRT: retinal thickness of fovea; IOP: intraocular pressure; RVO: retinal vein occlusion; DEX: dexamethasone intravitreal implant; CRVO: central retinal vein occlusion; BRVO: branch retinal vein occlusion.

All patients were divided into three groups: DEX combined with ranibizumab (combined group), DEX group, and ranibizumab group, with 33 cases (33 eyes), 24 cases (24 eyes), and 31 cases (31 eyes), respectively. The patients were analyzed in detail, and the treatment scheme was selected according to their personal wishes. The sex composition ratio ($\chi^2 = 0.426$), age ($\chi^2 = 1.273$), logMAR BCVA ($F = 0.394$), CRT ($F = 0.014$), IOP ($F = 0.105$), and RVO classification ($\chi^2 = 0.079$) of the three groups were compared.(**Table 1**).

Vitreous cavity injection was performed in an aseptic laminar flow operating room according to aseptic operation procedures. The patient was lying on his back on the operating table, and the eye drops of procaine were dripped into his eyes. During the operation, the eyelids and eyelashes of the eyes were disinfected with 5% povidone iodine, and the area around the eyes was covered with sterile cloth. The operation membrane was attached, and the eyelids were opened with an eyelid opener. After dilution with 5% povidone iodine, the conjunctival sac was disinfected, and it stayed for 90 s, and the conjunctival sac was washed with normal saline. Locate 3.5–4 mm behind the scleral margin of the superior or inferior temporal horn, use an injection needle to penetrate the surface of the eyeball vertically to the scleral wall, enter the vitreous cavity, inject 0.05 mL or 0.7 mg of ranibizumab towards the center of the ball, pull out the needle after the injection, press the injection site with a cotton swab, and monitor the patient's condition after the operation. After no discomfort, apply eye ointment to the conjunctival sac, and wrap the surgical eye with sterile gauze. All operations are completed by the same experienced deputy chief physician.

In the combined group, 3+1+on-demand (prn) therapy was adopted: the first intravitreal injection was ranibizumab (0.05 mL), and dexamethasone (0.7 mg) was administered one week later. This 1-week interval was chosen based on prior clinical studies suggesting that a short delay allows the initial anti-VEGF effect to stabilize retinal thickness and provides a safer environment for subsequent steroid therapy, thereby maximizing their synergistic benefits [10,11]. If macular edema did not completely resolve or reappear on subsequent evaluations, ranibizumab was re-administered on an as-needed basis with the same dosage as before. The DEX group was treated with 1+prn and treated as needed after a single intravitreal injection of DEX (the minimum injection interval was 3 months). The ranibizumab group was treated with a 3+prn regimen, with routine treatment of ranibizumab once a month for three consecutive times, followed by the treatment of ranibizumab as needed. All patients in the three groups were observed for 6 months. Re-treatment criteria: CRT ≥ 300 μm or single increase > 50 μm.

Review time: 1 week, 2 weeks, and every month after the first injection, followed up for 6 months. During the follow-up, the same equipment and methods were used before treatment to carry out relevant examinations. BCVA, CRT, FAZ area, SVC-MVD, DVC-MVD, CS, MD, IOP, and other indicators were observed, and retinal vascular perfusion was evaluated by FFA at 3 and 6 months. The times of intravitreal injection, the state of the lens before and after the operation, and the occurrence of complications were recorded. In the process of monitoring intraocular pressure, if the IOP of the patient's operating eye is more than or equal to IOP ≥ 25 mmHg, the intraocular pressure is controlled with intraocular pressure-lowering drugs, and if there

is a large area of retinal capillary without perfusion (> 10 optic disc area), local retinal laser photocoagulation is performed [12,13].

The software SPSS 26.0 was used for statistical analysis. According to the Shapiro-Wilk test, the measured data conform to the normal distribution and are represented by the mean standard deviation (S), while the non-normal distribution is represented by M(Q1, Q3), and the counting data is represented by the rate (%). The chi-square test, or Fisher exact probability method, is used to classify variables. The Levene test verifies the homogeneity of variance, conforms to the normal distribution, and has the homogeneity of variance. One-way analysis of variance is used for the comparison of differences between groups, and LSD-t test is used for the comparison of pairwise. For data with skewed distribution or inconsistent variance homogeneity, the Kruskal-Wallis H test was used for difference comparison, and the Wilcoxon rank sum test was used for pairwise comparison between groups. The index changes at different time points were analyzed by repeated measurement variance analysis (normal) and the Friedman M test (skewed). $p < 0.05$ is statistically significant $\chi \pm s$.

3. Results

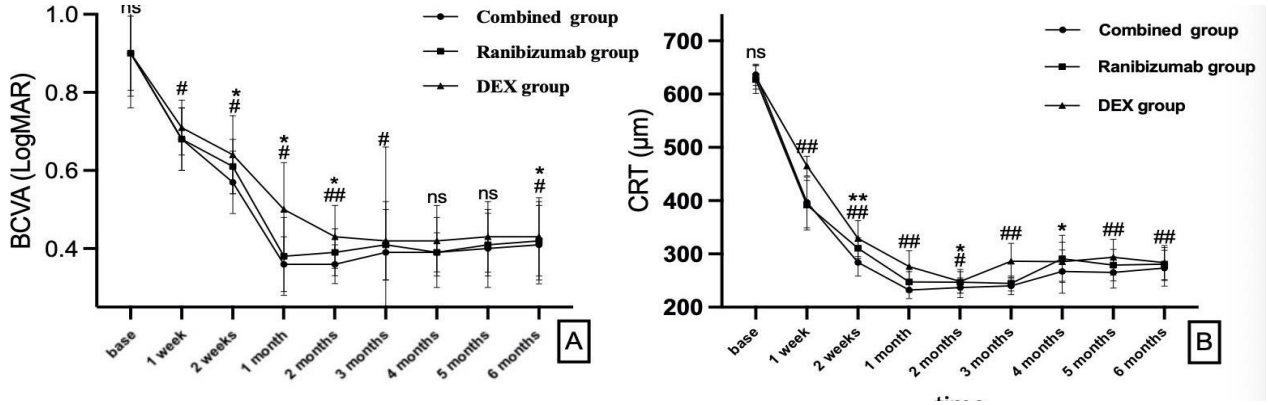

Figure 1. Comparison of BCVA and CRT in the combined group, DEX group, and ranibizumab group; * It is the difference of the same follow-up time point between the ranibizumab group and the combined group (*$P < 0.05$, ** $P < 0.01$); # is the difference between DEX and the combined group at the same follow-up time point (#$P < 0.05$, ##$P < 0.01$), and there is no statistical difference in ns. DEX: dexamethasone intravitreal implant; BCVA (LogMAR): minimum resolution angle logarithm best corrected vision, CRT: central retinal thickness.

During the follow-up period, there was no significant difference in baseline BCVA and CRT between the combined group, the ranibizumab group, and the DEX group ($p > 0.05$) (**Figure 1**). During the follow-up period, the BCVA and CRT of the three groups were significantly lower than the baseline after treatment, and the differences were statistically significant ($p < 0.01$) (**Table 2**). There were significant differences in BCVA between the three groups at 2 weeks, 1 month, 2 months, and 6 months after treatment ($p < 0.05$). There were significant differences in CRT between the three groups at 2 weeks, 1 month, and 2 months after treatment ($p < 0.05$). BCVA and CRT were improved in all patients within one week after treatment, and the maximum visual benefit time in the combined group was one month after treatment. Further comparison between groups showed that the improvement of BCVA in the combined group was better than that in the ranibizumab group at 2 weeks, 1 week, 2

months, and 6 months after treatment, and it was better than that in the DEX group at 1 week, 2 weeks, 1 month, 2 months, 3 months, and 6 months after treatment, with statistical significance ($p < 0.05$) (**Figure 1A**). At 2 weeks, 2 months, and 4 months after treatment, the improvement of CRT in the combined group was better than that in the ranibizumab group, and at other follow-up time points, the combined group was better than that in the DEX group, with statistical significance ($p < 0.05$) (**Figure 1B**).

Table 2. The follow-up time of BCVA (LogMAR) and CRT (μm) in three groups of patients was compared with the baseline (S) $\chi \pm s$.

Follow-up time	Combined group		Ranibizumab group		DEX group	
	BCVA	CRT	BCVA	CRT	BCVA	CRT
base	0.90 ± 0.14	636.48 ± 19.89	0.90 ± 0.95	627.58 ± 26.48	0.90 ± 0.11*	631.48 ± 22.16*
After treatment						
1 week	0.68 ± 0.08*	396.94 ± 47.60*	0.68 ± 0.08*	391.71 ± 46.47*	0.71 ± 0.07*	465.04 ± 18.56*
2 weeks	0.57 ± 0.08*	284.27 ± 26.01*	0.61 ± 0.07*	310.48 ± 19.25*	0.64 ± 0.10*	328.84 ± 33.80*
1 month	0.36 ± 0.07*	232.12 ± 15.92*	0.38 ± 0.10*	247.45 ± 19.14*	0.50 ± 0.12*	276.38 ± 29.94*
2 months	0.36 ± 0.05*	236.79 ± 18.47*	0.39 ± 0.06*	246.87 ± 19.98*	0.43 ± 0.08*	248.58 ± 22.10*
3 months	0.39 ± 0.27*	240.06 ± 16.31*	0.41 ± 0.09*	244.52 ± 14.01*	0.42 ± 0.10*	286.33 ± 33.44*
4 months	0.39 ± 0.05*	267.0 ± 40.55*	0.39 ± 0.09*	290.84 ± 44.36*	0.42 ± 0.09*	285．56 ± 36.71*
5 months	0.40 ± 0.10*	265.24 ± 29.22*	0.41 ± 0.08*	279.00 ± 29.33*	0.43 ± 0.09*	293.88 ± 33.81*
6 months	0.41 ± 0.10*	273.39 ± 33.57*	0.42 ± 0.10*	281.10 ± 31.01*	0.43 ± 0.10*	283.60 ± 32.03*

Note: DEX: dexamethasone intravitreal implant; BCVA (LogMAR): minimum resolution angle logarithm best corrected vision; CRT: central retinal thickness.; *$P < 0.01$.

Compared with the improvement of blood flow, there was no significant difference in the areas of SVC-MVD, DVC-MVD, and FAZ between the combined group, ranibizumab group, and DEX group ($p > 0.05$). During the follow-up period, the follow-up times of SVC-MVD and DVC-MVD in the three groups were significantly improved compared with the baseline ($p < 0.01$), and there was no significant difference in FAZ area (**Table 3** and **Figure 2C**). There were significant differences in SVC-MVD between the three groups at 2 weeks, 1 month, and 3 months after treatment ($p < 0.05$). There were significant differences in DVC-MVD among the three groups at 1, 2, 3, 4, and 6 months after treatment ($p < 0.05$). Further comparison between groups showed that the differences between SVC-MVD in the combined group and the ranibizumab group were statistically significant at 2 weeks, 1 month, and 3 months after treatment ($p < 0.05$), and those between the combined group and the DEX group at 2 weeks, 1 month, 2 months, and 3 months after treatment were statistically significant ($p < 0.05$) (**Figure 2A**). The improvement of DVC-MVD in the combined group was better than that in the ranibizumab group 1-6 months after treatment, and the improvement in the combined group was better than that in the DEX group at the 2nd week, 1st, 2nd, 3rd, 4th, and 6th months after treatment; the difference was statistically significant ($p < 0.05$) (**Figure 2B**). There was no significant difference in FAZ area between the three groups at each follow-up time after treatment ($p > 0.05$) (**Figure 2C**).

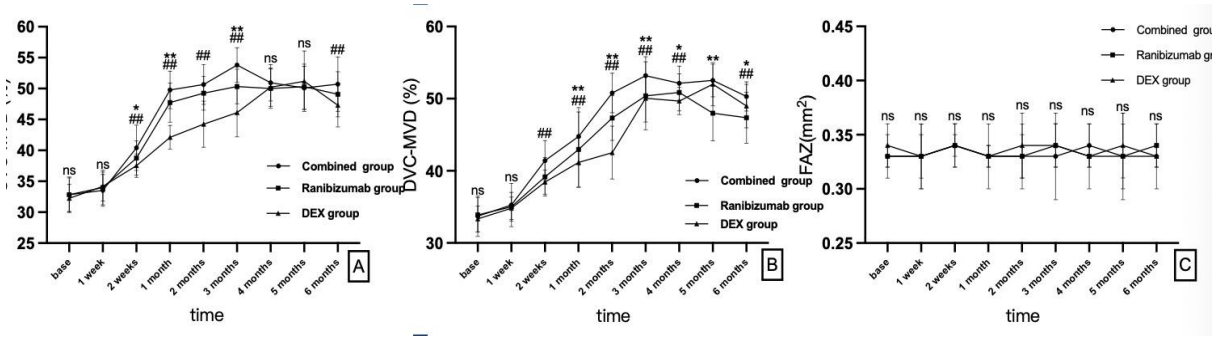

Figure 2. Comparison of SVC-MVD, DVC-MVD, and FAZ area differences among the combined group, DEX group, and ranibizumab group; * It is the difference of the same follow-up time point between the ranibizumab group and the combined group (*$P < 0.05$, ** $P < 0.01$); # is the difference between DEX and the combined group at the same follow-up time point (#$P < 0.05$, ##$P < 0.01$), and there is no statistical difference in ns. BCVA (LogMAR): minimum resolution angle logarithm best corrected vision; DEX: dexamethasone intravitreal implant; SVC-MVD: blood flow density of superficial vascular complex in macular area; DVC-MVD: blood flow density of deep vascular complex in macular area.

Table 3. Comparison of the follow-up time of SVC-MVD(%) and DVC-MVD(%) with baseline (S) $\chi \pm s$.

Follow-up time	Combined group		Ranibizumab group		DEX group	
	SVC-MVD	DVC-MVD	SVC-MVD	DVC-MVD	SVC-MVD	DVC-MVD
base	32.82 ± 2.71	33.71 ± 2.81	32.83 ± 2.85	33.89 ± 2.39	32.25 ± 2.24	33.33 ± 1.79
After treatment						
1 week	33.54 ± 2.57*	35.26 ± 2.99*	34.00 ± 2.80*	35.02 ± 2.00*	34.16 ± 2.36*	34.81 ± 1.56*
2 weeks	40.41 ± 3.67*	41.41 ± 2.78*	38.76 ± 2.76*	39.17 ± 2.66*	37.52 ± 1.90*	38.44 ± 1.68*
1 month	49.78 ± 3.03*	44.77 ± 3.98*	48.73 ± 3.17*	42.95 ± 5.21*	42.10 ± 1.93*	41.16 ± 3.45*
2 months	50.66 ± 3.23*	50.80 ± 2.74*	49.25 ± 2.73*	47.31 ± 3.09*	44.23 ± 3.74*	42.52 ± 3.67*
3 months	53.81 ± 2.80*	53.19 ± 2.62*	50.33 ± 2.80*	50.40 ± 4.71*	46.10 ± 3.90*	50.06 ± 3.30*
4 months	50.93 ± 2.94*	52.15 ± 2.37*	50.00 ± 3.20*	50.87 ± 2.56*	50.21 ± 3.10*	49.67 ± 1.88*
5 months	50.11 ± 3.48*	52.53 ± 2.26*	50.30 ± 3.66*	47.99 ± 3.83*	51.19 ± 4.90*	52.02 ± 3.00*
6 months	50.71 ± 4.41*	50.31 ± 2.03*	49.08 ± 3.64*	47.35 ± 3.53*	47.29 ± 3.50*	48.98 ± 3.01*

Note: DEX: dexamethasone intravitreal implant; SVC-MVD: blood flow density of superficial vascular complex in macular area; DVC-MVD: blood flow density of deep vascular complex in macular area; *$P < 0.01$.

Compared with the improvement of visual effect, there was no significant difference in baseline CS and MD between the combined group, ranibizumab group, and DEX group ($p > 0.05$) (**Figure 3**). During the follow-up period, the follow-up time CS and MD of the three groups were significantly higher than the baseline, and the differences were statistically significant ($p < 0.01$) (**Table 4**). After 2 weeks, 1, 2, 3, 4, and 6 months of treatment, there were significant differences in CS among the three groups ($p < 0.05$). There were significant differences in MD among the three groups at 2, 3, 5, and 6 months after treatment ($p < 0.05$). The improvement of the CS group was the most obvious one week after treatment, and that of the MD group was the most obvious one month after treatment. Further comparison between the two groups showed that at 2, 3, 5, and 6 months after treatment, the difference between the CS combined group and the ranibizumab group was statistically significant ($p < 0.05$),

and at each follow-up time point after treatment, the difference between the ranibizumab and DEX groups was statistically significant ($p < 0.05$) (**Figure 3A**); there was no difference between the MD combined group and the ranibizumab group at each time point ($p < 0.05$), and the improvement was better than that of the DEX group at 3 and 6 months after treatment, with statistical significance ($p < 0.05$) (**Figure 3B**).

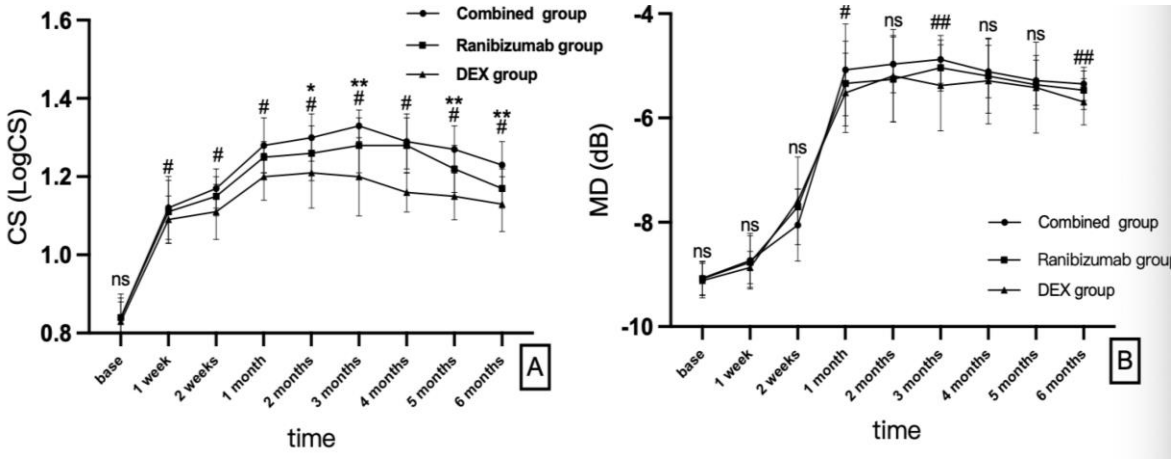

Figure 3. Comparison of CS and MD among the combined group, DEX group, and Rezhu single group; * It is the difference of the same follow-up time point between the ranibizumab group and the combined group (*$P < 0.05$, ** $P < 0.01$); # is the difference between DEX and the combined group at the same follow-up time point (#$P < 0.05$, ##$P < 0.01$), and there is no statistical difference in ns. LogCS: logarithmic value of contrast sensitivity; MD: average visual field defect.

Table 4. Comparison of follow-up time of CS (logCS) and MD (dB) with baseline in three groups of patients (S) $\chi \pm s$.

Follow-up time	Combined group		Ranibizumab group		DEX group	
	CS	MD	CS	MD	CS	MD
base	0.84 ± 0.05	−9.07 ± 0.32	0.84 ± 0.06*	−9.08 ± 0.32	0.83 ± 0.05	−9.12 ± 0.33
After treatment						
1 week	1.12 ± 0.08*	−8.73 ± 0.52*	1.11 ± 0.08*	−8.77 ± 0.51*	1.09 ± 0.06*	−8.87 ± 0.31*
2 weeks	1.17 ± 0.05	−8.05 ± 0.69*	1.15 ± 0.05*	−7.70 ± 0.34*	1.11 ± 0.07*	−7.59 ± 0.84*
1 month	1.28 ± 0.07*	−5.08 ± 0.88*	1.25+0.08*	−5.34 ± 0.81*	1.20 ± 0.06*	−5.52 ± 0.76*
2 months	1.30 ± 0.06*	−4.97 ± 0.55*	1.26 ± 0.07*	−5.26 ± 0.81*	1.21 ± 0.09*	−5.19 ± 0.89*
3 months	1.33 ± 0.04*	−4.88 ± 0.46*	1.28 ± 0.07*	−5.04 ± 0.44*	1.20 ± 0.10*	−5.38 ± 0.87*
4 months	1.29 ± 0.07*	−5.11 ± 0.50*	1.28 ± 0.07*	−5.20 ± 0.71*	1.16 ± 0.05*	−5.29 ± 0.82*
5 months	1.27 ± 0.06*	−5.28 ± 0.48*	1.22 ± 0.06*	−5.36 ± 0.47*	1.15 ± 0.06*	−5.42 ± 0.87*
6 months	1.23 ± 0.06*	−5.35 ± 0.32*	1.17 ± 0.05*	−5.47 ± 0.37*	1.13 ± 0.07*	−5.69 ± 0.44*

Note: DEX: dexamethasone intravitreal implant: CS: contrast sensitivity; MD: average visual field defect; *$P < 0.01$.

During the follow-up period, 11 patients (33.3%, 11/33), 17 patients (70.8%, 17/24), and 28 patients (90.3%, 11/31) in the combined treatment group, DEX treatment group, and ranibizumab treatment group received retreatment, respectively, and the difference was statistically significant. During the 6-month follow-up, the

course of treatment in the combined treatment group, the DEX treatment group, and the ranibizumab treatment group was (101.08, 13.76), (137.42, 19.08), and (161.25, 26.48) d, respectively, and the difference was statistically significant ($F = 174.87$, $p <$ Compared with the three groups, the average times of drug injection were (4.39, 0.55) in the combined group, (4.65, 0.92) in the ranibizumab group, and (1.79, 0.42) in the DEX group, and the differences were statistically significant ($p < 0.05$). The average number of injections in the combination group was significantly different from that in the ranibizumab group ($p < 0.05$).

Complications: There were 11 cases of subconjunctival hemorrhage after intravitreal injection of drugs in the combination group, the ranibizumab group, and the DEX group, which were 4 cases (2%), 3 cases (2%), and 4 cases (9%), respectively, with no statistical significance ($p > 0.05$). During the study, there were 4 cases (12%) with elevated intraocular pressure (IOP > 25 mmHg) in the combined group, including 2 cases with elevated intraocular pressure after one week of intravitreal injection of DEX and 6 cases (25%) with elevated intraocular pressure in the DEX group. No patients with elevated intraocular pressure in the Ranibizumab group, and patients with elevated intraocular pressure can be reduced to the normal range by using brinzolamide eye drops or Catilol eye drops. During the follow-up, FFA examination revealed a large area without perfusion, that is, retinal laser photocoagulation was performed, including 14 cases in the combined group (42.4%), 16 cases in the ranibizumab group (51.61%), and 10 cases in the DEX group (41.67%), with no statistical significance ($p > 0.05$). During the study, no patient needed cataract surgery because of the serious progress of cataracts. No serious complications, such as vitreous hemorrhage and endophthalmitis, occurred in all patients during the treatment (**Table 5**).

Table 5. Comparison of injection times and complications among three groups (S) $\chi \pm s$.

complication	**group**			**Inspection value**	***P***
	Combined group	**Ranibizumab group**	**DEX group**		
Injection times	4.39 ± 0.55	4.65 ± 0.92	1.79 ± 0.42		0.026
Subconjunctival hemorrhage (case) (%)	4(2%)	3(2%)	4(9%)	$\chi^2 = 0611$	0.737
Elevated intraocular pressure (case)	four	0	six	$\chi^2 = 8.424$	0.015
Cataract (case)	0	0	0	-	-
Laser (example)	14	16	10	$\chi^2 = 0.735$	0.692

Note: DEX: Dexamethasone intravitreal implant.

4. Discussion

At present, the pathogenesis of RVO is still unclear and complicated. The occurrence of RVO-ME is closely related to many factors, and the release of cytokines plays an important role in the development of ME. The release of cytokines stimulates inflammation and triggers an inflammatory cascade reaction. Causing macular edema and tissue damage [14]. Therefore, inhibiting inflammatory reaction is an important link in the treatment of RVO-ME. In this study, we included patients with central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). Although there are similarities in the pathological mechanism between CRVO and BRVO, they

may have differences in treatment response. CRVO usually affects a wider retinal area and may require more aggressive treatment strategies. BRVO may have a more local response to treatment in some cases. In order to evaluate the curative effect of RVO more accurately, we evaluated the curative effect of CRVO and BRVO patients, respectively. By comparing the data of the two groups before and after treatment, we found that CRVO patients may need more frequent treatment to maintain their vision stability, while BRVO patients may have a better short-term effect on a single treatment. Due to the small number of cases, they were not analyzed and discussed separately in detail.

In view of the limitations of single drug therapy and the different mechanisms of corticosteroids and anti-VEGF drugs in the treatment of RVO-ME, combined drugs can combine the characteristics of the rapid onset of ranibizumab and the long half-life of DEX and treat RVO-ME in different ways, with complementary advantages, achieving "synergistic" and "double" blocking effects on the pathological process of RVO-ME, so the combined therapy has certain prospects. Considering that there are some problems in the real world, such as poor treatment effect, high recurrence rate, poor follow-up compliance caused by frequent injection and reexamination, and it will increase the occurrence of complications after injection. DEX can be used as the first choice for RVO-ME patients when the therapeutic effect of anti-VEGF drugs is not good, or when personal/economic problems need to reduce the injection frequency, there are contraindications to anti-VEGF drugs, and it is complicated with systemic/ocular local inflammation [2]. DEX can alleviate ME through anti-inflammatory, anti-cell proliferation, and anti-angiogenesis effects, and the effect is lasting, thus reducing the frequency of drug injection and follow-up. However, the risk of eye adverse events, including accelerated cataract progress and increased intraocular pressure, increases [15,16]. Koss [17] Some scholars have found that some patients with RVO-ME have poor response to anti-VEGF therapy, and the level of VEGF in the vitreous is in the normal range, so anti-VEGF drugs are not suitable. Intravitreal injection of glucocorticoid can reduce the levels of inflammatory cytokines in the eye [6], improve ME, and improve vision from multiple mechanisms. Ding X [18] A retrospective study by other scholars compared the effects of anti-VEGF drugs and DEX in the treatment of RVO-ME. The results showed that, except for choroidal thickness, BCVA and CRT in both groups were significantly improved ($p < 0.01$), and anti-inflammatory therapy may be superior to anti-VEGF therapy in the height and resolution of serous retinal detachment.

At present, there have been many studies on the combined therapy of RVO-ME at home and abroad, and there are differences in medication strategies, especially the time interval and combined mode of the two drugs. Ren F. and other scholars [19] A retrospective study was conducted to evaluate the combined therapy. The method was to start receiving the initial intravitreal injection of ranibizumab, and all patients received a needle of DEX one month later, and they were followed up every month. Patients with recurrent or persistent RVO-ME could reconsider ranibizumab and observe it for one year. It was concluded that after the combined therapy, the patients had significantly improved in BCVA, IOP, CRT, and retinal vascular density (all $p < 0.05$). Du X and other scholars [20] A retrospective study was conducted for 6 months to explore the safety and effectiveness of simultaneous injection of DEX and

ranibizumab on CRVO-ME. The results showed that the combined method could significantly improve the visual acuity and anatomical prognosis of CRVO-ME patients, and no serious complications occurred. The choice of a combined treatment scheme should be based on the comprehensive evaluation of patients' condition, including the type of RVO, the severity of the condition, the individual differences of patients, and the expected response to treatment. To guide the choice of treatment scheme in clinical practice. At present, all the studies are about the combination of single-dose anti-VEGF drugs and DEX drugs. Considering the recommended administration mode of anti-VEGF drugs "3+prn" [2], this study chose the combination mode of 3+1+ prn treatment and explored whether the frequency of drug injection can be reduced while improving the curative effect on this basis. At the same time, the conventional BCVA and CRT indicators were observed, and other visual functions and macular microstructure indicators were observed so as to evaluate the combined treatment effect in multiple dimensions.

The results of this study show that both combined therapy and single drug therapy can significantly improve BCVA and reduce CRT in RVO-ME patients. At the first week of review, the visual benefit and anatomical results of the combined group and the ranibizumab group improved significantly, which can be attributed to the rapid onset of ranibizumab, while the DEX group demonstrated a longer duration of effect. Overall, the combined group still presented greater improvements in BCVA and CRT compared to either single-drug group. From a hemodynamic and biomechanical perspective, dexamethasone (as a potent corticosteroid) reduces local inflammation and stabilizes the blood–retinal barrier by decreasing vascular permeability, whereas ranibizumab inhibits VEGF-driven pathological neovascularization and further reduces vascular leakage. Their combined effect leads to enhanced vascular compliance—the ability of the retinal vasculature to adapt to changes in blood flow—and more stable hemodynamics by lowering venous pressure and restoring physiologic perfusion. Consequently, the microvascular environment recovers, allowing for better oxygen and nutrient delivery and facilitating fluid reabsorption from the retina. These mechanisms collectively promote faster resolution of macular edema and improve clinical outcomes in the combined group. Iu [21] Other scholars adopted the combined treatment plan, first applied the ranibizumab, then injected DEX within 4 weeks, and then injected it as needed. The follow-up period was 6 months. The results show that the combined therapy can improve vision more quickly and more permanently, which is consistent with the results of this study. It is speculated that the reason may be related to early ranibizumab inhibiting VEGF, controlling the proliferation of vascular endothelial cells, and reducing vascular permeability, thus reducing ME to some extent. With the progress of the disease, DEX promotes the recovery of the blood-retinal barrier and further promotes the regression of ME by inhibiting inflammatory factors, enhancing cell adhesion, and restoring the function of Müller cells.

In the study of analyzing the retinal blood flow density and the improvement of retinal vein occlusion, OCTA is used to observe the macular blood flow and structural characteristics of RVO patients. By non-invasive differentiation of MVD, it can partially reflect the therapeutic effect and accurately quantify the FAZ area, which can replace FFA to some extent. In patients with RVO, venous reflux is blocked, blood retention, vasodilation, and blood flow velocity are slowed down. These factors

together lead to the decrease of retinal blood flow density, which leads to the decrease of blood supply in the DVC layer and SVC layer. At the same time, the compensatory increase of blood flow in retinal tissue leads to the decrease of blood flow in choroidal layers, which is mainly manifested by the obvious decrease of MVD in the choroidal layer and choroidal capillary layer [22]. The more severe macular fovea edema also leads to blood reflux disorder and the formation of no perfusion area and also causes ischemia and hypoxia of retinal tissue. With the recovery of blood retinal integrity and the reduction of ME, blood perfusion improves. From a biological perspective, anti-VEGF therapy reduces pathological vascular permeability by downregulating VEGF-driven signaling, whereas corticosteroids diminish local inflammatory responses and stabilize the blood-retinal barrier. As intraretinal fluid is reabsorbed and inflammatory mediators subside, retinal capillary flow becomes less turbulent, thereby enhancing vascular compliance—the vessel's ability to accommodate and regulate changes in blood flow. This improvement in compliance leads to more stable hemodynamics and restores physiologic perfusion pressures in both the superficial and deep vascular complexes (SVC, DVC). Consequently, the observed increase in SVC-MVD and DVC-MVD on OCTA not only indicates an overall improvement in perfusion but also reflects a recovery in the biomechanical and functional properties of the microvasculature. Such structural and hemodynamic enhancements help alleviate macular edema and eventually contribute to better clinical outcomes. It is considered that the blood flow density in deep and shallow layers is negatively correlated with the thickness of the macular fovea and the neuroepithelial layer, while CRT is positively correlated with the thickness of the neuroepithelial layer and the height of subcortical effusion. Macular ischemia can be evaluated by measuring the size of FAZ. Vein occlusion leads to a significant expansion of the FAZ area in the superficial retina. During the development of the disease, the degree of ischemia reaches a certain level, or with the extension of the disease course, the vascular occlusion area gradually increases. However, there is no significant difference in the changes of the FAZ area among the three groups in this study, which is different from that of scholars such as Khalil. The conclusion is basically the same, which may be related to the short observation time [23]. At present, there is still controversy about the improvement of the FAZ area. After SVC-MVD and DVC-MVD treatment, the follow-up time points were generally improved compared with the baseline, and there was an obvious improvement trend after 2 weeks of treatment, and the combined group was better than the ranibizumab group and DEX group at 2 weeks, 1 month, 2 months, and 3 months after treatment, compared with Ruan Yimeng and other scholars. The research results are slightly different, which may be related to the different time of DEX combination, sample size, measurement methods, etc., but it is concluded that the combined group has achieved a good curative effect in SVC-MVD and DVC-MVD, which is better than the single drug group [24].

CS shows high sensitivity in detecting visual function, especially the damage of retinal and optic nerve fibers. Jay et al. [25] It is proved that the disorder of inner retinal tissue is significantly related to the decreased visual CS in RVO-ME patients. It may be caused by retinal capillary ischemia, which leads to retinal cell dysfunction and damages the visual pathway. During the 6-month follow-up period of this study, the CS of each group was significantly improved compared with the baseline after

treatment. The combined group showed a peak of CS improvement at 3 months after treatment, while the ranibizumab group remained stable at 1 month after treatment. The CS of the DEX group gradually increased at the first 2 months after treatment and began to decline at the third month. The overall combined group can improve CS early and permanently, considering the dual effects on capillary ischemia and the recovery of retinal cell function. At present, there is no research report on the correlation change of MD between hormone drugs and anti-VEGF drugs after RVO treatment. In this study, it was found that the MD of the three groups of patients decreased compared with the baseline at each time point after treatment, and the improvement effect of the combined group was generally better than that of the DEX group. The decline and treatment effect of the three groups were basically consistent with the improvement of BCVA and CRT.

The main complications in this study are subconjunctival hemorrhage and an increase in IOP following DEX use. Corticosteroids can alter the extracellular matrix in the trabecular meshwork, reducing aqueous humor outflow [26]. This mechanism involves upregulation of matrix metalloproteinases and changes in trabecular endothelial cells, leading to higher resistance in the outflow pathway. The severity of steroid-induced IOP elevation can vary from mild, transient increases to more significant elevations requiring pharmacological intervention [27,28]. In our study, most cases of elevated IOP were moderate and could be controlled effectively with topical antihypertensive medications (e.g., prostaglandin analogs, beta-blockers, carbonic anhydrase inhibitors). Additionally, regular monitoring of IOP and optic nerve head is critical; in cases where medical therapy is insufficient, laser trabeculoplasty or surgical intervention may be considered. By tailoring the frequency of DEX injections and promptly initiating IOP-lowering treatments when needed, it is possible to minimize the risk of long-term glaucomatous damage while benefiting from the anti-inflammatory effects of corticosteroids. No patient needs cataract surgery because of serious cataract progress, which proves that the combined treatment is safe. During the treatment period, there were patients in all three groups who didn’t need to be treated again after routine treatment, and the proportion of patients receiving retreatment in the combined group was the least compared with that in the single drug treatment group, which proved that the combined scheme could reduce the frequency of reinjection, shorten the total course of treatment, improve the early treatment effect of patients, and improve the maintenance state for a long time. In terms of injection times, the ranibizumab group had the highest number of injections, followed by the combined group, while the DEX group required the fewest injections overall. Consequently, the total treatment cost was lowest in the DEX group, followed by the combined group, and highest in the ranibizumab group In real-world practice, such differences in cost and injection frequency directly impact patient adherence and overall treatment burden. Although DEX monotherapy appears the most economical, its potential side effects (e.g., steroid-induced IOP elevation) may necessitate closer follow-up. Meanwhile, combined therapy provides relatively rapid and sustained efficacy, potentially reducing long-term clinic visits and injections of anti-VEGF agents. This can be particularly advantageous for patients with limited economic resources or those with poor compliance. By lowering the overall number of injections while maintaining good therapeutic outcomes, combined therapy may

strike a balance between efficacy, safety, and affordability. However, further research with a longer follow-up and health-economic evaluation is needed to clarify the cost-effectiveness and feasibility of adopting this regimen in broader clinical settings. Clinically, it can also be integrated with existing guidelines for fundus disease management in China, thus providing a flexible approach that accommodates individual economic constraints and compliance levels.

To sum up, the patients in the combined treatment group have good advantages in improving the visual function, macular microstructure, and visual effect in the short term, without serious adverse reactions, and can reduce the number of injections and relieve the treatment burden of patients. The results of this study show that the combination of ranibizumab and DEX has short-term advantages in improving visual function and macular microstructure. However, the long-term effect of treatment, the economic burden of patients, and the potential side effects should be considered when choosing the combined treatment. For example, for patients who need rapid vision recovery, combined therapy may be more suitable; for patients who are worried about long-term side effects, it may be necessary to consider more single-drug treatment or adjust the treatment plan. Future research should further explore the long-term efficacy and safety of different combined schemes. The limitation of this study is that only the clinical efficacy of combine therapy with ranibizumab and DEX is compared with that of single drug therapy for RVO-ME. Due to the limitations of research time and other conditions, the observation time is short and the sample size is small, so only the above short-term clinical observation results can be obtained. Besides, the therapeutic effects of different combined schemes are not compared. Therefore, we are still continuing this study. After combining the long-term observation of the course of disease with a larger sample size, we analyze and discuss the sub-component types of RVO patients, and at the same time, we compare them with other combined schemes that have advantages at present and supplement the application prospects of the combined scheme to guide clinical medication.

Author contributions: Conceptualization, LX and JH; methodology, LX; software, JH; validation, HJ, LX and XY; formal analysis, JH; investigation, JH; resources, LX; data curation, XC; writing—original draft preparation, JH; writing—review and editing, JH; visualization, LX; supervision, LX; project administration, LX; funding acquisition, LX. All authors have read and agreed to the published version of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: Nanchong City-University Strategic Science and Technology Cooperation Project (No.22SXQT0168), Chuanbei medical College Doctoral Initiation Fund (CBY21-QD28).

Ethical approval: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of North Sichuan Medical College (2021ER047-1, 2023-028).

Conflict of interest: The authors declare no conflict of interest.

References

1. Babiuch AS, Han M, Conti FF, et al. Association of Disorganization of Retinal Inner Layers With Visual Acuity Response to Anti–Vascular Endothelial Growth Factor Therapy for Macular Edema Secondary to Retinal Vein Occlusion. JAMA Ophthalmology. 2019; 137(1): 38. doi: 10.1001/jamaophthalmol.2018.4484
2. Ophthalmology Group of Ophthalmology Branch of Chinese Medical Association, Ophthalmologist Branch of Chinese Medical Association. Expert consensus on clinical diagnosis and treatment path of retinal vein occlusion in China. Chinese Journal of Ophthalmology. 2024; 40(3): 175-185.
3. Rattner A, Williams J, Nathans J. Roles of HIFs and VEGF in angiogenesis in the retina and brain. Journal of Clinical Investigation. 2019; 129(9): 3807-3820. doi: 10.1172/jci126655
4. Xu M, Fan R, Fan X, et al. Progress and Challenges of Anti-VEGF Agents and Their Sustained-Release Strategies for Retinal Angiogenesis. Drug Design, Development and Therapy. 2022; 16: 3241-3262. doi: 10.2147/dddt.s383101
5. Noma H, Yasuda K, Mimura T, et al. Relationship Between Choroidal Findings And Growth Factors, Cytokines, And Other Inflammatory Mediators After Intravitreal Ranibizumab Injection In Patients With Macular Edema Secondary To Branch Retinal Vein Occlusion. Retina. 2022; 42(4): 744-751. doi: 10.1097/iae.0000000000003362
6. Zhou Y, Qi J, Liu H, et al. Increased intraocular inflammation in retinal vein occlusion is independent of circulating immune mediators and is involved in retinal oedema. Frontiers in Neuroscience. 2023; 17. doi: 10.3389/fnins.2023.1186025
7. Tang Y, Cheng Y, wang S, et al. Review: The development of risk factors and cytokines in retinal vein occlusion. Front med (Lausanne). 2022; 9: 910600. doi: 10.3389/fmed. 2022.910600.
8. Liang X, Shen B, Ou Z, et al. Comparison of intravitreal ranibizumab monotherapy vs. ranibizumab combined with dexamethasone implant for macular edema secondary to retinal v ein occlusion. Front med (Lausanne). 2022; 9: 930508. doi: 10.3389/fmed.2022. 930508
9. Blanc J, Deschasse C, Kodjikian L, et al. Safety and long-term efficacy of repeated dexamethasone intravitreal implants for the treatment of cystoid macular edema secondary to retinal vein occlusion with or without a switch to anti-VEGF agents: a 3-year experience. Graefe's Archive for Clinical and Experimental Ophthalmology. 2018; 256(8): 1441-1448. doi: 10.1007/s00417-018-4016-7
10. Maturi RK, Glassman AR, Liu D, et al. Effect of Adding Dexamethasone to Continued Ranibizumab Treatment in Patients With Persistent Diabetic Macular Edema. JAMA Ophthalmology. 2018; 136(1): 29. doi: 10.1001/jamaophthalmol.2017.4914
11. Hoerauf H, Feltgen N, Weiss C, et al. Clinical Efficacy and Safety of Ranibizumab Versus Dexamethasone for Central Retinal Vein Occlusion (COMRADE C): A European Label Study. American Journal of Ophthalmology. 2016; 169: 258-267. doi: 10.1016/j.ajo.2016.04.020
12. Khayat M, Williams M, Lois N. Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion. Survey of Ophthalmology. 2018; 63(6): 816-850. doi: 10.1016/j.survophthal.2018.04.005
13. Hayreh SS. Photocoagulation for retinal vein occlusion. Progress in Retinal and Eye Research. 2021; 85: 100964. doi: 10.1016/j.preteyeres.2021.100964
14. Wang B, Zhang X, Chen H, et al. A Review of Intraocular Biomolecules in Retinal Vein Occlusion: Toward Potential Biomarkers for Companion Diagnostics. Frontiers in Pharmacology. 2022; 13. doi: 10.3389/fphar.2022.859951
15. Gao S, Zhang Y, Li X, et al. Comparative Efficacy of Pharmacotherapy for Macular Edema Secondary to Retinal Vein Occlusion: A Network Meta-analysis. Frontiers in Pharmacology. 2021; 12. doi: 10.3389/fphar.2021.752048
16. Massa H, Georgoudis P, Panos GD. Dexamethasone Intravitreal Implant (OZURDEX ®) for Macular Edema Secondary to Noninfectious Uveitis: a Review of the Literature. Therapeutic Delivery. 2019; 10(6): 343-351. doi: 10.4155/tde-2019-0024
17. Koss MJ, Pfister M, Rothweiler F, et al. Comparison of cytokine levels from undiluted vitreous of untreated patients with retinal vein occlusion. Acta Ophthalmologica. 2011; 90(2). doi: 10.1111/j.1755-3768.2011.02292.x
18. Ding X, Hu Y, Yu H, et al. Changes of Optical Coherence Tomography Biomarkers in Macular Edema Secondary to Retinal Vein Occlusion After Anti-VEGF and Anti-Inflammatory Therapies. Drug Design, Development and Therapy. 2022; 16: 717-725. doi: 10.2147/dddt.s351683
19. Ren F, Gong H, Zhang H, et al. Combination Therapy Using Anti-Vascular Endothelial Growth Factor (VEGF) Drugs and Steroids for Macular Edema in Retinal Vein Occlusions. Medical Science Monitor. 2023; 29. doi: 10.12659/msm.939277

20. Du X, Sheng Y, Shi Y, et al. The Efficacy of Simultaneous Injection of dexamethasone Implant and Ranibizumab Into Vitreous Cavity on Macular Edema Secondary to Central Reti nal Vein Occlusion. Front Pharmacol. 2022; 13: 842805. doi: 10.3389/fphar.2022. 842805.
21. Iu LP, Zhao P, Yeung IY, et al. Sequential therapy with ranibizumab and dexamethasone intravitreal implant is better than dexamethasone monotherapy for macular oedema due to retinal vein occlusion. British Journal of Ophthalmology. 2014; 99(2): 210-214. doi: 10.1136/bjophthalmol-2014-305661
22. Costanzo E, Parravano M, Gilardi M, et al. Microvascular Retinal and Choroidal Changes in Retinal Vein Occlusion Analyzed by Two Different Optical Coherence Tomography Angiography Devices. Ophthalmologica. 2019; 242(1): 8-15. doi: 10.1159/000496195
23. Ghasemi Falavarjani K, Iafe NA, Hubschman JP, et al. Optical Coherence Tomography Angiography Analysis of the Foveal Avascular Zone and Macular Vessel Density After Anti-VEGF Therapy in Eyes With Diabetic Macular Edema and Retinal Vein Occlusion. Investigative Opthalmology & Visual Science. 2017; 58(1): 30. doi: 10.1167/iovs.16-20579
24. Ruan Y, Yao D, Shi Y. Clinical study of ranibizumab combined with dexamethasone intravitreal implant in the treatment of macular edema secondary to retinal vein occlusion. China Journal of Clinical Pharmacology. 2023; 39(23): 3397-3400. doi: 10.13699/J.CNKI.1001-6821
25. Wang J, Cui Y, Vingopoulos F, et al. Disorganisation of retinal inner layers is associated with reduced contrast sensitivity in retinal vein occlusion. British Journal of Ophthalmology. 2020; 106(2): 241-245. doi: 10.1136/bjophthalmol-2020-317615
26. Chin EK, Almeida DRP, Velez G, et al. Ocular hypertension after intravitreal dexamethasone (Ozurdex) sustained-release implant. Retina. 2017; 37(7): 1345-1351. doi: 10.1097/IAE. 0000000000001364
27. Flaxel CJ, Adelman RA, Bailey ST, et al. Retinal Vein Occlusions Preferred Practice Pattern®. Ophthalmology. 2020; 127(2): P288-P320. doi: 10.1016/j.ophtha.2019.09.029
28. Zarranz-Ventura J, Sala-Puigdollers A, Velazquez-Villoria D, et al. Long-term probability of intraocular pressure elevation with the intravitreal dexamethasone implant in the real-world. Vavvas DG, ed. PLOS ONE. 2019; 14(1): e0209997. doi: 10.1371/journal.pone.0209997