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Article

Combined Use of Endonasal Retinalamin Electrophoresis and Lidase Magnetophoresis Enhances the Regenerative and Recovery Effects of Anti-VEGF Therapy in the Treatment of Non-Ischemic Branch Retinal Vein Occlusion: A Retrospective Cohort Study

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Abstract: Despite the documented efficacy and widespread clinical application of lidase magnetophoresis (LMP) and endonasal retinalamin electrophoresis (ERE) in Russia for the management of retinal vein occlusion (RVO), the synergistic potential of these methods remains insufficiently studied in current literature. **Purpose:** To evaluate the efficacy of LMP and ERE combined with intravitreal ranibizumab for the management of non-ischemic superior temporal RVO by analyzing longitudinal changes in central retinal thickness and total macular volume immediately post-treatment and at a three-month follow-up. **Materials and Methods:** In this retrospective, single-center, three-arm cohort study, we analyzed the clinical records of patients with non-ischemic superior temporal RVO who underwent LMP and ERE in combination with anti-VEGF therapy. In the final analysis were included 71 patients who underwent anti-VEGF monotherapy (control group). Additional to anti-VEGF therapy 71 patients passed LMP (LMP group) and 72 patients completed LMP and ERE (LMP + ERE group). Central retinal thickness and total macular volume were measured using optical coherence tomography at baseline, at one- and three-months post-treatment, and at the end of the follow-up period. Best-corrected visual acuity was evaluated at the same intervals. **Results:** A comparative analysis with anti-VEGF monotherapy revealed that combined application of ERE and LMP offers superior efficacy in reducing central retinal thickness by an additional 12.2% (t = 4.21, p-value = 0.0001, Cohen's d = 0.72) and total macular volume by 13.3% (t = 4.31, p-value = 0.0001, Cohen's d = 0.76) and in im-proving visual function by 66.7 (t = 30.2, p-value = 0.0001, Cohen's d = 6.5). **Conclusions:** Innovative complex use of ERE and LMP in the second month after the start of treatment with intravitreal anti-VEGF therapy enhances the protective and regenerative effect of anti-VEGF therapy. Application of this method leads to a more rapid reduction in central retinal thickness and total macular volume, which is critical for preventing permanent vision loss, scotoma, and optic nerve atrophy in patients following RVO.

Keywords: *retinal vein occlusion; lidase magnetophoresis; Endonasal retinalamin electrophoresis; anti-VEGF therapy; central retinal thickness; total macular volume; best-corrected visual acuity; SAN-questionnaire.*

1. INTRODUCTION

Retinal vein occlusion (RVO) represents a significant vascular pathology characterized by the partial or complete thrombotic blockage of the central retinal vein or its tributaries. This obstruction typically results in intraretinal hemorrhages and macular edema [1,2]. Globally, RVO is recognized as the second most prevalent retinal vascular disorder, surpassed only by diabetic retinopathy [3,4]. The gender epidemiology of RVO varies significantly by ethnicity. In Europe, RVO is approximately 1.7 times more common in men [5,6], whereas in Korea, the prevalence of this disease among women is 1.2 times higher [7,8]. In addition, there is a significant difference in the age of onset of the disease: in men, the pathology usually develops earlier, on average at the age of 48 years, while in women it develops at the age of 54 years [9]. According to some data, there are no significant differences between the sexes in the development of RVO [10]. Patients with RVO typically experience a sudden and painless onset of visual impairment. The degree of vision loss is dictated by the specific site of the occlusion and the severity of the resulting ischemia [11,12]. Common complications that exacerbate the clinical course include macular edema, vitreous hemorrhage, and neovascular glaucoma [13-20]

Retinal ischemia represents the most critical complication of RVO. It serves as a significant risk factor for the development of pathological neovascularization of the iris and retina, which frequently results in irreversible and critical acuity loss [21-27]. Although Fluorescein Angiography (FA) is still considered the gold standard for assessing capillary nonperfusion [28], Wide-Field OCT-Angiography has emerged as a vital non-invasive diagnostic method for detecting early ischemic signals [29,30]. Optical coherence tomography (OCT) allows for the identification of three unique morphological patterns of macular edema resulting from RVO [31,32,33]: diffuse retinal thickening [34], cystoid Macular Edema [35] and exudative retinal detachment [37,38]. Distinguishing between these patterns is essential, as they serve as key indicators for predicting visual outcomes and tailoring the aggressiveness of the therapeutic approach.

1.1. Anti-VEGF Therapy

In alignment with the European Society of Retina Specialists (EURETINA) and Royal College of Ophthalmologists' standards, intravitreal anti-VEGF agents (aflibercept, ranibizumab, bevacizumab) are strongly recommended as first-line treatment and the gold standard for reducing leakage and rapidly improving vision [15,16]. Overlapping pathobiological pathways in RVO indicate that targeting vascular stability beyond VEGF inhibition can improve treatment durability. Faricimab, a bispecific antibody that simultaneously targets VEGF and Angiopoietin-2, was approved by the U.S. Food and Drug Administration (FDA) in 2022. It is the first injectable RVO therapy to demonstrate 16-week dosing intervals in Phase 3 trials, showing a significant positive effect on RVO treatment [39,40,41]. The pathological sequelae following RVO are characterized by concurrent macular edema and neurosensory impairment. The multifactorial nature of this condition necessitates the development of innovative therapeutic strategies to potentiate the clinical outcomes of standard anti-VEGF therapy. These therapeutic modalities should provide protective, anti-inflammatory, and regenerative effects to accelerate the functional recovery of the retinal layers, photoreceptors, and nerve fibers. Consequently, innovative medical interventions have been developed in Russian ophthalmology to synergistically enhance the efficacy of anti-VEGF therapy in RVO management.

1.2. Endonasal Retinalamin Electrophoresis

Electrophoresis (also referred to as iontophoresis) is a non-invasive drug delivery modality that utilizes low-intensity electric current to facilitate the targeted migration of therapeutic agents across biological membranes, such as the skin or mucous mem-branes [42,43,44]. One of the earliest medical applications was documented in 1740 by Pivati for the treatment of arthritis [45]. The delivery process is primarily driven by two biophysical mechanisms: electromigration (the movement of charged ions) and electro-osmosis (convective solvent flow) [46, 47]. This method is particularly effective for the transport of hydrophilic and larger water-soluble molecules—including peptides and small proteins—which other-wise cannot penetrate biological barriers such as the blood-ocular barrier [48,49].

Extensive *in vitro* and in *vivo* research has demonstrated that charged and labeled compounds can migrate within a direct current field at rates of 2–10 mm/h along nerve fibers [50,51,52]. These findings suggest that electrical stimulation enhances in-tra-axonal transport between the cathode and anode, thereby promoting neuroregenerative processes within nerve fibers. Furthermore, iontophoresis applied along the cell surface can induce receptor aggregation (such as acetylcholine receptors) toward the cathodal pole within 30 minutes [53,54]. Emerging evidence also suggests a potential modulatory effect on receptors for transforming growth factor beta and fibroblast growth factor [55].

Given its long-standing history, this modality remains a vital tool in various medical fields, including contemporary ophthalmology. Besides its electrotherapeutic im-pact, electrophoresis exerts a dual action by incorporating a pharmacological component. By facilitating the iontophoresis of charged particles, this method effectively by-passes the inner blood-retinal barrier to deliver therapeutic agents directly to the neu-ral retina [56,57,58]. The resulting accumulation of Retinalamin—a bovine-derived complex of low-molecular-weight polypeptide fractions—enhances functional out-comes by stimulating photoreceptor activity and modulating vascular permeability [56,57,58,59]. Since 1988, research in laboratory animal models has elucidated the primary therapeutic effects of Retinalamin, which are driven by its neural and retinal regenerative and protective activities [60, 61]. Retinalamin is primarily authorized for use in Russia and several Commonwealth of Independent States countries, where it is manufactured by Geropharm and listed in national medicine registers.

1.3. Lidase Magnephoresis

Experimental and clinical evidence identifies external magnetic field therapy as a potent modulator of neural repair and survival, enhancing the regeneration of the op-tic nerve and retinal ganglion cells, accelerating synaptogenesis and increasing plasticity [62]. Other studies demonstrate that magnetic stimulation can stimulate nerve cell proliferation and differentiation by activating extracellular signal-regulated kinase and c-Jun N-terminal Kinase signaling pathways [63]. In addition, the restorative effect of magnetic stimulation has been experimentally proven, manifested in an in-crease in the function and resistance of cells due to the activation of Ca2+ and Na+/K+ channels in the cell membrane [64]. Additionally, external magnetic field therapy is used clinically to facilitate thrombolysis, enhance targeted drug delivery, and attenuate inflammatory responses within the retinal microenvironmen [65,66,67,68]. Beyond structural repair, external magnetic field therapy can potentiate the functional recovery of neuronal responses in the visual cortex [60]. Magnetophoresis is a physical phenomenon concerning the motion of magnetic particles in response to an external magnetic field by two mechanisms: magnetokinesis and alteration of barrier property of skin [69]. Concurrently with electrophoresis, magnetophoresis represents a sophisticated, non-invasive approach that leverages external magnetic field gradients to direct therapeutic agents, such as hyaluronidase (Lidase), toward occluded retinal vessels by penetrating the inner blood-retinal barrier. Recently, numerous experimental and clinical studies have validated the therapeutic potential of lidase magnetophoresis (LMP) following intravitreal anti-VEGF therapy in the treatment of RVO, demonstrating potent anti-inflammatory and anti-neovascularization effects [58].

Despite the documented high efficacy and widespread clinical adoption of these modalities in Russia for patients with retinopathy after RVO, there is a notable lack of publications evaluating their relative effectiveness or the extent of their synergistic potential when used in combination. To fill this knowledge gap, we conducted a retrospective study to evaluate the efficacy of LMP and endonasal retinalamin electrophoresis (ERE) combined with intravitreal ranibizumab for the management of non-ischemic superior temporal RVO by analyzing longitudinal changes in central retinal thickness and total macular volume immediately post-treatment and at a three-month follow-up.

2. MATERIALS AND METHODS

2.1 Study Design and Participants

In this retrospective, single-center three-arm cohort study we performed a retrospective analysis of clinical records for patients with RVO who underwent LMP and ERE in combination with anti-VEGF therapy between 2020 and 2024 in the ophthalmology department of the Rostov Regional Clinical hospital. This study is a part of the official scientific program of the Department of Sports Medicine and Medical Rehabilitation at Sechenov University.

2.1.1 Grouping Methodology

Eligibility Screening: A total of 526 medical records of patients with RVO who received anti-VEGF therapy, either alone or in combination with LMP and ERE, were initially screened. 111 records were excluded for failing to meet the predefined inclusion criteria.

Group Allocation: Propensity Score Matching method was applied to 415 patients, excluding 196 patients to obtain 3 matched groups by age, gender, central retinal thickness, and total macular volume. Of the remaining 219 patients 73 patients received only anti-VEGF therapy (control group). Additional to anti-VEGF therapy 72 patients under went

LMP (LMP group) and 74 patients completed combined LMP and ERE treatment (LMP + ERE group) (**Figure 1**). At the end of follow-up 5 patients were excluded from final analysis due to incomplete follow-up data. Consequently, the final analysis comprised 71 patients in the control group, 71 patients in the LMP group, and 72 patients in the LMP + ERE group.

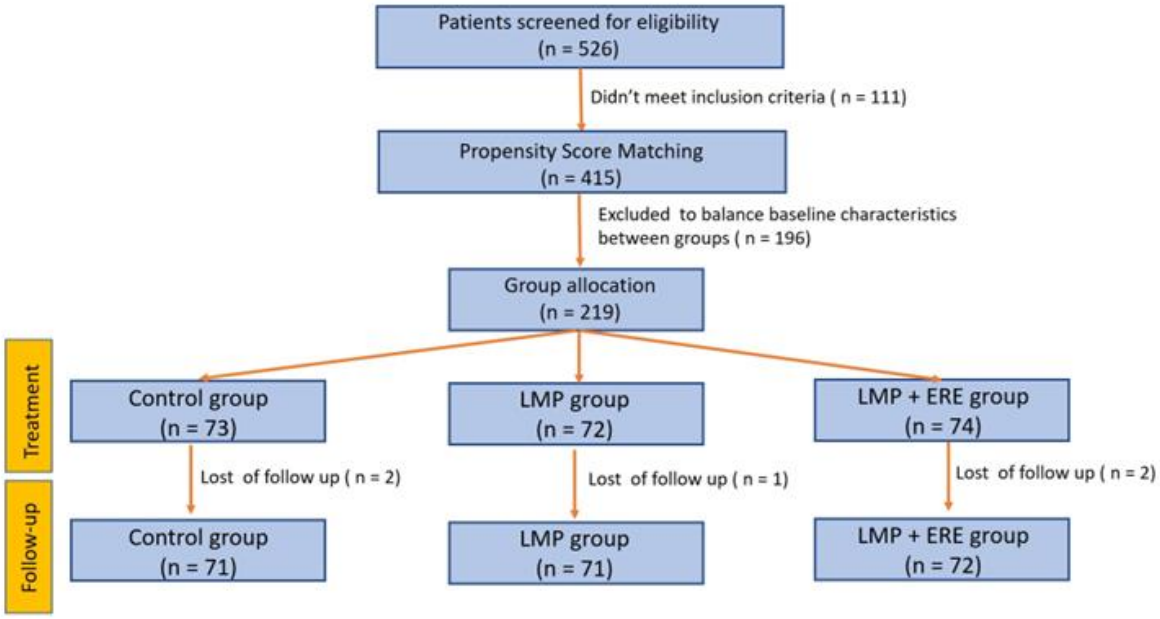


Figure 1. The CONSORT flow diagram. Note: LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis.

2.1.2. Participant Selection Criteria

Inclusion criteria:

1. Europeans;
2. men and women from 40 to 70 years old;
3. central retinal thickness less than 550 μm;
4. total macular volume less than 16 mm^3.

Exclusion criteria:

1. mental disorders;
2. thrombophilic disorders;
3. history of previously administered antiangiogenic therapy for the current condition;
4. non-compliance with follow-up protocols.

2.1.3. Consent to Participate

All study participants received a comprehensive explanation of the diagnostic and therapeutic procedures and provided documented consent for the medical interventions performed during their hospital stay. All study participants gave their documented, written informed consent to be included in this research. Additionally, they provided specific approval for their data and the study's conclusions to be published after personally reviewing the final manuscript. Neither the patients nor the researchers were given any form of financial payment for their involvement in the study.

2.1.4. Ethical Consideration

Ethical approval and a waiver of informed consent for this research were granted by the Institutional Review Board of Sechnov University (Moscow, Russia), as documented in Protocol No. 06-24 on March 14, 2024. All research protocols complied with the ethical principles set out in the 1984 Helsinki Declaration and its subsequent amendments.

2.2 Sample Size Calculation

An a priori power analysis performed with G*Power (version 3.1.9.4) determined that a minimum of 59 participants was necessary to achieve a statistical power of 0.95. This calculation was based on an effect size of 0.4, a significance level of 0.05, and a Type I error rate of 0.01. These parameters resulted in a noncentrality parameter of 3.35 and a critical *t*-value of 1.62.

2.3 Clinical Examination and Outcomes Evaluation

All participants received a comprehensive diagnostic protocol, which included uncorrected and best-corrected visual acuity measurement, anterior segment evaluation via slit-lamp biomicroscopy, fluorescein angiography and automated static perimetry for visual field mapping. The posterior segment was thoroughly assessed using funduscopy with a Goldmann three-mirror contact lens, supplemented by B-scan ultrasonography and high-resolution Optical Coherence Tomography (OCT).

2.3.1. Primary endpoints

Central retinal thicknessCentral retinal thickness is defined as the distance between the internal limiting membrane and the retinal pigment epithelium at the foveal center. Central retinal thickness refers to the central 1-mm subfield when using the Heidelberg Spectralis OCT. Central retinal thickness remains the definitive metric for diagnosing and monitoring RVO-associated macular edema [70]. While reductions in central retinal thickness over time are a positive sign, persistent or fluctuating thickness often predicts poorer long-term visual outcomes [71-76]. Quantitative central retinal thickness was obtained using a Heidelberg Spectralis OCT device (Heidelberg Engineering GmbH, Germany), which has been officially registered for medical practice in Russia since 2016 (Registration No. FSZ 2009/05829). OCT examination was performed before the start of therapy and repeated monthly for six months.

Total macular volume is the quantitative measurement of the entire neural retina's thickness within the central 6mm area of the macula, calculated by summing volumes from segmented sections (like the inner 3mm and outer 3-6mm rings) and is a key measurement of the macula's thickness and structure. For calculating total macular volume OCT is used [77,78,79]. In our study were included only patients with total macular volume of 9 -15 mm3. Total macular volume was assessed before treatment and repeated monthly for six months after treatment using a Heidelberg Spectralis OCT system (Registration No. FSZ 2009/05829).

2.3.2. Secondary Endpoints

Visual function was evaluated using Best Corrected Visual Acuity (BCVA), defined as the maximum resolution attainable with optimal refractive correction. BCVA assessments were conducted at baseline and subsequently repeated at monthly intervals for six months following the initiation of therapy

Well-being, Activity, and Mood (SAN) questionnaire was designed to assess both the physical and psychological dimensions of quality of life in both clinical and healthy populations. This instrument provides a differentiated self-assessment of an individual's functional status by measuring three core states: well-being, activity, and mood [80,81,82]. The SAN questionnaire is widely used in Russia to evaluate mental health and physical activity of patients after RVO [58,66].

2.4 Treatment Protocols

2.4.1. Anti-VEGF therapy

Patients received a 0.5 mg dose of ranibizumab via intravitreal injection, per-formed under strict aseptic conditions in an operating suite. Topical anesthesia was provided using 0.4% oxybuprocaine (Inocaine) drops. The medication was delivered into the vitreous cavity through a transscleral approach using a 30 G needle, with the entry point positioned

3.5 to 4 mm posterior to the limbus. A total of three doses were administered, with a 30-day interval between each session.

2.4.2. Lidase magnetophoresis

The patient received a course of magnetophoresis using a contact ophthalmic emitter while in a prone position. A gasket saturated with 64 units of Lidase solution was applied to the closed, affected eye. The therapy utilized a continuous, clockwise running magnetic field with an induction of 6 mT and a frequency of 12 Hz. Treatment sessions lasted 20 minutes and were administered on alternate days for a total of 15 procedures. The LMP procedures were initiated one month after the first ranibizumab injection and continued for a one-month duration. The procedures were performed using the POLIMAG-02 magnetic therapy device. The device was manufactured by JSC 'GPZ' in Ryazan region, Russia, registration number RZN 2017/6315 dated 03/10/2017. Lidase is a specific brand of hyaluronidase, an enzyme used to increase the ab-sorption and dispersion of other injected drugs. Hyaluronidase is approved by both the FDA and EMA under various brand names and in co-formulations.

2.4.3. Endonasal Retinalamin Electrophoresis

A 15-day regimen of retinalamin-mediated iontophoresis was performed using a bi-furcated endonasal anode. The procedure utilized a 0.25% peptide solution delivered via the nasal mucosa toward the ophthalmic structures, with a secondary 8 × 10 cm cathode placed at the upper cervical spine. Sessions lasted 15 minutes each with a tolerated current range of 0.6 to 1 mA. The endonasal electrophoresis sessions were ad-ministered immediately following the completion of the LMP procedure. The proce-dures were performed on alternate days. LMP and ERE protocols were started one month after the first ranibizumab injection and lasted for one month (**Figure 2**). Electrophoresis was performed using the Potok-1 (manufactured by EMA Plant CJSC, Yekaterinburg, Russia). The device holds a valid medical registration (No. FSR 2010/09713 dated 12/30/2010) for delivering galvanic current in clinical settings. Retinalamin primarily approved and manufactured in Russia by Geropharm (registration number LC-000684 – 07.07.2010) and is available in some neighboring Common-wealth of Independent States countries. Retinalamin is not U.S. Food and Drug Ad-ministration (FDA) or the European Medicines Agency (EMA) approved. Discussions of its efficacy can be framed as "experimental" or "region-specific" to maintain scientific rigor.

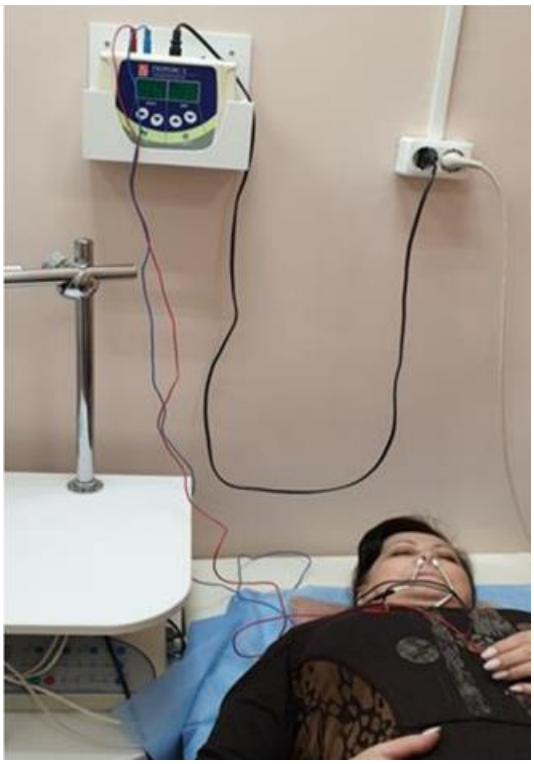


Figure 2. Technique of endonasal retinalamin electrophoresis application

2.5. Statistical Analysis

In this retrospective, single-center, three-arms cohort study, patients were divided into three comparable groups using SPSS for Windows (version 20) software. The primary endpoints in this research are the central retinal thickness and total macular volume. The secondary endpoints were best corrected visual acuity and quality of life. To negotiate differences, in baseline values between groups, Propensity Score Matching method were performed. To assess significant differences between groups, data were summarized as mean (M) and standard deviation (SD). Inter-group comparisons were performed using Student's t-test, with statistical significance defined at p-value ≤ 0.05. Furthermore, effect sizes were calculated using Cohen's d to quantify the magnitude of the observed differences. Data normality was assessed using the Shapiro-Wilk test. The equality of variances of two or more groups was determined using the Levene test. To minimize the risk of Type I errors during simultaneous hypothesis testing, the Bonferroni correction was applied to adjust for multiple comparisons. In our study, comparative analysis was conducted only between two groups for one specific symptom. To compare the mean pre-treatment values of a four groups analysis of variance (ANOVA) was used.

3. RESULTS

3.1. Patient Demographics and Characteristics

Mean age of the participants was 55.4 ± 9.1 years. Mean duration of RVO symptoms was 8.45 ± 3.20 days. Data from optical coherence tomography (OCT) indicated an increase in central retinal thickness averaging 419 ± 50.5 μm, alongside an elevated total macular volume of 12.4 ± 2.30 mm^3 (**Table 1**).

Table 1. Characteristics of the participants

Characteristic	Control group	LMP group	LMP+ ERE group	F*	*P*-value**
Number of the participants, n	71	71	72		
Male/Female	39/32	38/33	39/33	0.028#	0.98
Age (year)	55.4 ± 9.22	55.1 ± 9.5	55.9 ± 10.1	0.125	0.88
Duration of symptoms (days)	8.80 ± 3.58	8.45 ± 3.87	8.25 ± 3.41	0.41	0.66
Central retinal thickness (mm)	426 ± 56	416 ± 61	415 ± 64	0.72	0.49
Total macular volume ($mm^{3)}$	12.4 ± 2.20	12.5 ± 2.60	12.2 ± 2.41	0.28	0.75

*Note: LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis, Mean ± Standard deviation (SD), * F – F-value by ANOVA test, ** p-value by ANOVA test. #- chi-square statistic.*

In our study were included only patients with non-ischemic superior temporal RVO with development of superotemporal quadrant (upper-outer section) edema. All patients showed foveal involvement, with 93.9% (n = 214) exhibiting additional spread into the inferior macular region. Morphometric analysis identified that isolated cystoid macular edema occurred in 38.8% of cases, while isolated diffuse retinal thickening was the least frequent pattern at 6.1%. A combined pattern of cystoid macular edema and diffuse retinal thickening (mixed-type) was the dominant type, occurring in 55.1% of patients. Further subgroup analysis, as shown in **Figure 3**, confirmed that this pr-portional distribution remained consistent across all patient categories (chi-square statistic = 1.1005, p-value = 0.8942).

3.2. Primary Clinical Outcomes

3.2.1. Central Retinal Thickness

At baseline, central retinal thickness ranged from 350 to 500 μm, with a mean of 419 ± 50.5 μm. No statistically significant differences were observed across the study groups at baseline (F = 0.72, p-value = 0.49). Following the first month of anti-VEGF monotherapy, a significant reduction in central retinal thickness was observed in control group, LMP group and LMP+ERE group by 20.4%, 18.0% and 19.3%, respectively.

After the application of LMP and ERE was found more decrease of this thickness by 12.9% after LMP and by 16.4% following LMP+ERE treatment and only by 5.89% in control group. At the end of treatment both LMP and LMP+ERE groups demonstrated statistical superiority over the control group in reducing central retina1 thickness by 6.89% and

12.3%, respectively. At the end of the follow-up, a mild continued decrease in central retinal thickness by 5.37% was observed in LMP+ERE group, but not in the control and LMP groups (**Figure 4**).

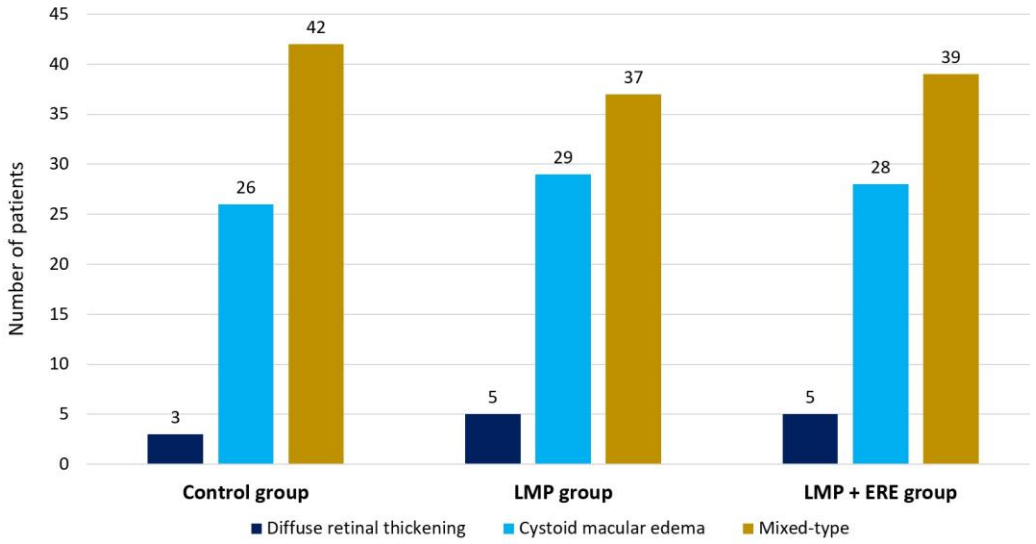
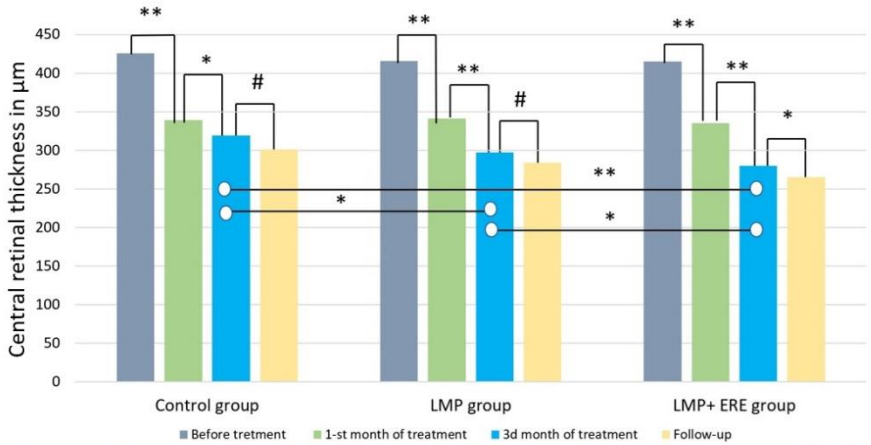


Figure 3. The relative distribution of morphometric variations in macular edema across the analyzed groups.
Note: *LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis.*



	Before treatment	After Treatment		Follow up	Significant difference		
		1-st month	3-d month		1	2	3
Control group	426 ± 56 95% CI [412.0 – 438.0]	339 ± 55 95% CI [326.2 – 351.8]	319 ± 58 95% CI [305.5 – 332.4]	301 ± 60 95% CI [287.0 – 314.9]	t = 9.06 p = 0.0001 Cohen's d = 1.56	t = 2.10 p = 0.04 Cohen's d = 0.35	t = 1.88 p = 0.06 Cohen's d = 0.30
LMP group	416 ± 61 95% CI [401.8 – 430.1]	341 ± 54 95% CI [328.4 – 353.6]	297 ± 51 95% CI [285.1 – 308.8]	284 ± 52 95% CI [271.9 – 296.0]	t = 7.75 p = 0.0001 Cohen's d = 1.33	t = 4.99 p = 0.0001 Cohen's d = 0.83	t = 1.50 p = 0.135 Cohen's d = 0.25
LMP+ ERE group	415 ± 64 95% CI [400.2 – 429.8]	335 ± 51 95% CI [323.2 – 346.7]	280 ± 49 95% CI [268.7 – 291.3]	265 ± 45 95% CI [254.6 – 275.3]	t = 8.23 p = 0.0001 Cohen's d = 1.48	t = 6.47 p = 0.0001 Cohen's d = 1.05	t = 2.04 p = 0.04 Cohen's d = 0.31

Significant difference between groups		
LMP group / Control group	t = 2.40, p = 0.02 Cohen's d = 0.40	t = 2.04, p = 0.04 Cohen's d = 0.30
LMP –ERE group / LMP group	t = 2.02, p = 0.04 Cohen's d = 0.34	t = 2.33 p = 0.02 Cohen's d = 0.39
LMP+ ERE group / Control group	t = 4.26, p = 0.0001 Cohen's d = 0.72	t = 4.06, p = 0.0001 Cohen's d = 0.64

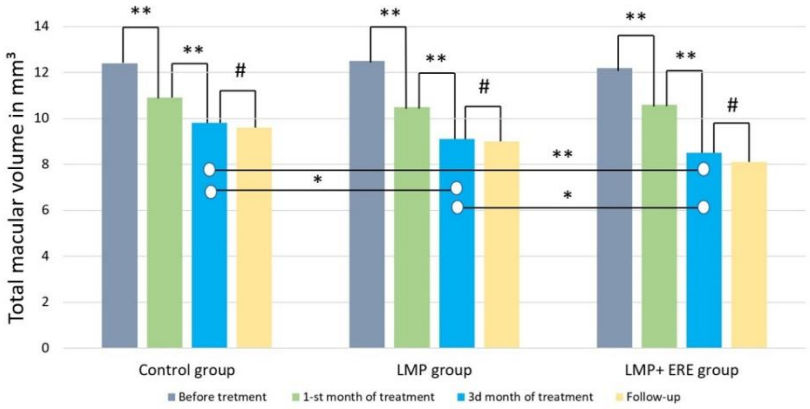
Figure 4. Dynamics if central retinal thickness in the observed groups in µm.
*Notes: LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis, # - p-value > 0.05, * - p-value ≤ 0.05, ** - p-value ≤ 0.01.*

3.2.2. Total Macular Volume

Prior to treatment, all study groups exhibited elevated total macular volume, with an overall mean of 12.4 ± 2.30 mm³. Statistical analysis con-firmed that the studied groups were homogeneous at baseline, with no significant inter-group differences detected (F = 0.28, *p*-value = 0.75).

After the first month of treatment by anti-VEGF monotherapy the decrease of this anatomical value was detected in control group by 12.1%, in LMP group by 16.0% and in LMP+ERE group by 13.1%. The application of LMP and ERE led to an additional significant decrease in total macular volume by 13.3% in the LMP group and 19.8% in the LMP+ERE group. In contrast, the control group exhibited a more modest decrease of 10.1%. Meanwhile, LMP and LMP+ERE groups showed superior efficacy over control group, reducing total macular volume by 7.14% and 13.3%. At the end of the follow-up period, the improvement achieved was maintained without negative dynamics (**Figure 5**).

4.



	Before treatment	After Treatment		Follow up	Significant difference		
		1-st month	3-d month		1	2	3
Control group	12.4 ± 2.2 95% CI [11.9 –12.9]	10.9 ± 2.1 95% CI [10.4 – 11.4]	9.80 ± 1.9 95% CI [9.35 – 10.2]	9.60 ± 1.8 95% CI [9.17 – 10.0]	t = 4.51 p = 0.0001 Cohen's d = 0.70	t = 3.86 p = 0.0002 Cohen's d = 0.52	t = 0.64 p = 0.52 Cohen's d = 0.10
LMP group	12.5 ± 2.6 95% CI [11.9 – 13.1]	10.5 ± 2.3 95% CI [9.96 – 11.0]	9.12 ± 1.8 95% CI [8.69 – 9.54]	9.00 ± 1.7 95% CI [8.60 – 9.39]	t = 4.80 p = 0.0001 Cohen's d = 0.81	t = 4.03 p = 0.0001 Cohen's d = 0.68	t = 0.34 p = 0.73 Cohen's d = 0.05
LMP+ ERE group	12.2 ± 2.4 95% CI [11.6 – 12.7]	10.6 ± 2.3 95% CI [0.1 – 11.2]	8.50 ± 1.7 95% CI [8.10 – 8.89]	8.11 ± 1.6 95% CI [7.74 – 8.48]	t = 4.80 p = 0.0001 Cohen's d = 0.68	t = 6.23 p = 0.0001 Cohen's d = 0.91	t = 1.45 p = 0.81 Cohen's d = 0.23
Significant difference between groups							
LMP group / Control group			t = 2.25, p = 0.02 Cohen's d = 0.37	t = 2.04, p = 0.04 Cohen's d = 0.34			
LMP –ERE group / LMP group			t = 2.04, p = 0.04 Cohen's d = 0.33	t = 3.20, p = 0.001 Cohen's d = 0.53			
LMP+ ERE group / Control group			t = 4.31, p = 0.0001 Cohen's d = 0.76	t = 5.26, p = 0.0001 Cohen's d = 0.83			

Figure 5. Dynamics if total macular volume in the observed groups in mm3.
Notes*: LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis, # - p-value > 0.05, * - p-value ≤ 0.05, ** - p-value ≤ 0.01.*

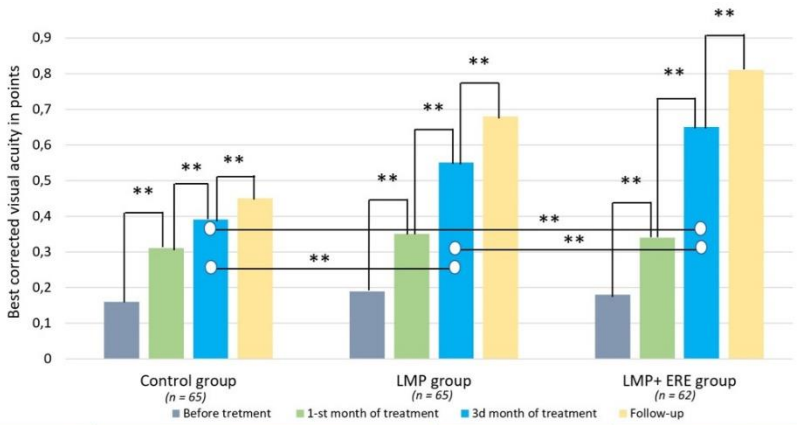
3.3. Secondary Clinical Outcomes

3.3.1. Best Corrected Visual Acuity

At baseline, visual function was significantly impaired across all participants, with a mean BCVA of 0.17 ± 0.08. The study groups were well-matched, with no significant differences detected (F = 2.19, *p*-value = 0.11) (**Figure 6**).

Following the initial anti-VEGF monotherapy all groups showed significant improvement in BCVA. The average improvement rate was 93.7% in the control group, 84.2% in the LMP group, and 88.9% in the LMP+ERE group. After the application of LMP and LMP+ERE treatment BCVA improvements were recorded by 57.1% in the LMP group and 91.2% in the LMP+ERE group, while the control group improved by only 10.7%. Consequently, treatment efficacy in the LMP and LMP+ERE groups exceeded that of the control group by 41% and 67%, respectively. At the end of follow-

up compared to the results obtained after 3 months of treatment continuing improvement was observed in LMP group by 15.4%, in LMP+ERE group by 23.6%. This positive decline in BCVA was higher than in control group by 51.1 % in LMP group and by 80% % in LMP+ERE group. By the end of the follow-up period, the LMP group showed an additional 15.4% improvement, while the LMP+ERE group demonstrated significant improvement of 24.6%. This continued progress significantly exceeded that of the control group, by 51.1% in LMP group and by 80% in LMP+ERE group.



	Before treatment	After Treatment		Follow up	Significant difference		
		1-st month	3-d month		1	2	3
Control group	0.16 ± 0.08 95% CI [0,141 — 0,179]	0.31 ± 0.04 95% CI [0,300–0,320]	0.39 ± 0.05 95% CI [0,378 — 0,402]	0.45 ± 0.06 95% CI [0,440–0,460]	t = 21.4 p = 0.0001 Cohen's d = 3.75	t = 10.7 p = 0.0001 Cohen's d = 1.76	t = 6.19 p = 0.0001 Cohen's d = 1.08
LMP group	0.19 ± 0.09 95% CI [0,168–0,212]	0.35 ± 0.04 95% CI [0,340–0,360]	0.55 ± 0.04 95% CI [0,540–0,560]	0.68 ± 0.05 95% CI [0,660 — 0,692]	t = 20.0 p = 0.0001 Cohen's d = 3.53	t = 14.3 p = 0.0001 Cohen's d = 2.50	t = 16.4 p = 0.0001 Cohen's d = 2.20
LMP+ ERE group	0.18 ± 0.09 95% CI [0,158–0,202]	0.34 ± 0.05 95% CI [0,328 — 0,352]	0.65 ± 0.04 95% CI [0,640–0,660]	0.81 ± 0.07 95% CI [0,790 — 0,827]	t = 19.9 p = 0.0001 Cohen's d = 3.53	t = 38.1 p = 0.0001 Cohen's d = 6.84	t = 15.6 p = 0.0001 Cohen's d = 4.05
Significant difference between groups							
LMP group / Control group			t = 21.0, p = 0.0001 Cohen's d = 3.53	t = 10.3, p = 0.0001 Cohen's d = 4.16			
LMP –ERE group / LMP group			t = 12.6, p = 0.04 Cohen's d = 2.20	t = 12.1 p = 0.0001 Cohen's d = 2.13			
LMP+ ERE group / Control group			t = 31.6, p = 0.0001 Cohen's d = 6.50	t = 30.1, p = 0.0001 Cohen's d = 5.52			

Figure 6. Dynamics of best corrected visual acuity in the observed groups in points.
Notes: *LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis, ** - p-value ≤ 0.01.*

3.3.2. Quality of Life

Well-being Aspect: The baseline mean for well-being was 3.04 ± 0.6 points, with no significant intergroup differences observed (F = 0.58; *p*-value = 0.56). By the end of the follow-up period, well-being scores had improved by 12.1% in the control group, 38.9% in the LMP group, and 51.1% in the LMP+ERE group. Compared to the control group, these improvements were significantly higher in the LMP group by 21.1% and the LMP+ERE group by 37.4% (**Figure 7**).

Activity Aspect: The average pretreatment activity score was 2.16 ± 0.5 points, with statistical homogeneity across study groups (F = 0.81; *p*-value = 0.44). Post-treatment analysis revealed positive dynamics of 46.4% in the control group, 76.4% in the LMP group, and 97.2% in the LMP+ERE group. In comparison to the control group, the improvement in activity was significantly greater in the LMP group by 27.4% and in the LMP+ERE group by 40.5%.

Mood Aspect: Prior to treatment, mood indicators were uniformly reduced across all groups, averaging 2.57 ± 0.5 (F = 0.46; p-value = 0.63). Post-treatment results demonstrated significant improvements in all groups, most notably in the LMP and LMP+ERE groups, which exhibited increases of 42.9% and 70%, respectively. In contrast, the control group's improvement remained below 17%. When compared directly to the control group, the efficacy of the LMP and LMP+ERE interventions were 26% and 49.1% higher, respectively.

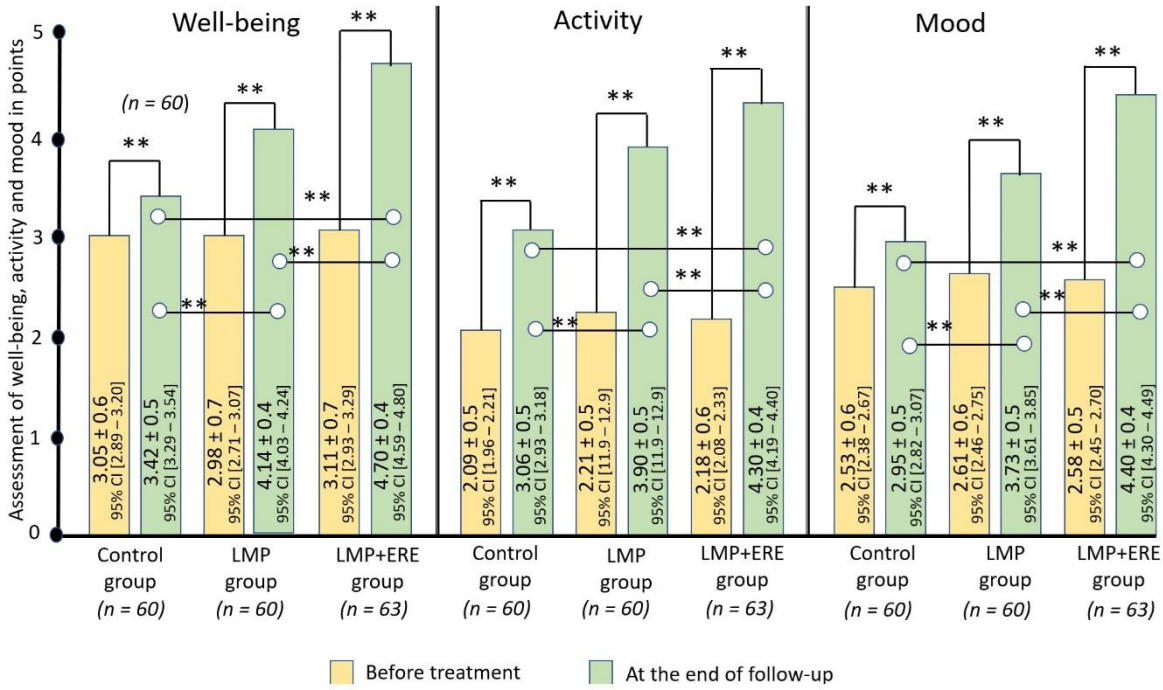


Figure 7. Dynamics of SAN-questionnaire aspects in the observed groups.
Notes: *LMP – lidase magnetophoresis, ERE – endonasal retinalamin electrophoresis, ** - p-value ≤ 0.01.*

3.4. Side Effects

No side effects were observed after LMP and ERE procedures.

4. DISCUSSION

This large-scale retrospective study investigated the efficacy of combining novel physical therapy techniques with anti-VEGF therapy for patients with RVO. Existing literature on the efficacy of LMP and ERE in ophthalmology is sparse. Available studies are predominantly published in Russian and limited by small sample sizes. Additionally, there is a lack of research comparing these two methods or investigating their potential clinical benefits when used in combination. Accordingly, the objective of this study was to evaluate the efficacy of LMP and ERE combined with intravitreal ranibizumab for the management of non-ischemic superior temporal RVO by analyzing longitudinal changes in central retinal thickness and total macular volume immediately post-treatment and at a three-month follow-up.

In this study, we performed a retrospective review of medical records for patients with non-ischemic superior temporal RVO. The analysis included patients who had received anti-VEGF therapy, either as a monotherapy or in combination with LMT or ERE. Anti-VEGF therapy consisted of three monthly intravitreal ranibizumab injection. The LMT and ERE protocols were initiated one month after the first injection and continued for a one-month duration.

4.1. Anti-VEGF Therapy

The control group received anti-VEGF monotherapy, as did the other groups during the first month of treatment before the inclusion of LMP and ERE methods. Reductions in central retinal thickness and total macular volume were noticeable after the first injection, with a gradual decrease in these values after each subsequent injection. Regression of anatomical abnormalities was accompanied by a significant improvement in BCVA and quality of life. While the effectiveness of anti-VEGF therapy is well-established, clinical success remains variable, depending on the choice of drug, total treatment duration, and the severity of baseline ischemic conditions [82-86].

4.2. Lidase Magnetophoresis

Our findings demonstrate that the combined use of LMP significantly potentiates the efficacy of anti-VEGF therapy, resulting in a more pronounced reduction in both central retinal thickness and total macular volume. Significantly, the recovery of BCVA following LMP therapy far exceeded the degree of anatomical restoration. This disparity suggests that LMP potentiates visual function not only through retinal recovery effect but also via direct neuromodulation of the optic nerve fibers, retinal receptors, and the visual cortex [60,62]. Comparative analysis with other published results is limited by the novelty of this treatment protocol in clinical practice. While previous studies have explored magnetic stimulation, they are largely focused on other ophthalmological disorders, leaving a significant gap in research regarding its effectiveness for RVO [87,88,89,90,91]. Nevertheless, several clinical studies focusing on the management of RVO have recently been published. These investigations demonstrate the high efficacy of combining LMP with anti-VEGF therapy in promoting retinal regeneration and the regression of central retinal thickness and total macular volume [58,65,66,67].

The primary advantage of LMP lies in its dual therapeutic effect: first, the beneficial regenerative and neuroprotective impact of the magnetic field on the retina and optic nerve; and second, the potentiation of the drug's pharmacological activity. By establishing a stable magnetic field, this method facilitates the targeted movement of charged lidase particles, enabling them to penetrate the inner blood-retinal barrier and reach otherwise inaccessible areas of retinal ischemia and damage [58,67]. Lidase in addition to enhancing fluid resorption and structural stabilization, promotes an-ti-inflammatory activity, facilitates tissue recovery, and improves the transretinal penetration of concomitant pharmacological agents [92].

4.3. Combined Application of Endonasal Retinalamin Electrophoresis with Lidase Magnetophoresis

The evidence from our study clarifies that the combined application of ERE with LMP demonstrated superior efficacy in enhancing the positive results achieved with the complex use of LMP and anti-VEGF therapy in reducing central retinal thickness by 5.72% ($t = 2.02$, p-value = 0.04, Cohen's $d = 0.34$) and total macular volume by 6.6% ($t = 2.04$, p-value = 0.04, Cohen's $d = 0.33$). Nevertheless, the effect size remains below 0.5, suggesting that while a measurable difference exists between the groups, its clinical significance is marginal.

Of particular note, a comparative analysis with anti-VEGF monotherapy revealed that combined application of ERE with LMP offers superior efficacy in promoting the regression of anatomical abnormalities. Specifically, this method outperformed anti-VEGF monotherapy by reducing central retinal thickness by an additional 12.2% ($t = 4.21$, p-value = 0.0001, Cohen's $d = 0.72$) and total macular volume by 13.3% ($t = 4.31$, p-value = 0.0001, Cohen's $d = 0.76$), with both outcomes exhibiting a strong effect size.

Notably, the improvement in visual function achieved with this method exceeded the effectiveness of LMP by 18,8% ($t = 12.3$, p-value = 0.0001, Cohen's $d = 2.2$) and the effectiveness of anti-VEGF monotherapy by 66.7 % ($t = 30.2$, p-value = 0.0001, Cohen's $d = 6.5$).

The use of electrophoresis in ophthalmology is an innovative and understudied scientific field. However, its effectiveness has been proven in improving clinical and electrophysiological parameters of optic nerve function and bulbar microcirculation [58,65,66,67,93].

In addition to the inherent benefits of electrical stimulation ERE operates through a second mechanism involving the targeted transport of retinalamin to the retina, effectively bypassing the inner blood-retinal barrier [58,65,66,67]. Retinalamin is a pharmacotherapeutic agent composed of a standardized complex of water-soluble polypeptide fractions, with a low molecular weight profile under 10,000 Da. Typically administered via intramuscular injection, it is used to decrease degenerative processes and accelerate tissue repair within the retina. These clinical benefits are achieved through a multifaceted metabolic mechanism that activates retinal metabolism, enhances intracellular protein synthesis, and regulates lipid peroxidation. Beyond its antioxidant properties, retinalamin enhances the homeostatic relationship between the retinal pigment epithelium and photoreceptor outer segments [61].

The observed improvement in quality of life across all treatment groups was most pronounced with the combined use of ERE, LMP, and anti-VEGF therapy, which showed a 2 times greater improvement than anti-VEGF monotherapy and 38% superiority compared to the LMP and anti-VEGF combination. This result correlates directly with the anatomical and functional advantages recorded for the combined ERE, LMP, and anti-VEGF therapy.

Thus, the complex application of LMP and ERE demonstrates a pronounced quadruple synergistic effect, which combines the distinct mechanisms of action of both LMP and ERE. This multifactorial strategy significantly potentiates the efficacy of anti-VEGF therapy and accelerates the achievement of clinical outcomes.

5. LIMITATIONS

This study is not without limitations. The first limitation is that his study did not include a placebo-only group, as withholding established effective treatment for retinal vein occlusion during the acute phase would be ethically impermissible. Addition-ally, we also could not conduct a comparative analysis between LMP and ERE separately because this study is retrospective and the number of patients who underwent ERE in combination with anti-VGEF therapy without LMP is too small to constitute a separate comparable group. An important limitation of our study is the scarce nature of the procedures and substances used, specifically Retinalamin, which is primarily used in Russia and a limited number of other countries. Additionally, it must be noted that our results are viable only in the Caucasian population and specifically for non-ischemic branch retinal vein occlusion; therefore, these findings should not be generalized to central retinal vein occlusion or ischemic branch retinal vein occlusion.

6. CONCLUSIONS

Innovative complex use of ERE and LMP in the second month after the start of treatment with intravitreal anti-VEGF therapy enhances the protective and regenerative effect of anti-VEGF therapy. Application of this method lead to an earlier reduction in central retinal thickness and decrease in total macular volume, which is important for the prevention of the development of permanent vision loss, scotoma and optic nerve atrophy in patients after RVO. Moreover, this method directly and simul-taneously impacts photoreceptors, the optic nerve, and the visual cortex, which significantly accelerate vision recovery and markedly improve patients' psychological and physical quality of life.

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Informed Consent Statement: Written informed consent has been obtained from the patients to publish this paper.

The authors confirm that they have obtained all necessary patient consent forms. In the form, the patients gave their consent for the publication of their images and other clinical information in the journal. The patients understand that their names and initials will not be published and appropriate steps will be taken to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of Interest: The authors declare no conflict of interest.

REFERENCES:

1. Jonas J.B., Monés J., Glacet-Bernard A., Coscas G. Retinal vein occlusions. *Dev Ophthalmol* **2017**; 58: 139-167. https://doi.org/10.1159/000455278.
2. Khayat M., Williams M., Lois N. Ischemic retinal vein occlusion: characterizing the more severe spectrum of retinal vein occlusion. *Surv Ophthalmol* **2018**; 63(6): 816-850. https://doi.org/10.1016/j.survophthal.2018.04.005.
3. Song P., Xu Y., Zha M., et al. Global epidemiology of retinal vein occlusion: a systematic re-view and meta-analysis of prevalence, incidence, and risk factors. *J Glob Health* **2019**; 9(1): 010427. https://doi.org/10.7189/jogh.09.010427.
4. Li W., Bian L., Ma B., et al. Interpretable detection of diabetic retinopathy, retinal vein occlusion, age-related macular degeneration, and other fundus conditions. *Diagnostics (Basel)* **2024**; 14 (2): 121. https://doi.org/10.3390/diagnostics14020121.
5. Ponto K.A., Elbaz H., Peto T., et al. Prevalence and risk factors of retinal vein occlusion: the Gutenberg Health Study. *J Thromb Haemost* **2015**; 13 (7): 1254-1263. https://doi.org/10.1111/jth.12982.
6. Smekalkina L.V., Safonicheva O.G., Kabardina E.V., et al. Current understanding of retinal vein thrombosis in older adults: A review of the literature. *Clin Interv Aging* **2025;** 3 (20): 2399-2407. https://doi.org/10.2147/CIA.S548403.
7. Hariprasad S.M., Holz F.G., Asche C.V., et al. Clinical and socioeconomic burden of retinal diseases: Can biosimilars add value? A narrative review. *Ophthalmol Ther* **2025;** 14 (4): 621-641. https://doi.org/10.1007/s40123-025-01104-3.
8. Park S.J., Choi N.K., Park K.H., Woo S.J. Nationwide incidence of clinically diagnosed retinal vein occlu-sion in Korea, 2008 through 2011: preponderance of women and the impact of aging. *Ophthalmology* **2014;** 121 (6): 1274-1280. https://doi.org/10.1016/j.ophtha.2013.12.024.

9. Shin K.U., Lee J.Y., Han K., Song S.J. Sex-specific age threshold for increased risk of retinal vein occlusion in Koreans. *Thromb Res* **2018**; 167: 60-63. https://doi.org/10.1016/j.thromres.2018.05.020.
10. Song P., Xu Y., Zha M., et al. Global epidemiology of retinal vein occlusion: a systematic re-view and meta-analysis of prevalence, incidence, and risk factors. *J Glob Health* **2019;** 9 (1): 010427. https://doi.org/10.7189/jogh.09.010427.
11. Zhang X.T., Zhong Y.F., Xue Y.Q., et al. Clinical features of central retinal vein occlusion in young patients. *Ophthalmol Ther* **2022;** 11 (4): 1409-1422. https://doi.org/10.1007/s40123-022-00534-7.
12. Darabuş D.M., Dărăbuş R.G., Munteanu M. The diagnosis and treatment of branch retinal vein occlusions: An update. *Biomedicines* **2025;** 5 (13): 105. https://doi.org/10.3390/biomedicines13010105.
13. Lang G.E., Lang S.J. Venöse Gefäßverschlüsse der Retina [Retinal Vein Occlusions]. *Klin Monbl Augenheilkd* **2018;** 235 (11): 1297-1315. (In German) https://doi.org/10.1055/a-0662-1197.
14. Devi V.L.J., Panigrahi P.K., Minj A., Hanisha D. Clinical profile of patients with retinal vein occlusion and its correlation with serum homocysteine levels. *BMC Ophthalmol* **2025**; 25 (1): 458. https://doi.org/10.1186/s12886-025-04285-4.
15. Schmidt-Erfurth U., Garcia-Arumi J., Gerendas B.S., et al. Guidelines for the management of retinal vein occlusion by the European Society of Retina Specialists (EURETINA). *Ophthalmologica* **2019;** 242 (3): 123-162. https://doi.org/10.1159/000502041.
16. Sivaprasad S., Amoaku W.M., Hykin P. RVO Guideline Group. The Royal College of Ophthalmologists Guidelines on retinal vein occlusions: executive summary. *Eye (Lond)* **2015;** 29 (1): 1633-1638. https://doi.org/10.1038/eye.2015.164.
17. Basilious A., Duncan J., Smuck B., et al. Treatment discontinuation patterns of anti-VEGF in retinal vein occlusion. *Can J Ophthalmol* **2024;** 59 (5): 341-349. https://doi.org/10.1016/j.jcjo.2023.08.005.
18. Spooner K.L., Fraser-Bell S., Hong T., et al. Long-term outcomes of anti-VEGF treatment of retinal vein occlusion. *Eye (Lond)* **2022;** 36 (6): 1194-1201. https://doi.org/10.1038/s41433-021-01620-z.
19. Namvar E., Yasemi M., Nowroozzadeh M.H., Ahmadieh H. Intravitreal injection of anti-vascular endothelial growth factors combined with corticosteroids for the treatment of macular edema secondary to retinal vein occlusion: A systematic review and meta-analysis. *Semin Ophthalmol* **2024;** 39 (1): 109-119. https://doi.org/10.1080/08820538.2023.2249527.
20. Nicholson L., Talks S.J., Amoaku W., et al. Retinal vein occlusion (RVO) guideline: ex-ecutive summary. *Eye (Lond)* **2022;** 36 (5): 909-912. https://doi.org/10.1038/s41433-022-02007-4.
21. Zhang X.T., Zhong Y.F., Xue Y.Q., et al. Clinical features of central retinal vein occlusion in young patients. *Ophthalmol Ther* **2022;** 11 (4): 1409-1422. https://doi.org/10.1007/s40123-022-00534-7.
22. Rehak M., Wiedemann P. Retinal vein thrombosis: pathogenesis and management. *J. Thromb. Haemost* **2010;** 8: 1886–1894. https://doi.org/10.1111/j.1538-7836.2010.03909.x
23. Noma H., Yasuda K., Shimura M. Cytokines and pathogenesis of central retinal vein occlusion. *J Clin Med* **2020;** 9 (11): 3457. https://doi.org/10.3390/jcm9113457
24. Darabuş D.M., Dărăbuş R.G., Munteanu M. The diagnosis and treatment of branch retinal vein occlusions: An update. *Biomedicines* **2025;** 13 (1): 105. https://doi.org/10.3390/biomedicines13010105.
25. Noh S.Y., Lee J.H., Jeong, W.J. Branch retinal vein occlusion with arteriovenous crossing. *J. Retin* **2023;** 8: 36–41. https://doi.org/10.21561/jor.2023.8.1.36.
26. Lendzioszek M., Bryl A., Poppe E., et al. Retinal vein occlusion-background knowledge and foreground knowledge prospects-A review. *J Clin Med* **2024;** 13 (13): 3950. https://doi.org/10.3390/jcm13133950.
27. Cochran M.L., Mahabadi N., Czyz C.N. Branch retinal vein occlusion. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2025, Available from: https://www.ncbi.nlm.nih.gov/books/NBK535370/
28. Ashraf M., Souka A.A., Singh, R.P. Central retinal vein occlusion: modifying current treatment protocols. *Eye (Lond).* **2016;** 30 (4): 505-514. https://doi.org/10.1038/eye.2016.10.
29. Casselholmde Salles M., Kvanta A., Amrén U., Epstein D. Optical coherence tomography angiography in central retinal vein occlusion: correlation between the foveal avascular zone and visual acuity. *Invest Ophthalmol Vis Sci* **2016;** 57 (9): OCT242-6. https://doi.org/10.1167/iovs.15-18819.
30. Soecknick F., Breher K., Nafar Z., et al. The clinical evaluation of a widefield lens to expand the field of view in optical coherence tomography (OCT-A). *Sci Rep* **2024**; 14: 6936. https://doi.org/10.1038/s41598-024-57405-3.
31. Burchard C.V., Roider J., Kepp T. Analysis of OCT scanning parameters in AMD and RVO. *Diagnostics (Basel)* **2024;** 14 (5): 516. https://doi.org/10.3390/diagnostics14050516.
32. Gupta S., Thapa R., Pradhan E., et al. Patterns of macular edema in branch retinal vein occlusion diagnosed by optical coherence tomography. *Nepal J Ophthalmol* **2023**; 15 (30): 55-62. doi: 10.3126/nepjoph.v15i2.29763.
33. Haydinger C.D., Ferreira L.B., Williams K.A., Smith J.R. Mechanisms of macular edema. *Front Med (Lausanne)* **2023;** 7 (10): 1128811. https://doi.org/10.3389/fmed.2023.1128811.
34. Martinet V., Guigui B., Glacet-Bernard A., et al. Macular edema in central retinal vein occlusion: correlation between optical coherence tomography, angiography and visual acuity. *Int Ophthalmol* **2012;** 32 (4): 369-377. https://doi.org/10.1007/s10792-012-9578-5.
35. Rotsos T.G., Moschos M.M. Cystoid macular edema. *Clin Ophthalmol* **2008;** 2 (4): 919-930. https://doi.org/10.2147/opth.s4033.
36. Ravalico G., Battaglia Parodi M. Exudative retinal detachment subsequent to retinal vein occlusion. *Ophthalmologica* **1992;** 205 (2): 77-82. https://doi.org/10.1159/000310316.

37. Qi Y., Scotland D.H., Zhang C., Xu, J. Changes of choroidal thickness and choroidal vascularity index in patients with macular edema secondary to branch retinal vein occlusion after intravitreal ranibizumab. *Int J Retina Vitreous* **2025;** 11 (1): 99. https://doi.org/10.1186/s40942-025-00727-9.
38. Şekeroğlu M.A., Taşkale F.B., Doğuizi S., Yılmazbaş P. Prevalence of serous macular detachment in recurrent macular edema secondary to retinal vein occlusion. *Turk J Ophthalmol* **2022;** 52 (4): 276-280. https://doi.org/10.4274/tjo.galenos.2021.02582.
39. Jing Y., Li D. Faricimab for retinal vein occlusion: a review of current evidence and future perspectives. *Front Pharmacol* **2025;** 14 (16): 1646806. https://doi.org/10.3389/fphar.2025.1646806.
40. Shirley M. Faricimab: first approval. *Drugs* **2022;** 82 (7): 825-830. https://doi.org/10.1007/s40265-022-01713-3.
41. Hattenbach L.O., Abreu F., Arrisi P., et al. BALATON and COMINO: Phase III randomized clinical trials of faricimab for retinal vein occlusion: study design and rationale. *Ophthalmol Sci* **2023;** 3 (3): 100302. https://doi.org/10.1016/j.xops.2023.100302.
42. Al-Zamil M., Kulikova N.G., Vasil`eva E.S., Zhuk Y.M. The effectiveness of electrophoresis with caripain in the treatment of discogenic radiculopathy in the cervical spine. Clinical case. *Russian Journal of Physiotherapy, Balneology and Rehabilitation* **2020;** 19 (1): 65-68. (In Russian). https://doi.org/10.17816/1681-3456-2020-19-1-10
43. Dagash H., McCaffrey S., Mellor K., et al. Tap water iontophoresis in the treatment of pediatric hyperhidrosis. *J Pediatr Surg*, **2017**; 52 (2,): 309-312. https://doi.org/10.1016/j.jpedsurg.2016.11.026.
44. Wang Y., Thakur R., Fan Q., Michniak B. Transdermal iontophoresis: combination strategies to improve transdermal iontophoretic drug delivery. *Eur J Pharm Biopharm* **2005**; 60: 179–191.
45. Sheikh N.K., Dua A. Iontophoresis analgesic medications, **2023**, 31. In: StatPearls [Internet]. Treasure Is-land (FL): StatPearls Publishing; 2025 Jan–. PMID: 31971730.
46. Cázares-Delgadillo J., Planard-Luong L., Gregoire S., et al. Investigation of different iontophoretic currents profiles for short-term applications in cosmetics. *Pharmaceutics*. **2018,** 10, 266.
47. Bakshi P., Vora D., Hemmady K., Banga A.K. Iontophoretic skin delivery systems: success and failures. *Int J Pharm* **2020;** 586: 119584.
48. Liatsopoulou A., Varvaresou A., Mellou F., Protopapa E. Iontophoresis in dermal delivery: A review of applications in dermato-cosmetic and aesthetic sciences. *Int J Cosmet Sci* **2023**; 45 (2): 117-132. https://doi.org/10.1111/ics.12824.
49. Kim K.T., Lee J., Kim M.H., et al. Novel reverse electrodialysis-driven ion-tophoretic system for topical and transdermal delivery of poorly permeable therapeutic agents. *Drug Deliv* **2017;** 24: 1204–1215.
50. Swift M.J., Crago P.E., Grill W.M. Applied electric fields accelerate the diffussion rat and increase the dif-fusion distance of DiI in fixed tissue. *J Neurosci Methods* **2005**; 141: 155–163. https://doi.org/10.1016/j.jneumeth.2004.06.011.
51. Madison R.D., Robinson G.A., Krarup C., et al. In vitro electrophoresis and in vivo electrophysiology of peripheral nerve using DC field stimulation. *J Neurosci Methods* **2014;** 30 (225): 90-96. https://doi.org/10.1016/j.jneumeth.2014.01.018.
52. Kiernan M.C., Bostock H. Effects of membrane polarization and ischaemia on the excitability properties of human motor axons. *Brain* **2000;** 123 (Pt 12): 2542-2551. https://doi.org/10.1093/brain/123.12.2542.
53. Poo M., Lam J.W., Orida N., Chao A.W. Electrophoresis and diffusion in the plane of the cell membrane. *Biophys J.* **1979;** 26 (1): 1-21. https://doi.org/10.1016/S0006-3495(79)85231-5.
54. Stollberg J., Fraser S.E. Acetylcholine receptors and concanavalin A-binding sites on cultured Xenopus muscle cells: electrophoresis, diffusion, and aggregation. *J Cell Biol* **1988;** 107 (4): 1397-1408. https://doi.org/10.1083/jcb.107.4.1397.
55. Zhao M., Dick A., Forrester J.V., McCaig C.D. Electric field-directed cell motility involves up-regulated expression and asymmetric redistribution of the epidermal growth factor receptors and is enhanced by fibronectin and laminin. *Mol Biol Cell* **1999;** 10 (4): 1259-1276. https://doi.org/10.1091/mbc.10.4.1259.
56. Astakhov Yu.S., Kiryanova V.V., Maksimov A.V., et al. Optimization of treatment of the dry form of age-related macular degeneration by endonasal electrophoresis with the drug "Retinalamin". *Ophthalmological Reports* **2010;** 3 (1): 69-77.
57. Antonov A,A. Experimental studies of Retinalamin efficacy. *National Journal of Glaucoma* **2024;** 23 (2): 45-52. (In Russian)
58. Kabardina E.V., Smekalkina L.V., Shurygina I.P., Khripunova O.V. Prospects for the use of pharmaco-physiotherapeutic methods in the complex treatment of macular retinal edema in patients with postthrombotic retinopathy. *Journal of New Medical Technologies* **2023**; 3: 101-107. (In Russian). https://doi.org/10.24412/2075-4094-2023-3-3-5
59. Saidov T., Yangieva N. Khamidullaev F., et al. Clinical and functional effectiveness of endonasal electro-phoresis in combination with electrostimulation in complex therapy of glaucomatous optic neuropathy. *The American Journal of Medical Sciences and Pharmaceutical Research* **2021**; 3 (3): 138-144. https://inlibrary.uz/index.php/archive/article/view/13877.
60. Antonov A.A., Makarova A.S., Reshchikova V.S. Experimental studies of Retinalamin efficacy. *National Journal of Glaucoma.* 2017,16, 3, 98-102. (In Russian)
61. Antonov A.A. Experimental studies of Retinalamin efficacy. *National Journal of Glaucoma* **2024;** 23 (2): 45-52. (In Russian)
62. Khalili M.R., Shadmani A., Sanie-Jahromi F. Application of electrostimulation and magnetic stimulation in patients with optic neuropathy: A mechanistic review. *Dev Neurobiol* **2024;** 84 (3): 236-248. https://doi.org/10.1002/dneu.22949.
63. Wu H., Li C., Masood M., et al. Static magnetic fields regulate T-type calcium ion channels and mediate mesenchymal stem cells proliferation. *Cells* **2022;** 11 (15): 2460. https://doi.org/10.3390/cells11152460.
64. Yan J., Dong L., Zhang B., Qi N. Effects of extremely low-frequency magnetic field on growth and differ-entiation of human mesenchymal stem cells. *Electromagn Biol Med* **2010;** 29 (4): 165-176. https://doi.org/10.3109/01676830.2010.505490.

65. Smekalkina L.V., Shurygina I.P., Kabardina EV. Long-term results of complex pharmacotherapy and physiotherapy in anti-angiogenic therapy for macular edema in patients with post-thrombotic retinopathy. *Modern Problems of Science and Education* **2023;** 3. https://doi.org/10.17513/spno.32597 (In Russian)
66. Kabardina E.V., Smekalkina L.V., Shurygina I.P. Comprehensive rehabilitation of patients after thrombosis of the superior temporal branch of the central retinal vein using physiotherapeutic treatment methods. In: Abstract Book of the VIII All-Russian Congress "Physiotherapy. Exercise Therapy. Rehabilitation. Sports Medicine" **2025**: 15-16. (In Russian)
67. Kabardina E.V., Smekalkina L.V., Naprienko M.V., et al. Clinical and rehabilitative aspects of retinal vein occlusions: A text-book. Moscow: Sechenov University Publishing House; 2025. 60 p. (In Russian)
68. Davydov D.V., Yakovlev A.E., Vybornaya T.R. Clinical functional results of the continuous electromag-netic stimulation in patients with optic nerve partial atrophy. *Ophthalmology Reports* **2017;** 10 (2,): 29-35. https://doi.org/10.17816/OV10229-35.
69. Murthy S.N., Sammeta S.M., Bowers C. Magnetophoresis for enhancing transdermal drug delivery: Mechanistic studies and patch design. *J Control Release* **2010;** 148 (2): 197-203. https://doi.org/10.1016/j.jconrel.2010.08.015.
70. Ahn S.J. Retinal thickness analysis using optical coherence tomography: diagnostic and monitoring applications in retinal diseases. *Diagnostics (Basel)* **2025**; 15 (7): 833. https://doi.org/10.3390/diagnostics15070833.
71. Dhoot D.S., Shah C.P., Silva F.Q., et al. Impact of central sub-field thickness fluctuations on visual outcomes in neovascular age-related macular degeneration in the VIEW trials. *J Vitreoretin Dis* **2025;** 20: 24741264251359902. https://doi.org/10.1177/24741264251359902.
72. Rattanalert K., Bhurayanontachai P., Ratanasukon M., et al. Correlation of retinal thickness, macular volume, and their fluctuation with visual outcomes in patients with macular edema due to retinal vein occlusion. *Int J Retina Vitreous* **2025;** 11 (1): 67. https://doi.org/10.1186/s40942-025-00693-2.
73. Chan A., Duker J.S., Ko T.H., et al. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. *Arch Ophthalmol* **2006;** 124 (2): 193-198. https://doi.org/10.1001/archopht.124.2.193.
74. Oderinlo O., Bogunjoko T., Hassan A.O., et al. Normal central foveal thickness in a thousand eyes of healthy patients in Sub Saharan Africa using fourier domain optical coherence tomography. *Nigerian Journal of Clinical Practice* **2023;** 26 (3): 331-335. https://doi.org/10.4103/njcp.njcp_318_22
75. Mititelu M., Uschner D., Doherty L., et al. Retinal thickness and morphology changes on OCT in youth with type 2 diabetes: findings from the TODAY study. *Ophthalmol Sci* **2022**; 2 (4): 100191. https://doi.org/10.1016/j.xops.2022.100191.
76. Liu T., Hu A.Y., Kaines A., et al. A pilot study of normative data for macular thickness and volume measurements using cirrus high-definition optical coherence tomography. *Retina* **2011;** 31 (9): 1944-1950. https://doi.org/10.1097/IAE.0b013e31820d3f13.
77. Arruabarrena C., Rodríguez-Miguel A., de Aragón-Gómez, F., et al. Normative data for macular thickness and volume for optical coherence tomography in a diabetic population without maculopathies. *J Clin Med* **2023;** 12 (16): 5232. https://doi.org/10.3390/jcm12165232.
78. Pokharel A., Shrestha G.S., Shrestha J.B. Macular thickness and macular volume measurements using spectral domain optical coherence tomography in normal Nepalese eyes. *Clin Ophthalmol* **2016;** 21 (10): 511-519. https://doi.org/10.2147/OPTH.S95956.
79. Al-Zamil W.M., Al-Zwaidi F.M., Yassin S.A. Macular thickness in healthy Saudi adults. A spectral-domain optical coherence tomography study. *Saudi Med J* **2017;** 38 (1): 63-69. https://doi.org/10.15537/smj.2017.1.17565.
80. Mikhailova O.B., Farennikova E.S. Specifics of psychological well-being of different occupational groups' representatives during the COVID-19 pandemic. *World of Science. Pedagogy and Psychology* **2020**; 4 (8): 67PSMN420 Available at: https://mir-nauki.com/PDF/67PSMN420.pdf (In Russian)
81. Zhmerenetsky K.V., Rzyankina M.F., Potapova K.E. Psychosocial aspects of self-assessment of the health of children and adolescents in changed epidemiological conditions. *Mental Health* **2022;** 17 (7): 24-28. https://doi.org/10.25557/2074-014X.2022.07.24-28
82. Campa C., Alivernini G., Bolletta E., et al. Anti-VEGF therapy for retinal vein occlusions. *Curr Drug Targets* **2016;** 17 (3): 328-336. https://doi.org/10.2174/1573399811666150615151324.
83. Dinah C., Dodds M., Lotery A., et al. Treatment patterns and long-term outcomes in anti-VEGF-treated macular oedema secondary to retinal vein occlusion: a retrospective observational study. *Eye (Lond)* **2025;** 14. https://doi.org/10.1038/s41433-025-04089-2.
84. Corazza P.D., Alterio F.M., Savastano M.C., et al. Long-term outcomes of anti-VEGF treatment of macular oedema due to retinal vein occlusions. *Eur J Ophthalmol* **2022;** 32 (6): 3536-3546. https://doi.org/10.1177/11206721221085870.
85. Subhi Y., Potapenko I., Hajari J.N., la Cour M. Prognostic modelling of number of patients with retinal vein occlusion in anti-VEGF therapy. *Acta Ophthalmol* **2024;** 102 (3): 318-325. https://doi.org/10.1111/aos.15721.
86. Chen K.Y., Chan H.C., Chan C.M. Effectiveness and safety of anti-vascular endothelial growth factor therapies for macular edema in retinal vein occlusion: A systematic review and network meta-analysis of randomized controlled trials. *Surv Ophthalmol* **2025;** 70 (6): 1067-1089. https://doi.org/10.1016/j.survophthal.2025.05.008.
87. Özmert E., Arslan U. Management of deep retinal capillary ischemia by electromagnetic stimulation and platelet-rich plasma: preliminary clinical results. *Adv Ther* **2019;** 36 (9): 2273-2286. https://doi.org/10.1007/s12325-019-01040-2.
88. Makarov I.A., Voronkov Yu.I. The role of low-frequency TRANS-orbital magnetic stimulation in normalization of intraocular pressure in patients with primary open-angle glaucoma. *Ophthalmology in Russia* **2016;** 13 (4): 273-277. (In Russian). https://doi.org/10.18008/1816-5095-2016-4-273-277
89. Joseph J.T., Jammigumpula A., Jaise J., et al. Safety of repetitive transcranial magnetic stimulation in retinal detachment: A case report and brief review. *J ECT* **2024;** 40 (3): e11-e12. https://doi.org/10.1097/YCT.0000000000001000.

90. Khalili M.R., Shadmani A., Sanie-Jahromi F. Application of electrostimulation and magnetic stimulation in patients with optic neuropathy: A mechanistic review. *Dev Neurobiol* **2024;** 84 (3): 236-248. https://doi.org/10.1002/dneu.22949.
91. Davydov D.V., Yakovlev A.E., Vybornaya T.R. Clinical functional results of the continuous electromag-netic stimulation in patients with optic nerve partial atrophy. *Ophthalmology Reports* **2017;** 10 (2): 29-35. https://doi.org/10.17816/OV10229-35.
92. Ibraheem M., El-Fakharany E., Husseiny S., Mohammed F. An overview on Hyaluronidase enzyme types, mode of action, assay and therapeutic applications. *Journal of Scientific Research in Science.* **2024;** 41: 1-17. https://doi.org/10.21608/jsrs.2024.273369.1125.
93. Razumovskaya A.M., Razumovsky M.I., Koroviansky Yu.A., Razumovsky E.S. Estimation of therapeutic effect of endonasal electrophorosis with methylethylpyridinol in partial optic nerve atrophy. *Ophthalmology in Russia* **2018;** 15 (2): 219-224. (In Russian). https://doi.org/10.18008/1816-5095-2018-2-219-224.