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Posterior Subtenon Autologous Platelet-Rich Plasma in Non-Arteritic Anterior Ischemic Optic Neuropathy: An Exploratory Randomized Study

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Posterior Subtenon Autologous Platelet-Rich Plasma in Non-Arteritic Anterior Ischemic Optic Neuropathy: An Exploratory Randomized Study

Running title: Posterior Sub-Tenon PRP in Acute NAION

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ABSTRACT

Introduction: To evaluate the short-term functional, structural, and safety outcomes of posterior sub-Tenon autologous platelet-rich plasma (PRP) injection in acute nonarteritic anterior ischemic optic neuropathy (NAION).

Methods: This prospective, exploratory, open-label randomized study included 39 patients with acute NAION allocated to posterior sub-Tenon PRP injection (n=21) or observation (n=18). PRP was administered at baseline and Weeks 3 and 6. Best-corrected visual acuity (BCVA), global retinal nerve fiber layer (RNFL) thickness, visual field mean deviation (MD), and visual field index (VFI) were assessed over 16 weeks. Baseline-adjusted linear mixed-effects models using available post-baseline measurements were used for longitudinal analyses. Exploratory Week 16 comparisons were performed using baseline-adjusted ANCOVA.

Results: The 39 randomized participants had a mean age of 59.28 ± 9.50 years, and 26 (66.7%) were male. Thirty-one participants (15 PRP and 16 control) contributed to the longitudinal analyses. No significant group-by-time interaction was observed for BCVA ($p=0.094$), RNFL thickness ($p=0.655$), MD ($p=0.124$), or VFI ($p=0.559$). Significant overall time effects were observed for BCVA ($p=0.006$) and RNFL thickness ($p<0.001$), but changes did not differ significantly between groups. Baseline-adjusted Week 16 comparisons also showed no significant between-group differences in BCVA, RNFL thickness, MD, or VFI. No serious ocular or systemic adverse events were documented.

Discussion: Posterior sub-Tenon autologous PRP did not show evidence of a short-term functional or structural advantage over observation in acute NAION. Interpretation is limited by the small sample size, incomplete follow-up, and absence of sham control and masking. Larger, adequately powered randomized trials with standardized PRP characterization and systematic safety monitoring are warranted.

Clinical Trial Registration: ClinicalTrials.gov: NCT07330713 (retrospectively registered on December 28, 2025).

INTRODUCTION

Non-arteritic anterior ischemic optic neuropathy (NAION) is a common cause of acute, painless, and predominantly unilateral visual loss in patients aged 50 and older [1]. Its annual incidence is reported to range from 2 to 10 cases per 100,000 in the general population [2]. Clinically, it is characterized by sudden vision loss, arcuate or altitudinal visual defects, and edema at the optic nerve head, often accompanied by peripapillary flame-shaped retinal hemorrhages [3]. The visual prognosis is highly variable; however, a significant proportion of cases result in permanent vision loss [1].

Although the underlying mechanisms remain incompletely elucidated, current evidence suggests that NAION is primarily related to impaired perfusion of the optic nerve head, mainly supplied by the short posterior ciliary arteries, resulting in ischemic injury and optic disc edema. Subsequent axonal damage and retinal ganglion cell loss may occur as part of the secondary degenerative process [4].

Currently, there is no standard treatment protocol for NAION. Several treatment options, including corticosteroids, antioxidants, antiplatelet agents, neuroprotective pharmacological drugs, hyperbaric oxygen therapy, and surgical methods, have been evaluated to date. Some of these approaches have yielded encouraging findings in animal models and early clinical observations. However, evidence from these studies remains limited due to small sample sizes, the absence of control groups, and a lack of convincing evidence for long-term therapeutic benefit [1, 4-6].

In recent years, platelet-rich plasma (PRP) has become popular in ophthalmology for treating various diseases due to the growth factors, cytokines, and other bioactive molecules it contains [7-11]. PRP has been shown to yield positive results with topical application in ocular surface diseases, fibrin formation in macular hole closure, and intravitreal or periocular injections for various retinal diseases, such as retinitis pigmentosa [7-11]. Furthermore, experimental studies have demonstrated the favorable effects of PRP on axonal regeneration and functional improvement in peripheral nerve injuries, suggesting that PRP may be a potential treatment option for NAION involving optic nerve damage [12].

In this exploratory randomized study, we aimed to evaluate the short-term functional, structural, and safety outcomes of posterior subtenon autologous PRP injection compared with observation alone in patients with acute NAION.

MATERIALS AND METHODS

This prospective, single-center, randomized controlled clinical study was conducted at Bursa Uludag University, Department of Ophthalmology, between January 2022 and January 2024. The diagnosis of acute NAION was based on the presence of sudden painless visual loss, decreased visual acuity and/or visual field defects, typically altitudinal, optic disc edema, and a relative afferent pupillary defect when clinically applicable, after excluding other causes of optic neuropathy.

The prespecified primary outcome was the change in best-corrected visual acuity (BCVA), expressed in logarithm of the minimum angle of resolution (logMAR) units, from baseline to week 16. Secondary outcomes included changes in peripapillary retinal nerve fiber layer (RNFL) thickness (μm), visual field mean deviation (MD, dB), and visual field index (VFI, %) from baseline to week 16. Outcome measures were summarized using means and standard deviations or medians and ranges, as appropriate to the distribution of the data. Safety outcomes included ocular and systemic adverse events recorded throughout the 16-week follow-up period.

Eligible participants were randomized with an equal allocation probability (1:1) to the PRP or control group using computer-generated simple randomization. The randomization sequence was generated by G.O. Participants were enrolled by G.U.G., and group allocation was implemented by S.N.T. The allocation sequence was concealed within the electronic randomization system and was revealed only after participant enrollment and eligibility confirmation. No stratification or block randomization was applied. The PRP group received posterior sub-Tenon autologous PRP injections at baseline, Week 3, and Week 6, whereas the control group was managed with observation alone. No sham injection was performed. No additional NAION-specific treatments were administered to participants in either group during the study period. Concomitant medications for pre-existing systemic conditions were continued as clinically indicated. Consequently, participants and treating ophthalmologists were aware of treatment allocation after randomization. Outcome assessors were also not masked to group assignment; therefore, the study was open-label. Treatment adherence, completion of the scheduled injections, and any deviations from the protocol were documented. Participants in the control group were followed according to the same assessment schedule.

Inclusion criteria were as follows: 1) acute and painless vision loss or visual field defect, 2) symptom onset within 14 days, 3) age 40 years or older, and 4) ability to cooperate with visual acuity and visual field examinations. Exclusion criteria were as follows: 1) arteritic anterior ischemic optic neuropathy, including suspected giant cell arteritis, 2) posterior ischemic optic neuropathy, 3) age under 40 years, 4) concomitant retinal or optic nerve disease that could affect visual acuity or visual field assessment, such as glaucoma, diabetic

macular edema, retinal dystrophy, or other relevant ocular conditions, 5) demyelinating disease or intracranial mass affecting the optic nerve, 6) inability to cooperate with visual acuity or visual field testing, and 7) systemic hematological disease that could affect PRP preparation.

All patients were assessed for systemic risk factors and were referred to the relevant specialties for the management and optimization of existing conditions, including hypertension, diabetes mellitus, hyperlipidemia, and obstructive sleep apnea syndrome.

A comprehensive evaluation was performed on all patients on the day of presentation. Demographic data (age, gender), symptom duration, concomitant systemic diseases, and systemic medications were recorded. A detailed ophthalmological examination, including best-corrected visual acuity (BCVA), intraocular pressure (IOP), biomicroscopy, funduscopy, and visual field testing, was performed. BCVA values were converted to LogMAR units according to the Holladay method. Automated perimetry (Zeiss Humphrey Field Analyzer 3, Germany) was used for the visual field (30-2) test. At baseline, the visual field examination was performed in both eyes. To minimize the learning effect, two additional 30-2 examinations were subsequently performed only in the study eye; the mean deviation (MD) and visual field index (VFI) values from the third examination were used for analysis. Visual field tests were considered reliable if fixation losses, false-positive responses, and false-negative responses were within the reliability limits recommended by the device software. Tests not meeting these reliability criteria were excluded from MD and VFI analyses. Optic disc photography was taken with a fundus camera (Zeiss Visucam 500, Germany). Peripapillary RNFL thickness was measured using the Spectralis SD-OCT system (Heidelberg Engineering, Heidelberg, Germany; software version 5.3.3.0). A 3.5-mm diameter circular scan protocol consisting of 768 A-scans was used. Real-time eye tracking (TruTrack™) was enabled during image acquisition to reduce motion artifacts. RNFL thickness was automatically segmented by the device software as the distance between the internal limiting membrane and the outer border of the RNFL. Global and sectoral RNFL thicknesses (superior, inferior, nasal, temporal, superotemporal, superonasal, inferonasal, and inferotemporal) were recorded for analysis. Only scans with an image quality score (Q score) of ≥20, correct centration, and reliable automated segmentation were included. Scans with motion artifacts or segmentation errors were excluded. Visual evoked potential (VEP) testing was performed, and P100 latencies were noted. Serum erythrocyte sedimentation rate and C-reactive protein (CRP) levels were measured to rule out arteritic ischemic optic neuropathy. Therefore, patients presenting with chalky-white optic disc edema, elevated erythrocyte sedimentation rate or CRP levels, absent temporal artery pulsation, temporal artery tenderness, or systemic symptoms suggestive of giant cell arteritis, such as headache or jaw claudication, were excluded. All

patients underwent cranial and orbital magnetic resonance imaging to exclude alternative intracranial or orbital causes of optic neuropathy, and those with abnormal imaging findings were not included in the study. None of the enrolled patients had received pulse corticosteroid therapy before enrollment.

All patients underwent a thorough ophthalmological examination at weeks 1, 3, 6, 8, and 16 after presentation. At each visit, BCVA, visual field testing, optic disc photography, OCT, and RNFL measurements were repeated. The main efficacy assessment focused on longitudinal BCVA changes during the 16-week follow-up. Secondary longitudinal outcomes included global RNFL thickness, visual field MD, and VFI. Exploratory Week 16 outcome comparisons were also performed among patients with valid Week 16 measurements.

Autologous PRP was prepared using the Dr. PRP® Kit (Dr. PRP USA LLC, USA) according to the manufacturer's instructions with a refrigerated centrifuge to minimize premature platelet activation and preserve platelet integrity during processing. On the day of injection, 18 mL of peripheral venous blood was drawn from patients in the PRP group using 20-mL syringes containing 2 mL of sodium citrate. A two-stage centrifugation protocol (first spin: 3000 rpm for 3–4 minutes; second spin: 3250 rpm for 6 minutes) was applied. After removal of the platelet-poor plasma fraction, approximately 3–4 mL of PRP was obtained. Based on the manufacturer’s specifications, the final PRP product was estimated to contain a platelet concentration approximately 8–10 times higher than baseline physiological levels. The final platelet concentration was not measured in individual preparations. The obtained PRP (2 mL) was injected into the posterior sub-Tenon space through an inferonasal approach by an experienced ophthalmologist (S.D. or G.U.G.).

The posterior subtenon injection technique was as follows: After topical anesthesia and povidone-iodine antisepsis, an eyelid speculum was inserted. A small conjunctival and Tenon's incision was made approximately 5–10 mm posterior to the inferonasal limbus. A blunt subtenon cannula was introduced through the incision and advanced along the curvature of the globe into the posterior subtenon space until the tip passed beyond the equator. Subsequently, 2 mL of PRP was injected slowly.

The study protocol was approved by the Turkish Ministry of Health and Bursa Uludag University Ethics Committee with the number (2019-21/36). All participants provided written informed consent, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki. This study was retrospectively registered at ClinicalTrials.gov (NCT07330713) on December 28, 2025, as patient enrollment had already commenced at the time of registration. This randomized clinical trial was reported in accordance

with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. A completed CONSORT checklist is provided as an additional file.

The target sample size was determined based on feasibility considerations during the planned recruitment period, given that acute NAION is an uncommon condition and strict inclusion criteria were applied. Therefore, this study was designed as an exploratory prospective randomized study rather than a definitive efficacy trial. The sample size was not intended to provide sufficient statistical power to detect small or moderate between-group treatment effects.

IBM SPSS Statistics, version 29.0.2.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous variables are presented as mean ± standard deviation or median (minimum–maximum), as appropriate, and categorical variables are presented as numbers and percentages. Baseline demographic and clinical characteristics were summarized descriptively and compared between groups using the independent-samples t-test or Mann–Whitney U test for continuous variables and the Pearson chi-square test, Fisher's exact test, or Fisher–Freeman–Halton test for categorical variables, as appropriate. Baseline p-values were considered descriptive and were not interpreted as evidence of baseline equivalence. Because of the small sample size and non-normal distribution of several outcome variables, unadjusted between-group comparisons at each visit were performed using the Mann–Whitney U test. These visit-specific comparisons were considered descriptive and were not used as the primary basis for evaluating longitudinal treatment effects.

Because of the exploratory nature of the study, incomplete follow-up measurements, and baseline differences in BCVA, the main longitudinal analyses were performed using baseline-adjusted linear mixed-effects models. Separate models were fitted for BCVA, global RNFL thickness, MD, and VFI using available post-baseline measurements as dependent variables. Treatment group, time, the group-by-time interaction, and the corresponding baseline outcome value were included as fixed effects. Time was modeled as a categorical repeated factor. The group-by-time interaction was used to evaluate whether longitudinal changes differed between the PRP and control groups. Alternative within-subject covariance structures, including first-order autoregressive [AR(1)], compound symmetry, and unstructured structures, were evaluated separately for each outcome. Covariance structures were selected based on model convergence, information criteria, and parsimony, with particular consideration of the Bayesian information criterion. An unstructured covariance structure was selected for BCVA and RNFL, whereas an AR(1) structure was selected for MD and VFI. Models used available outcome-specific post-baseline observations without imputation.

As exploratory supportive analyses, Week 16 outcomes were compared between groups using ANCOVA adjusted for the corresponding baseline value among participants with valid Week 16 measurements. Adjusted between-group mean differences with 95% confidence intervals were reported.

Analyses were performed using outcome-specific available data. No imputation was performed for missing follow-up measurements because of the small sample size and exploratory design. The number of participants and observations included in each longitudinal model was reported separately. No adjustment was made for multiple comparisons; therefore, secondary and exploratory findings were interpreted cautiously. All tests were two-sided, and $p<0.05$ was considered statistically significant.

RESULTS

A total of 39 patients with acute NAION were randomly allocated to the PRP group (n=21) or the control group (n=18). Among the 39 randomized participants, 26 (66.7%) were male, and the mean age was 59.28 ± 9.50 years. The right eye was affected in 21 patients (53.8%) and the left eye in 18 patients (46.2%). Baseline demographic and clinical characteristics of the randomized study population are summarized in Table 1. A CONSORT flow diagram illustrating patient allocation, exclusions, and follow-up is presented in Figure 1.

Thirty-one participants, including 15 in the PRP group and 16 in the control group, contributed data to the longitudinal analytic dataset. The number of valid observations varied by outcome and visit; outcome- and visit-specific sample sizes are reported in Tables 2 and 3. For MD and VFI, 118 valid post-baseline observations were available for descriptive analyses, but four observations from one participant in the PRP group were excluded from the baseline-adjusted mixed-effects models because the corresponding baseline values were missing. Consequently, each model included 114 observations from 30 participants (Table 4).

Baseline comparisons were considered descriptive and were not interpreted as evidence of baseline equivalence. Among participants included in the longitudinal BCVA analysis, baseline BCVA was descriptively worse in the control group than in the PRP group [0.50 (0.0–3.0) vs 0.30 (0.0–2.0) logMAR], and the longitudinal analyses were therefore adjusted for baseline BCVA.

Unadjusted visit-specific BCVA comparisons are presented in Table 2. These comparisons were considered descriptive. No statistically significant between-group differences in BCVA were observed at baseline or at any individual follow-up visit.

Unadjusted visit-specific comparisons of global RNFL thickness, MD, and VFI are presented in Table 3. Global RNFL thickness decreased over the follow-up period in both groups. No statistically significant

between-group differences were observed for global RNFL thickness, MD, or VFI at any individual follow-up visit.

The baseline-adjusted longitudinal mixed-effects analyses are summarized in Table 4. No statistically significant group-by-time interaction was observed for BCVA (p=0.094), global RNFL thickness (p=0.655), MD (p=0.124), or VFI (p=0.559), indicating no evidence that the longitudinal trajectories differed between the PRP and control groups for any of the evaluated outcomes. Significant overall time effects were observed for BCVA (p=0.006) and global RNFL thickness (p<0.001), whereas the time effects for MD (p=0.293) and VFI (p=0.428) were not statistically significant. An overall group effect was observed for VFI (p=0.022); however, in the absence of a significant group-by-time interaction, this finding was not interpreted as evidence of a differential longitudinal treatment effect. Baseline BCVA, MD, and VFI were significantly associated with their respective longitudinal measurements (all p<0.001), whereas the association with baseline RNFL thickness was not statistically significant (p=0.080).

In exploratory supportive analyses restricted to participants with valid Week 16 measurements and the corresponding baseline values, baseline-adjusted ANCOVA showed no statistically significant between-group differences in any outcome. The analyses included 10 PRP and 6 control participants for BCVA, 8 PRP and 8 control participants for global RNFL thickness, and 6 PRP and 6 control participants for MD and VFI. The adjusted PRP-minus-control mean difference was 0.411 logMAR for BCVA (95% CI, −0.287 to 1.110; p=0.226), −7.598 μm for global RNFL thickness (95% CI, −26.059 to 10.863; p=0.390), −6.908 dB for MD (95% CI, −15.497 to 1.680; p=0.102), and −22.890 percentage points for VFI (95% CI, −53.053 to 7.273; p=0.120). Thus, the exploratory Week 16 comparisons did not provide evidence of a between-group difference and were consistent with the absence of significant group-by-time interactions in the longitudinal analyses.

No serious ocular or systemic adverse events were documented during scheduled follow-up. Immediate post-injection safety parameters, including transient chemosis, acute intraocular pressure elevation, proptosis, and injection-related discomfort, were not systematically graded.

DISCUSSION

Currently, there is no established standard treatment for NAION, and most proposed therapeutic approaches remain empirical, targeting mechanisms such as neurodegeneration, inflammation, thrombosis, or vascular dysregulation [1,5]. PRP has attracted interest in ophthalmology and regenerative medicine because it contains platelet-derived mediators, cytokines, and neurotrophic factors that may contribute to tissue repair and

modulation of inflammation [3,12-16]. These biological properties have raised the question of whether PRP could have a therapeutic role in optic nerve disorders such as NAION. However, the clinical relevance of these mechanisms in acute ischemic optic nerve injury remains uncertain.

The demographic characteristics of the study population were broadly consistent with those reported in previously published NAION series [17]. Among participants contributing to the longitudinal BCVA analysis, baseline BCVA was descriptively worse in the control group than in the PRP group; therefore, the longitudinal BCVA model was adjusted for baseline BCVA.

In the present study, posterior sub-Tenon autologous PRP injection was not associated with a differential longitudinal BCVA trajectory compared with observation alone during the 16-week follow-up. In the baseline-adjusted longitudinal mixed-effects model, BCVA changed significantly over time, but the group-by-time interaction was not statistically significant. Similarly, the exploratory supportive Week 16 ANCOVA among participants with valid Week 16 BCVA measurements showed no statistically significant adjusted between-group difference.

Recently, Jin et al. [3] evaluated subtenon PRP injections in NAION patients with symptom duration of up to two months, administering two injections 10 days apart and conducting a one-month follow-up. In contrast, our study included patients with shorter symptom duration (≤14 days), used three injections at 3-week intervals, and extended follow-up to 16 weeks. We did not observe a consistent visual acuity benefit of PRP compared with observation alone. Differences in patient selection, injection protocol, follow-up duration, and outcome assessment may partly explain the differences between studies.

Jin et al. [3] also reported an increase in radial peripapillary capillary perfusion density using OCT angiography. In the present study, we assessed structural neuroretinal changes using OCT-derived RNFL measurements but did not evaluate optic nerve head or peripapillary microvascular perfusion with OCT angiography. Therefore, this study cannot determine whether PRP had any short-term effect on peripapillary microcirculation.

Acute NAION is typically characterized by optic disc edema in the early phase, followed by progressive RNFL thinning as edema resolves and axonal loss evolves [18]. In the present study, global RNFL thickness changed significantly over time, with decreasing values during follow-up in both groups. Visit-specific comparisons showed no significant between-group differences. The baseline-adjusted mixed-effects model showed no significant group-by-time interaction. Descriptive differences in early RNFL trajectories may reflect differences in the resolution of optic disc edema rather than true axonal preservation.

Visual field outcomes also did not demonstrate a consistent treatment-related benefit. In the baseline-adjusted longitudinal mixed-effects models, the group-by-time interaction was not statistically significant for either MD or VFI. Although an overall group effect was observed for VFI, there was no significant group-by-time interaction, and the exploratory Week 16 adjusted comparison was also not statistically significant. The overall VFI group effect therefore did not indicate a differential treatment response over time. Overall, posterior sub-Tenon PRP injection did not demonstrate a measurable short-term advantage in visual field outcomes over observation alone. Visual field defects in NAION commonly develop early in the disease course and may show limited recovery during follow-up [19,20].

The PRP preparation protocol used in this study did not include an exogenous activation agent. This approach was chosen to avoid the use of additional exogenous substances, and PRP may be activated upon contact with collagen and local tissue factors within the subtenon space. However, the absence of exogenous activation may have influenced the timing and immediate bioavailability of growth factor release. The dose, frequency, and interval of PRP injections were selected empirically because no established PRP protocol exists for acute NAION. The optimal dose, injection volume, frequency, and interval remain unknown.

This study has several important limitations. First, the study was limited by its small sample size and feasibility-based design. Although random allocation was used, the small sample size limits the ability to ensure balance across all potential prognostic factors and reduces the statistical power to detect small or moderate treatment effects. Baseline BCVA was descriptively worse in the control group, and although baseline adjustment was performed, residual imbalance in other prognostic factors cannot be excluded. Moreover, the absence of statistically significant between-group differences should not be interpreted as definitive evidence of treatment inefficacy, particularly given the possibility of spontaneous functional changes during the natural course of NAION. Therefore, the findings should be interpreted as exploratory and hypothesis-generating rather than confirmatory. Second, no sham injection was performed, and the control group was managed with observation alone. This design may have introduced expectation bias in patients and potential detection bias in outcome assessment. In addition, outcome assessors were not masked to treatment allocation. Third, incomplete follow-up measurements were present, and the number of valid observations varied by outcome and visit. Although the mixed-effects models incorporated available repeated measurements without imputation, their validity relies on assumptions regarding the missing-data mechanism, and residual bias due to informative missingness cannot be excluded. The small number of valid visual field measurements at later visits and the lack of adjustment for multiple secondary comparisons further limit the interpretation of the exploratory VFI

findings. Fourth, immediate post-injection safety parameters, including transient chemosis, acute IOP elevation, proptosis, and injection-related discomfort, were not systematically graded. Fifth, PRP composition was not fully characterized because platelet concentration, leukocyte content, and erythrocyte content were not measured in individual preparations. Additionally, ganglion cell complex measurements were not available, limiting our ability to assess macular ganglion cell loss as a complementary structural outcome alongside peripapillary RNFL thickness. Finally, the study was limited by the short follow-up duration and lack of OCT angiography assessment.

In conclusion, this exploratory randomized study did not demonstrate a consistent short-term functional or structural advantage of posterior sub-Tenon autologous PRP injection over observation alone in patients with acute NAION. Although no serious ocular or systemic adverse events were documented during scheduled follow-up, the immediate safety profile of the 2-mL posterior sub-Tenon PRP injection cannot be fully determined from the present dataset. These findings do not currently support the routine clinical use of posterior sub-Tenon PRP for acute NAION. Larger, adequately powered, sham-controlled randomized trials with longer follow-up and systematic safety monitoring are needed to clarify its potential therapeutic role.

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Table 1. Baseline demographic and clinical characteristics of the randomized study population.

		PRP group (n = 21 patients)	Control group (n = 18 patients)	p value
Age, years		59.48 ± 8.98	59.05 ± 10.34	0.893[1]
Sex, male		13 (61.9)	13 (72.2)	0.496[2]
Laterality (OD)		11 (52.4)	10 (55.6)	0.843[2]
ESR, mm/h		11.0 (3.0–25.0)	8.5 (2.0 – 30.0)	0.321[3]
VEP P100 latency, ms		124.1 (110.7 – 232.8)	129.05 (105.3 – 148.2)	0.779[3]
CRP <5 mg/L, n (%)		15 (71.4)	14 (77.8)	0.726[4]
Systemic diseases	**Hypertension**	7 (33.3)	9 (50.0)	0.560[5]
	Diabetes mellitus	4 (19.0)	2 (11.1)	
	Hyperlipidemia	1 (4.8)	2 (11.1)	
	None	9 (42.9)	5 (27.8)	

Values are presented as mean ± standard deviation, median (minimum–maximum), or n (%), as appropriate. P values are descriptive and should not be interpreted as evidence of baseline equivalence. PRP: platelet-rich plasma; OD: oculus dexter; NAION: non-arteritic anterior ischemic optic neuropathy; ESR: erythrocyte sedimentation rate; VEP: visual evoked potentials; CRP: C-reactive protein.
[1]Independent t-test, [2]Pearson Chi-square test, [3]Mann-Whitney U test, [4]Fisher's exact test, [5]Fisher-Freeman-Halton test.

Table 2. Unadjusted comparison of BCVA (logMAR) between the PRP and control groups at baseline and each follow-up visit.

BCVA (logMAR)	n	PRP group (n = 15 patients)	n	Control group (n = 16 patients)	p value
Baseline	15	0.30 (0.0 – 2.0)	16	0.5 (0.0 – 3.0)	0.119
Week 1	15	0.30 (0.0 – 2.0)	16	0.6 (0.0 – 3.0)	0.110
Week 3	15	0.40 (0.0 – 2.0)	16	0.5 (0.0 – 3.0)	0.264
Week 6	15	0.30 (0.0 – 2.0)	16	0.45 (0.0 – 3.0)	0.188
Week 8	15	0.30 (0.0 – 2.0)	16	0.4 (0.0 – 3.0)	0.299
Week 16	10	0.25 (0.0 – 2.0)	6	0.5 (0.0 – 1.0)	0.562

Values are presented as median (minimum–maximum), with the number of valid observations shown for each visit. P values represent unadjusted between-group comparisons using the Mann–Whitney U test at each visit. PRP: platelet-rich plasma; BCVA: best-corrected visual acuity.

Table 3. Unadjusted comparison of global RNFL thickness, MD, and VFI between the PRP and control groups at baseline and each follow-up visit.

Outcome measures	Visits	n	PRP group (n = 15 patients)	n	Control group (n = 16 patients)	p value
RNFL thickness, µm	**Baseline**	15	172 (112;326)	16	198 (130;259)	0.379
	Week 1	15	135 (87;309)	16	148 (76;232)	0.740
	Week 3	15	109 (66;338)	16	100 (42;190)	0.232
	Week 6	15	80 (55;211)	10	77 (39;176)	0.495
	Week 8	13	66 (49;124)	10	67 (41;84)	0.483
	Week 16	8	56.5 (50;82)	8	62 (41;84)	0.645
Mean deviation, dB	**Baseline**	14	-14.03 (-31.82;-7.73)	16	-16.59 (-31.64;-5.65)	0.951
	Week 1	15	-17.53 (-32.02;-8.2)	16	-17.03 (-32.18;-6.6)	0.740
	Week 3	15	-18.15 (-32.52;-5.94)	16	-14.19 (-32.29;-4.6)	0.446
	Week 6	15	-16.33 (-32.33;-7.44)	11	-16.18 (-36.7;-5.2)	0.799
	Week 8	10	-17.34 (-31;-8.59)	8	-17.48 (-30.42;-5.47)	0.633
	Week 16	6	-17.95 (-30.88;-9.8)	6	-14 (-29.51;-6.18)	0.394
Visual field index, %	**Baseline**	14	62 (2;86)	16	54.5 (2;93)	0.667
	Week 1	15	51 (0;84)	16	52.5 (0;93)	0.922
	Week 3	15	55 (0;89)	16	59 (0;95)	0.495
	Week 6	15	48 (1;88)	11	59 (0;94)	0.683
	Week 8	10	48.5 (1;77)	8	47 (3;92)	0.696
	Week 16	6	45.5 (3;73)	6	61 (9;89)	0.589

Values are presented as median (minimum–maximum), with the number of valid observations shown for each visit. P values represent unadjusted between-group comparisons using the Mann–Whitney U test at each visit. RNFL: retinal nerve fiber layer; MD: mean deviation; VFI: visual field index; PRP: platelet-rich plasma.

Table 4. Baseline-adjusted linear mixed-effects models for longitudinal visual and structural outcomes.

Outcome	No. of patients	No. of observations	Covariance structure	Group effect p	Time effect p	Group × time interaction p	Baseline covariate p
BCVA (logMAR)	31	140	UN	0.260	0.006	0.094	**<0.001**
Global RNFL thickness	31	126	UN	0.243	**<0.001**	0.655	0.080
MD	30	114	AR(1)	0.160	0.293	0.124	**<0.001**
VFI	30	114	AR(1)	0.022	0.428	0.559	**<0.001**

Values are p values from baseline-adjusted linear mixed-effects models. Each model included treatment group, time as a categorical factor, the group-by-time interaction, and the corresponding baseline outcome value. Alternative within-subject covariance structures were evaluated separately for each outcome; an unstructured (UN) covariance structure was selected for BCVA and RNFL, whereas a first-order autoregressive [AR(1)] structure was selected for MD and VFI based on model convergence, information criteria, and parsimony. Analyses were based on available outcome-specific observations without imputation. BCVA, best-corrected visual acuity; logMAR, logarithm of the minimum angle of resolution; RNFL, retinal nerve fiber layer; MD, mean deviation; VFI, visual field index.

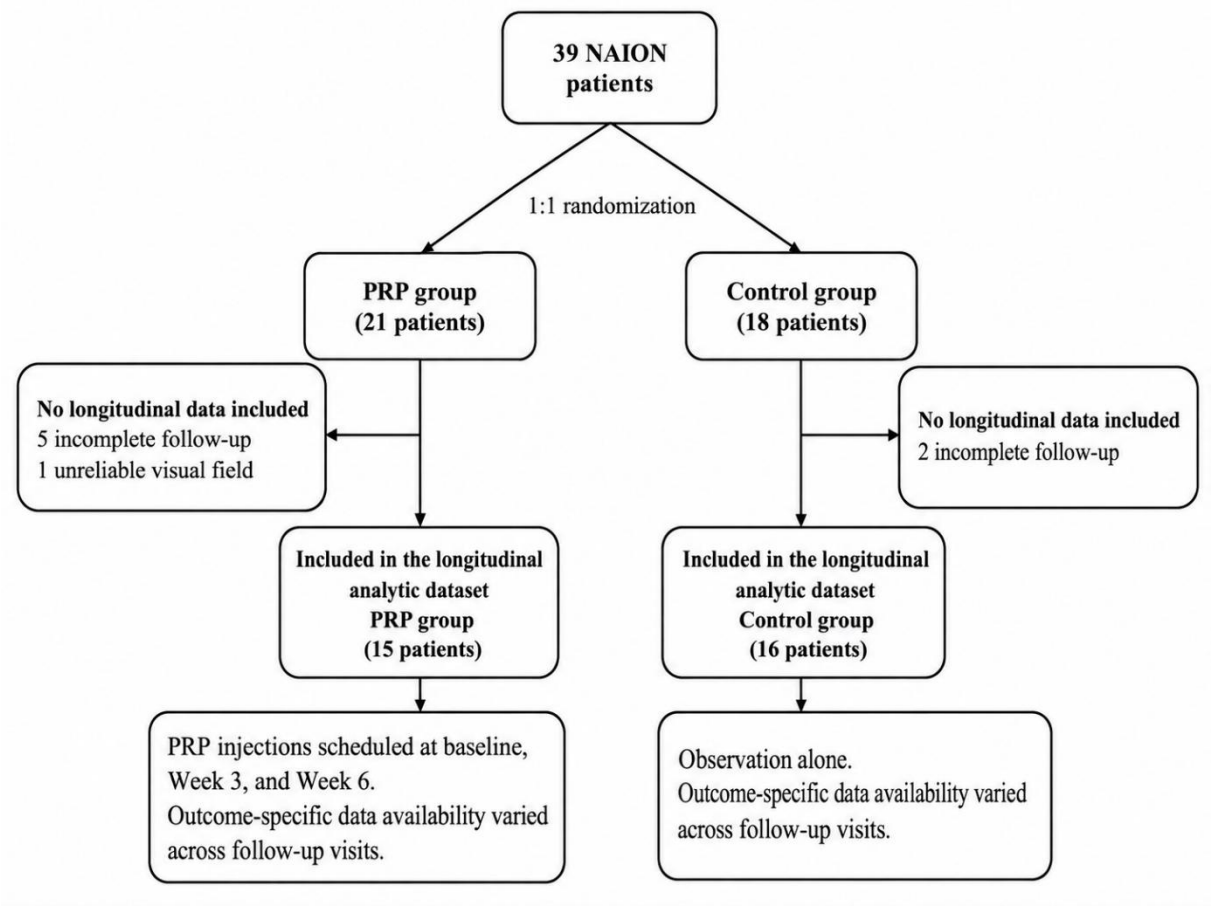

Figure 1. CONSORT flow diagram showing randomization, availability of follow-up data, and inclusion in the longitudinal analytic dataset. Outcome-specific sample sizes varied across visits and are reported in Tables 2 and 3.

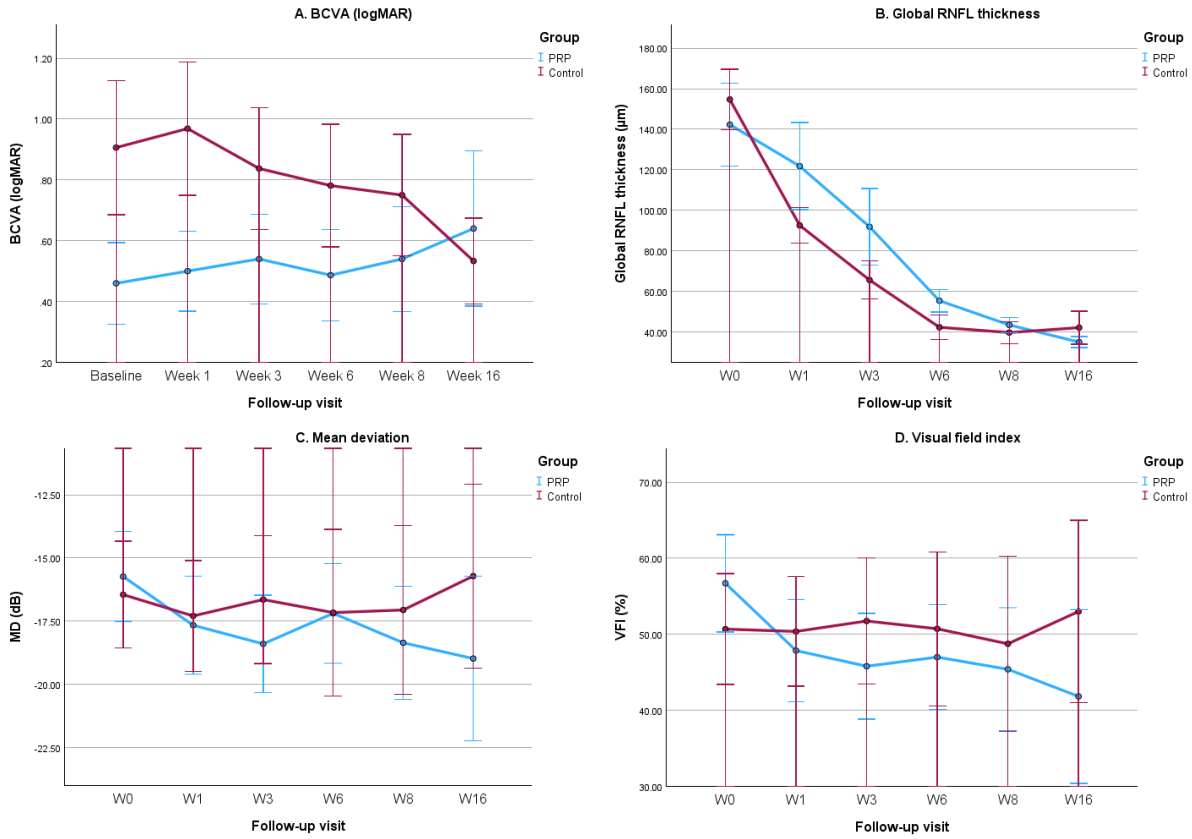

Figure 2. Longitudinal changes in the main structural and functional outcomes during the 16-week follow-up. Panel A shows best-corrected visual acuity (BCVA, logMAR), Panel B global retinal nerve fiber layer (RNFL) thickness, Panel C visual field mean deviation (MD), and Panel D visual field index (VFI). Values represent unadjusted observed means ± standard error for descriptive purposes. The number of valid observations varied by outcome and visit and is reported in Tables 2 and 3.

ABBREVIATIONS

BCVA: Best-corrected visual acuity

CRP: C-reactive protein

IOP: Intraocular pressure

MD: Mean deviation

NAION: Non-arteritic anterior ischemic optic neuropathy

PRP: Platelet-rich plasma

RNFL: Retinal nerve fiber layer

VEP: Visual evoked potential

VFI: Visual field index

DECLARATIONS

Ethical Approval and Informed Consent: The study protocol was approved by the Turkish Ministry of Health and Bursa Uludağ University Ethics Committee with the number (2019-21/36). All participants provided written informed consent, and the study was conducted in accordance with the principles outlined in the Declaration of Helsinki. This randomized controlled study was conducted and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) statement.

Consent for publication: Not applicable.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Conflicting Interest: The authors declare that they have no conflicts of interest related to this manuscript.

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