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ORIGINAL RESEARCH

Structural-Functional Correlation in Non-Arteritic Acute Ischemic Optic Neuropathy

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Purpose: This study investigated the relationships between structural and functional parameters in non-arteritic ischemic optic neuropathy (NAION).

Methods: This retrospective study enrolled 29 patients (58.2 ± 10.4 years old) with unilateral NAION. During the acute phase, we performed comprehensive evaluations including best-corrected visual acuity (BCVA), optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), visual fields (VF), visual evoked potentials (VEP), electroretinography (ERG), and multifocal ERG (mf-ERG). At three months post-presentation, patients underwent follow-up assessments comprising visual acuity testing, perimetry, and advanced retinal imaging.

Results: During the acute phase, affected eyes demonstrated increased mean retinal nerve fiber layer (RNFL) thickness, while ganglion cell-inner plexiform layer (GCIPL) thickness decreased. Both visual fields mean deviation (MD) and VEP P100 amplitude were reduced, accompanied by prolonged peak latency. We also observed decreased P1 response density in mf-ERG. Analysis revealed significant direct correlations between GCIPL parameters and electrophysiological measurements, particularly VEP P100 amplitude and mf-ERG P1 response density. Mean GCIPL thickness, VF MD, and VEP P100 amplitude showed negative correlations with baseline logMAR VA. Baseline VF MD, VEP P100 amplitude, and minimum GCIPL thickness showed negative correlations with logMAR VA at 3-month follow-up.

Conclusion: Retinal ganglion cell layer thickness serves as a valuable indicator to objective evaluate optic nerve function in acute NAION patients. Decreases in both VEP amplitude and mf-ERG response density showed significant correlations with retinal ganglion cell layer thickness. Baseline visual field performance, VEP measurements, and minimum GCIPL thickness exhibited negative correlations visual acuity at 3-month follow-up.

Trial Registration: Clinical Research Ethics Committee of Xi'an People's Hospital (NO. 20220018). Registered 27 September 2022-Retrospectively registered, https://www.medicalresearch.org.cn/. Informed consent was obtained from each participant.

Keywords: ischemic optic neuropathy, OCTA, OCT, visual field, visual electrophysiology

Introduction

Anterior ischemic optic neuropathy without arteritis (NAION) represents a leading cause of optic nerve edema and dysfunction among individuals aged 50 and above.[1–4] While the complete pathophysiological mechanism remains to be fully understood, current evidence suggests that reduced blood flow through the short posterior ciliary arteries to the optic nerve plays a central role in disease development.[1,5] Recently, the focus on correlation between morphological indicators and functional condition has been increased. Ganglion cell–inner plexiform layer (GCIPL) analysis was reported as a useful biomarker for ganglion cell damage, which significantly correlated with best-corrected visual acuity (BCVA), visual field indices (mean deviation (MD) and visual field index (VFI)) in NAION patients.[6,7] Nerve fiber layer (NFL) and ganglion cell complex (GCC) losses were also found to correlate well with visual field (VF) losses in both magnitude

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and location in NAION patients.[8] As conventional measurements of visual function, such as visual acuity (VA) and VF are subjective tests, and the reliability of both examination results is questionable when patients suffered severe visual loss, as well as unsatisfactory cooperation of some patients, while visual electrophysiological tests can make up for this defect.[8,9] After analyzing morphology optic disc and evaluating electrophysiology and VA of NAION patients in chronic phase, Barbano et al found VA changes were correlated to the impaired morphology and function of inner retina.[10]

Conventionally, it's widely accepted that visual evoked potentials (VEP) reflect visual function of NAION patients, while multifocal electroretinography (mf-ERG) represent local retina function in macula. Lately, new attention of role of multifocal electroretinography (mf-ERG) in optic neuropathy started to be paid, and meanwhile contribution of retinal ganglion cells (RGCs) to mf-ERG wave is getting to be explored.[11–14] Consequently, assessing the changes of mf-ERG may widen its application in optic neuropathy.

Thus, in this study, we aimed to explore whether there was a correlation between morphological involvement in the optic nerve as well as macula and function changes of RGCs, to investigate whether vision changes is associated to this morpho-functional condition in the acute phase of NAION, and to find indicators that can evaluate the prognosis.

Methods

Design and Materials

This retrospective analysis evaluated consecutive clinical data from 29 individuals (15 male and 14 female patients, averaging 58.24 ± 10.36 years of age) who presented with single-eye NAION at our institution between September 2020 and June 2024, the demographic characteristics of all the NAION patients are provided in Table 1. This research protocol was approved by the Clinical Research Ethics Committee of Xi'an People's Hospital and followed Helsinki Declaration guidelines. Informed consent was obtained from each participant. Each patient received ophthalmic examinations during acute disease phase (within 30 days of onset), including BCVA, intraocular pressure, slit-lamp biomicroscope, fundus examination, optical coherence tomography angiography (OCT-A), VF, pattern and flash VEP, full-field electroretinogram (ERG) and mf-ERG. BCVA, VF and OCTA follow-up examinations were repeated at 3 months post treatment.

According to the disease course, defined as the time between symptom onset and presentation, the NAION patients were divided into Group A (less than 1 week), Group B (1–2 weeks), and Group C (2 weeks-1 month).

Study participants met established diagnostic criteria for NAION, including acute unilateral vision deterioration without pain, demonstrable relative afferent pupillary dysfunction, sectoral optic disc elevation, and characteristic visual field abnormalities.[15] Patients with unilateral NAION, age over 40, and first visit within 30 days onset were included in this study. Exclusion criteria included an opacity of media, history of glaucoma, any fundus diseases other than NAION, NAION history in the fellow eye, or other neurological diseases.

Octa

We performed multimodal imaging using the AngioPlex™ CIRRUS™ HD-OCT platform (model 5000, Carl Zeiss Meditec, Inc., Dublin, USA). The imaging protocol included bilateral 6×6 mm^2 scans, with separate acquisitions focused

Table 1 The Demographic Characteristics of All the NAION Patients

Characteristics		Whole (n = 29)
Sex	Female	14 (48.3%)
	Male	15 (51.7%)
Age	Mean ± SD	58.2 ± 10.4
	Range	40–74
Duration of onset	Mean ± SD	15.6 ± 8.1
	Range	4–30
BCVA (logMAR)	NE	0.4 ± 0.5
	FE	0.1 ± 0.2

Abbreviations: SD, standard deviation; NE, NAION eye; FE, fellow eye.

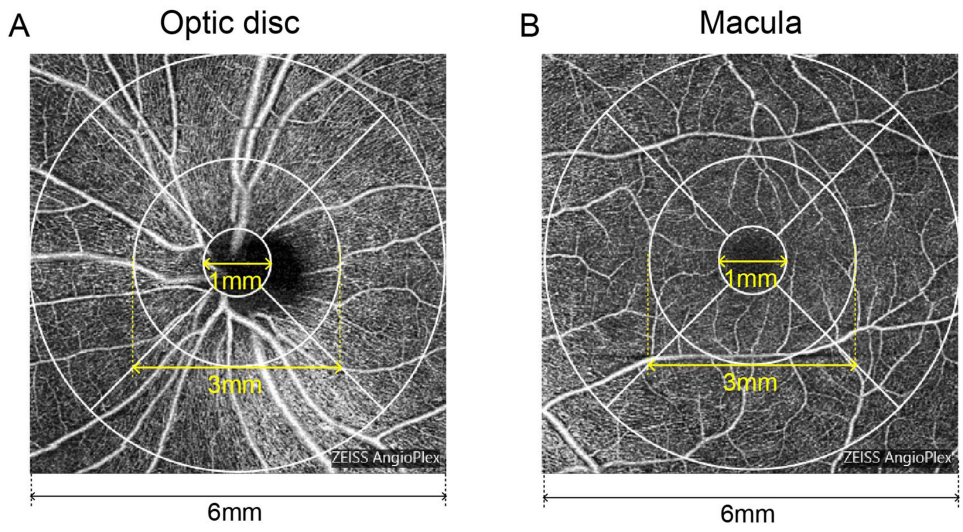

Figure 1 OCT-A measurement of the radial peripapillary capillaries (RPC, Figure 1**A**) and macular superficial capillary plexus (mSCP, Figure 1**B**). The scanned area was 6×6 mm^2, and the areas in the range of 1 mm, 1–3 mm, and 3–6 mm scanned diameter centered on the optic nerve head (ONH) or central macula were defined as the center-RPC or center mSCP, inner-RPC or inner-mSCP and outer-RPC or outer-mSCP, respectively.

on macular and optic nerve head (ONH) regions. Image analysis included OCTA scans that demonstrated signal strength exceeding 7, minimal motion blurring, and no significant floaters or media opacities.

During image analysis, we employed automated segmentation software to delineate the retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL). We then evaluated differences in both mean and minimum GCIPL measurements between affected and fellow eyes across three temporal groups (A, B, and C). An automatic segmentation algorithm was performed to segment the radial peripapillary capillaries (RPC) and macular superficial capillary plexus (mSCP). The center-RPC, center-mSCP, inner-RPC, inner-mSCP, outer-RPC and outer-mSCP were defined as areas with scanning diameters of 1 mm, 1–3 mm, and 3–6 mm centered on the ONH or central fovea, respectively (Figure 1).For each analyzed region, vessel density (VD) represented the percentage of area occupied by both large vessels and microvessels.[16]

Measurement of Visual Pathway Function

Best-corrected visual acuity (BCVA) was determined using Snellen chart and converted to logMAR values. Visual field testing was performed with the Humphrey Field Analyzer II 750 (Carl-Zeiss Meditec, Dublin, CA, USA) using the 24–2 Swedish interactive threshold algorithm. The mean deviation (MD) of the VF was recorded.

All visual electrophysiological tests (VEP, ERG and mf-ERG) were conducted using the GT-2008V-IV 8.1 system (Guote, Chongqing, China), following International Society of Clinical Visual Electrophysiology (ISCEV) standards.[17–19] The amplitude (μV) and peak time (ms) of P100 in P-VEP, the amplitude (μV) and peak time (ms) of b wave in scotopic 3.0 ERG responses and the P1 response density of mf-ERG were recorded and compared.

Statistical Analysis

Quantitative data were presented as mean ± standard deviation (SD). Paired-samples *t*-test was performed to analyze the differences in retinal morphology and visual function between the NAION eye (NE) and the fellow eye (FE) in the acute phase and 3-month follow-up, and the differences in logMAR of BCVA, OCT and OCTA parameters at 3-month follow-up versus the acute phase. The association between retinal morphology and visual function, as well as the correlation between visual acuity, disease course, and retinal morphology and function were analyzed by Spearman correlation tests. All statistical analyses were performed using IBM-SPSS 23.0 (IBM Inc., Armonk, NY, United States), and $P < 0.05$ was considered to be statistically significant.

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Results

Morphological results of the Retina in the Acute Phase

Analysis of acute phase measurements revealed substantially increased mean RNFL thickness in affected eyes (236.89 ± 60.24 μm) compared to fellow eyes (103.69 ± 13.75 μm), demonstrating statistical significance (t = 11.068, P < 0.001, Figure 2A). Conversely, a significant decrease of the mean GCIPL in NE (73.89 ± 16.76 μm) was displayed compared with FE (85.58 ± 9.30 μm) (t = 2.936, P = 0.007, Figure 2A). To further analyze, all patients were divided into 3 subgroups (A: less than 1 week, B:1–2 weeks, C: 2 weeks −1 month) according to disease course. The significant mean GCIPL thinning was shown in Group B and Group C in NE when compared to FE (t = 2.157, P = 0.04 and t = 2.103, P = 0.04, respectively) (Figure 2B). Besides, among three groups, similar differences of RNFL thickness in the NE were all significantly thicker than FE in Group A (t = 8.756, P = 0.001), B (t = 6.456, P < 0.001) and C (t = 6.594, P < 0.001) (Figure 2C).

When examining minimum GCIPL thickness, NE demonstrated significantly lower values (64.12 ± 23.50 μm) compared with FE (81.38 ± 11.02 μm) during the acute phase (t = 3.391, P = 0.002, Figure 3). According to disease course, the significant minimum GCIPL thinning was also observed in Group B and Group C in NE when compared to FE (t = 2.46, P = 0.036 and t = 3.037, P = 0.011, respectively) (Figure 3).

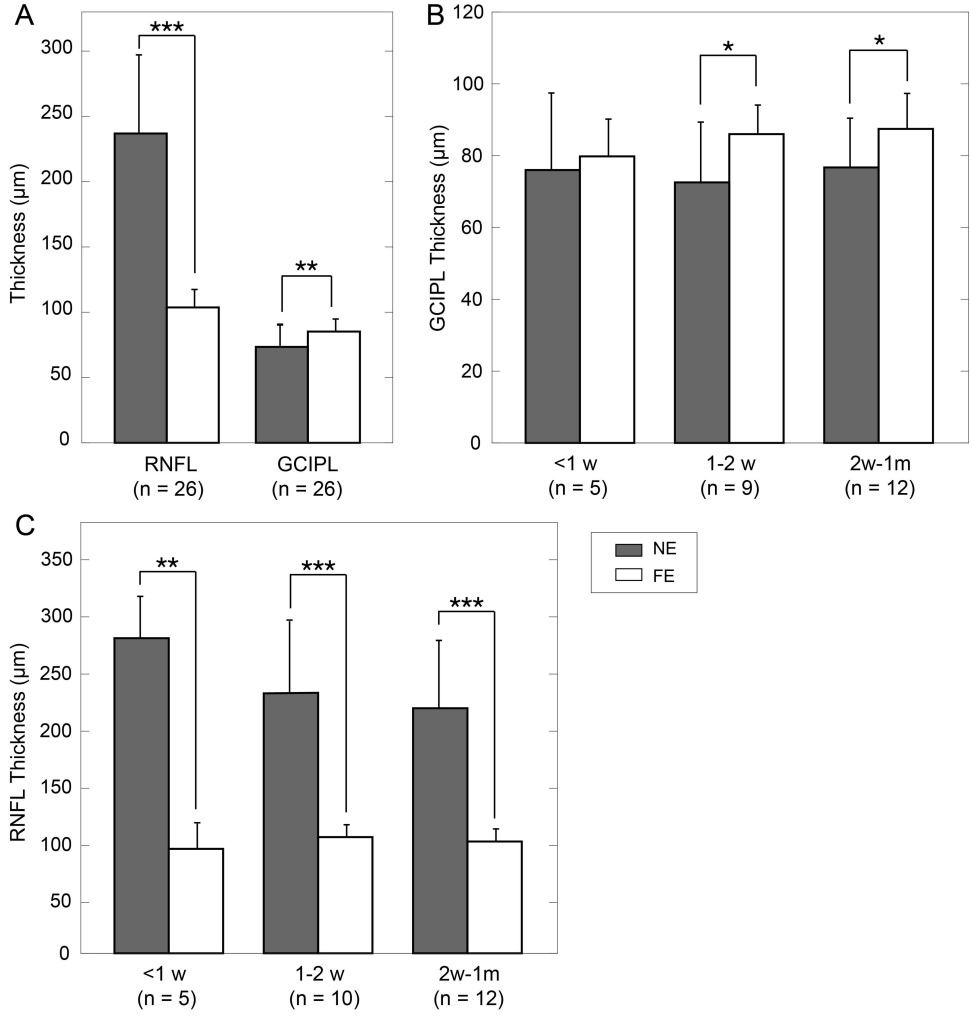

Figure 2 (**A**) The difference of the retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) between the NAION eyes (NE) and the fellow eyes (FE). In acute phase, the mean RNFL thickness of NE was significantly thicker than FE and the mean GCIPL thickness was thinner in NE compared to FE. (**B**) Differences in GCIPL thickness between NE and FE at different timepoint of onset in the acute phase (Group (**A**) <1 week, Group (**B**) 1–2 weeks, Group (**C**) 2–4 weeks). Solid columns represent NE, hollow columns represent FE, and error lines represent standard deviation (SD). The thinning of mean GCIPL thickness in NE was after 7 days of onset. The results of the paired t-tests are shown: *P < 0.05, **P < 0.01, ***P < 0.001.

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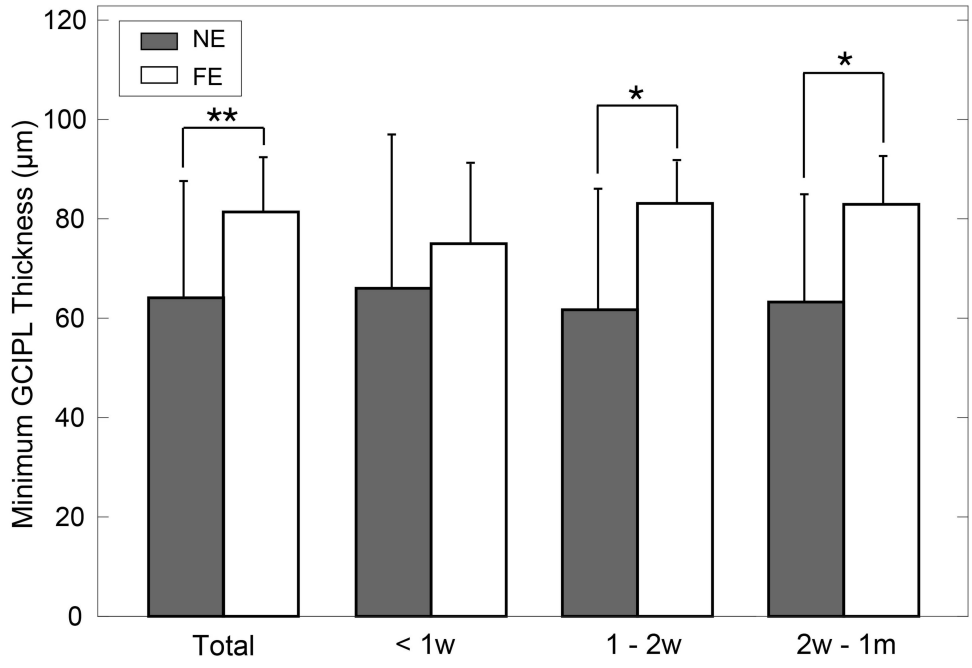

Figure 3 The difference of the minimum ganglion cell-inner plexiform layer (GCIPL) thickness between the NAION eyes (NE) and the fellow eyes (FE) in acute phase and at different timepoint of onset in the acute phase (Group (A) <1 week, Group (B) 1–2 weeks, Group (C) 2–4 weeks). In acute phase, the minimum GCIPL thickness was thinner in NE compared to FE. The thinning of minimum GCIPL thickness in NE was after 7 days of onset. Solid columns represent NE, hollow columns represent FE, and error lines represent standard deviation (SD). The results of the paired t-tests are shown: *$P < 0.05$, **$P < 0.01$.

On OCTA (Figure 4), vessel density on SCP was analyzed in ONH region and in the macula. In NAION-affected eyes, vessel density analysis demonstrated regional variations across the radial peripapillary capillary network. Values ranged from 12.69 ± 4.45% centrally to 17.43 ± 1.35% in the inner region, with outer zone and total measurements of 15.98 ± 2.15% and 15.33 ± 2.81%, respectively. While in FE, the VD in the same regions were 9.25 ± 4.77%, 17.49 ± 1.63%, 16.89 ± 2.43% and 15.74 ± 2.44%, respectively. The VD in the center-, inner-, outer- and whole mSCP were 5.80 ± 3.65%, 14.09 ± 4.19%, 14.90 ± 2.87%, and 14.46 ± 3.08% in NE and 4.62 ± 2.82%, 14.06 ± 3.53%, 15.30 ± 2.68% and 14.72 ± 2.81% in FE, respectively. A significant vessel density difference between NE (12.69 ± 4.45%) and FE (9.25 ± 4.77%) was identified specifically in the center-RPC ($t = 3.046$, $P = 0.005$), but not in inner-RPC or outer-RPC regions. However, regarding VD of SCP in the macula, no difference between NE and FE was found in center-mSCP, inner-mSCP or outer mSCP ($P > 0.5$).

Visual Pathway Function in the Acute Phase

By visual field test, the mean deviation declined in NE (−19.93 ± 1.75 dB) when compared with FE (−5.79 ± 1.95 dB) ($t = 7.119$, $P < 0.001$, Figure 5A). On visual electrophysiological test, lower amplitudes (7.13 ± 2.89 μV vs 15.96 ± 5.60 μV; $t = 7.175$, $P < 0.001$) and prolonged peak time (109.21 ± 14.77 ms vs 100.76 ± 4.95 ms; $t = 3.388$, $P = 0.002$) of P100 waves were shown in NAION patients (Figure 5B). Additionally, we also found that the P1 response density of mf-ERG in NE was significantly lower than FE (45.70 ± 22.99 nV/degree^2 vs 67.35 ± 21.90 nV/degree^2; $t = 5.607$, $P < 0.001$) (Figure 5C).

Similarly, P1 response density of mf-ERG was further analyzed according to disease course and compared among A, B and C subgroups. The P1 response density was lower in Group B and Group C in NE when compared to FE ($t = -3.16$, $P = 0.013$ and $t = -4.497$, $P = 0.001$, respectively) (Figure 5D).

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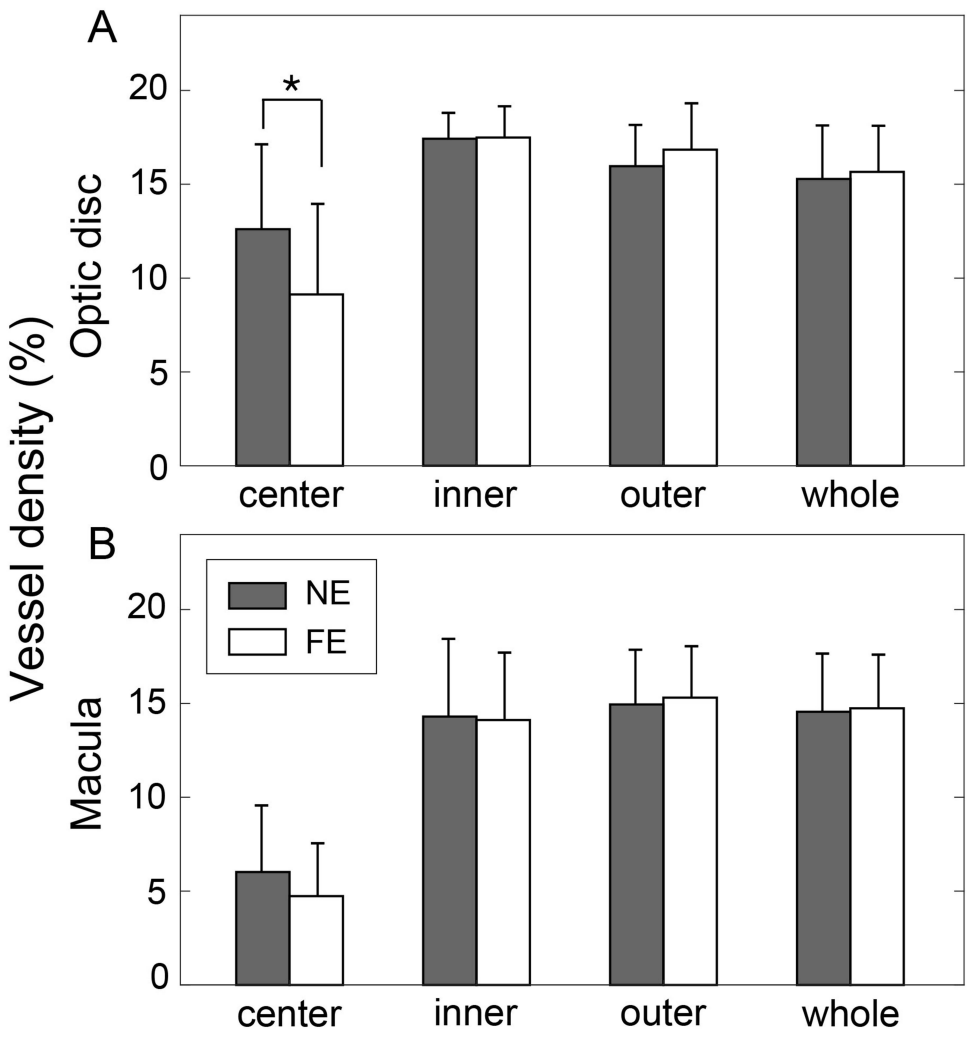

Figure 4 Differences in vessel density (VD) between the NAION eyes (NE) and the fellow eyes (FE) in the superficial capillary layer in the optic disc (**A**) and macula (**B**). Solid columns represent NE, hollow columns represent FE, and error lines represent standard deviation (SD). Only the center-peripapillary capillaries (RPC) of VD was thickening in NE. The results of the paired t-tests are shown: *$P < 0.05$.

Correlation Between Retinal Morphology and Visual Pathway Function in the Acute Phase as Well as Influence Factors

Mean and minimum GCIPL thickness showed positive correlations with P100 wave amplitude ($r = 0.452$, $P = 0.012$; $r = 0.585$, $P = 0.001$) and mf-ERG P1 response density ($r = 0.427$, $P = 0.017$; $r = 0.425$, $P = 0.017$) (Figure 6). However, no significant correlation between RNFL thickness and visual function was observed. And no significant correlation was displayed between the VD in the optic disc and macular region and the peak time of P100 wave, or the P1 response density of mf-ERG ($P > 0.05$, for all). Furthermore, VD in the optic disc and macular showed no significant correlation with either mean GCIPL or RNFL thickness ($P > 0.05$, for all).

Baseline logMAR visual acuity demonstrated inverse relationships with multiple parameters: mean GCIPL thickness ($r = -0.366$, $P = 0.033$), visual field mean deviation ($r = -0.405$, $P = 0.043$), and PVEP P100 amplitude ($r = -0.633$, $P < 0.001$) (Figure 7).

Comparison of Retinal Morphological Factors and logMAR Visual Acuity at 3-month of NAION

After 3 months, there was a slight improvement in visual acuity in NE (0.31 ± 0.40 vs 0.40 ± 0.48), while no statistical significance was found ($t = 0.393$, $P = 0.699$). The RNFL of NE was significantly thinner than the

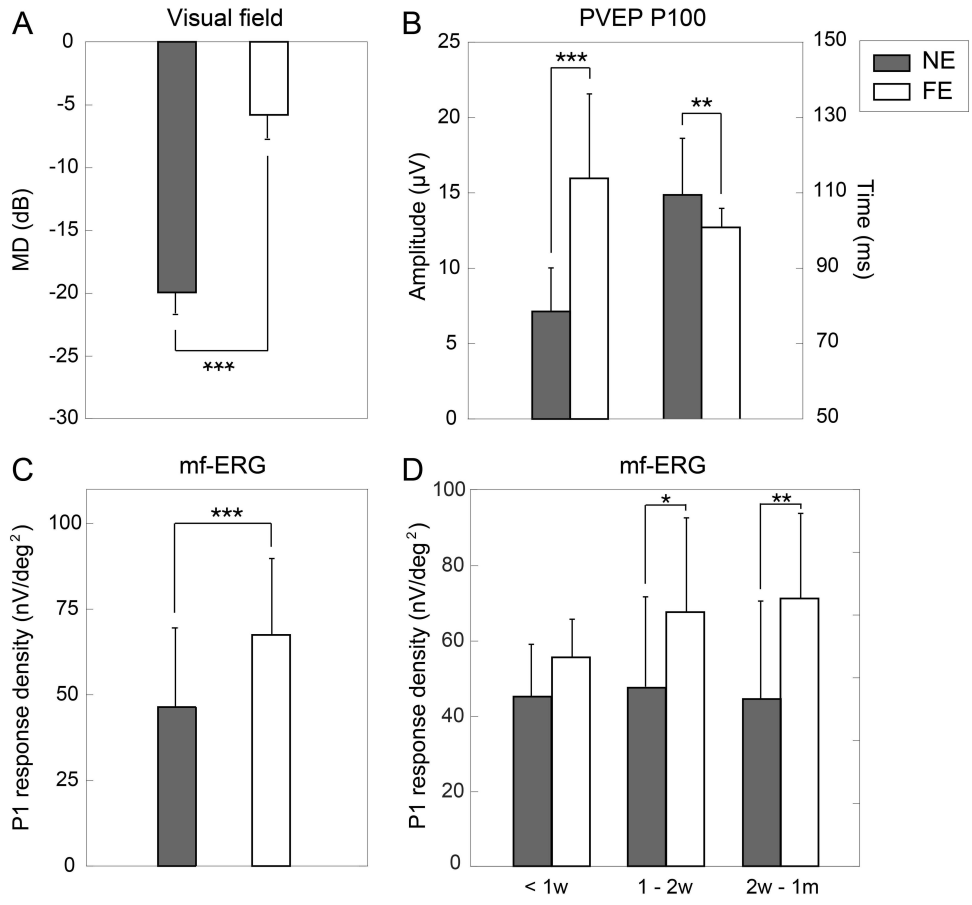

Figure 5 The differences of mean deviation (MD) of the visual field (**A**), amplitude and peak time of pattern visual evoked potentials (PVEP) P100 (**B**), and the P1 response density of multifocal electroretinography (mf-ERG) (**C**) between the NAION eyes (NE) and the fellow eyes (FE). The P1 response density decreased in Group B (1–2 weeks) and Group C (2 weeks – 1 month) in NE when compared to FE (**D**). Solid columns represent NE, hollow columns represent FE, and error bars represent standard deviation (SD). In NE, the mean deviation (MD) of the visual field, P100 amplitude and the P1 response density of mf-ERG reduced significantly. The peak timing of P100 wave prolonged. The results of the paired t-tests are shown: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

baseline (72.42 ± 9.81 μm vs 236.89 ± 60.24 μm, $t = 3.059$, $P = 0.002$, Figure 8A). Similarly, the mean and minimum GCIPL thickness of NE also declined than baseline (61.92 ± 10.49 μm vs 73.89 ± 16.76 μm, $t = 2.536$, $P = 0.011$, Figure 8B; 53.08 ± 11.22 μm vs 64.12 ± 23.50μm, $t = 2.434$, $P = 0.033$, Figure 8C). Additionally, on OCTA, the VD in the center- (6.49 ± 4.96% vs 12.69 ± 4.45%, $t = 3.664$, $P = 0.005$), inner- (12.80 ± 3.20% vs 17.43 ± 1.35%, $t = 4.575$, $P = 0.001$) and outer-RPC (13.02 ± 2.39% vs 15.98 ± 2.15%, $t = 2.915$, $P = 0.017$) in optic disc of NE were thinner than the baseline (Figure 9). The difference between NE and FE (Figure 9) were significant in the VD in the inner- (12.80 ± 3.20% vs 18.06 ± 0.93%, $t = 5.258$, $P = 0.001$), outer- (13.02 ± 2.39% vs 17.87 ± 1.57%, $t = 6.612$, $P < 0.001$) and whole-RPC (12.75 ± 2.44% vs 17.64 ± 1.21%, $t = 7.013$, $P < 0.001$).

To evaluate visual acuity improvement and biomarkers at baseline in NAION patients, the correlations between logMAR visual acuity of NE at 3-month and the baseline morpho-functional data were analyzed. MD on VF ($r = -0.513$, $P = 0.03$), PVEP P100 amplitude ($r = -0.519$, $P = 0.011$), and the minimum GCIPL thickness ($r = -0.439$, $P = 0.012$) of NE at baseline showed a negative correlation with logMAR visual acuity at 3-month follow-up (Figure 10).

Discussion

Optical coherence tomography has emerged as the primary method for evaluating and monitoring changes in both retinal nerve fiber layer and ganglion cell thickness in patients with neuro-ophthalmologic conditions.[6,7,10,20,21] In our investigation of NAION patients, we obtained OCT measurements of RNFL thickness at baseline and three-month follow-up

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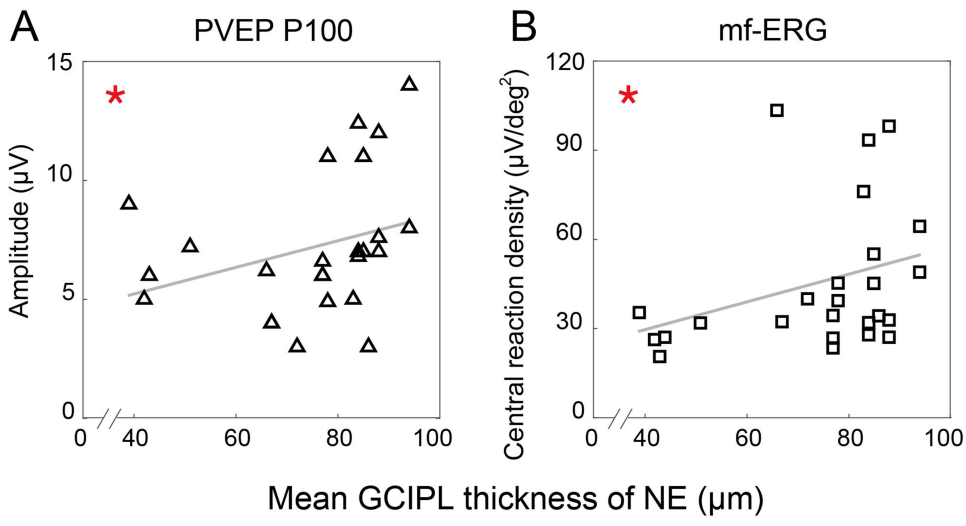

Figure 6 The correlation between mean ganglion cell-inner plexiform layer (GCIPL) thickness and the amplitude of P100 wave of pattern visual evoked potentials (PVEP) (**A**) and the P1 response density of multifocal electroretinography (mf-ERG) (**B**) in NAION eyes (NE). X-axis represents mean GCIPL thickness of NE, and Y-axis represents P100 amplitude and the P1 response density of mf-ERG. Positive correlations were revealed between GCIPL thickness and P100 amplitude or the P1 response density of mf-ERG. The results of the Spearman correlation test are shown in the figure: **P* < 0.05.

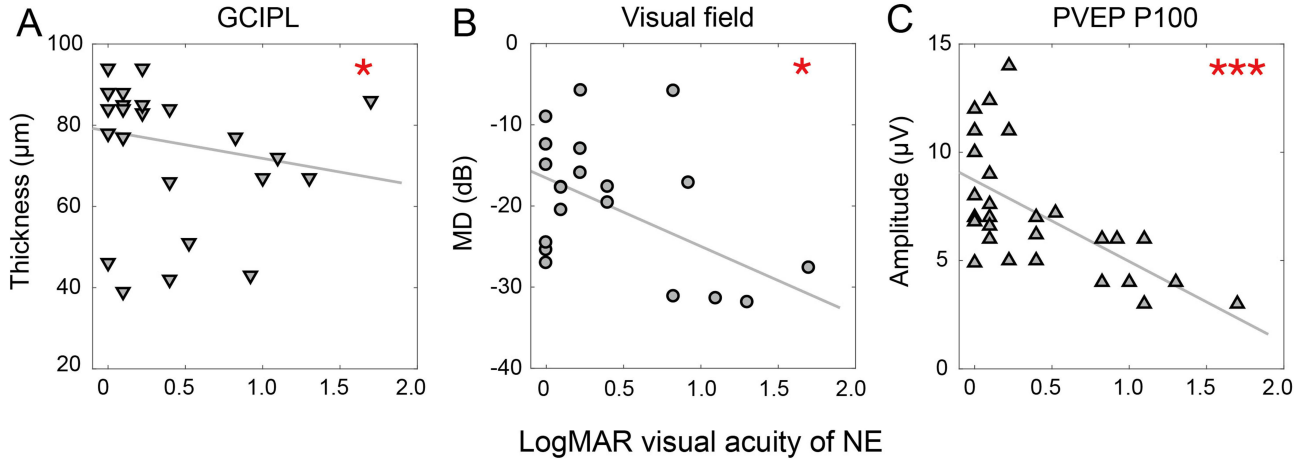

Figure 7 Correlation of logMAR visual acuity of the NAION eyes (NE) with mean ganglion cell-inner plexiform layer (GCIPL) thickness (**A**), the mean deviation (MD) of the visual field (**B**), and the amplitude of pattern visual evoked potentials (PVEP) P100 (**C**). X-axis represents the logMAR visual acuity of NE, and Y-axis represents the mean GCIPL thickness, MD of the visual field, and amplitude of PVEP P100. Each symbol represents each patient, and the gray line represents the best linear fit. GCIPL thickness, MD of the visual field, and P100 amplitude were all significantly negatively correlated with visual acuity. The results of Spearman correlation test are shown in the figure: **P* < 0.05, ****P* < 0.001.

intervals, comparing them with unaffected fellow eyes. We selected the first 30 days after symptom onset as inclusion criteria, given the significant pathological and clinical changes expected during this period. Our measurements revealed substantial RNFL thickening during the first month post-onset, while GCIPL attenuation became detectable via OCT. Akbari M et al found a significant GCIPLmin thinning at presentation.[22] In this study, we observed GCIPL became thinner at least one week after onset, while RNFL became thicker within one week, suggesting that the initial onset was acute optic disc edema. However, the GCIPL could be used to detect early axonal damage in the acute phase that cannot be used by measuring the RNFL, which is masked by its edema.[6,7,10,20,21]

Our analysis demonstrated a significant correlation between GCIPL thickness and baseline visual acuity, while RNFL thickness showed no such relationship with visual function. This finding highlighted both the predictive potential of GCIPL measurements and their increased susceptibility to early impairment during ischemic events compared to RNFL parameters. The progressive GCIPL thinning observed throughout the three-month follow-up period likely reflects

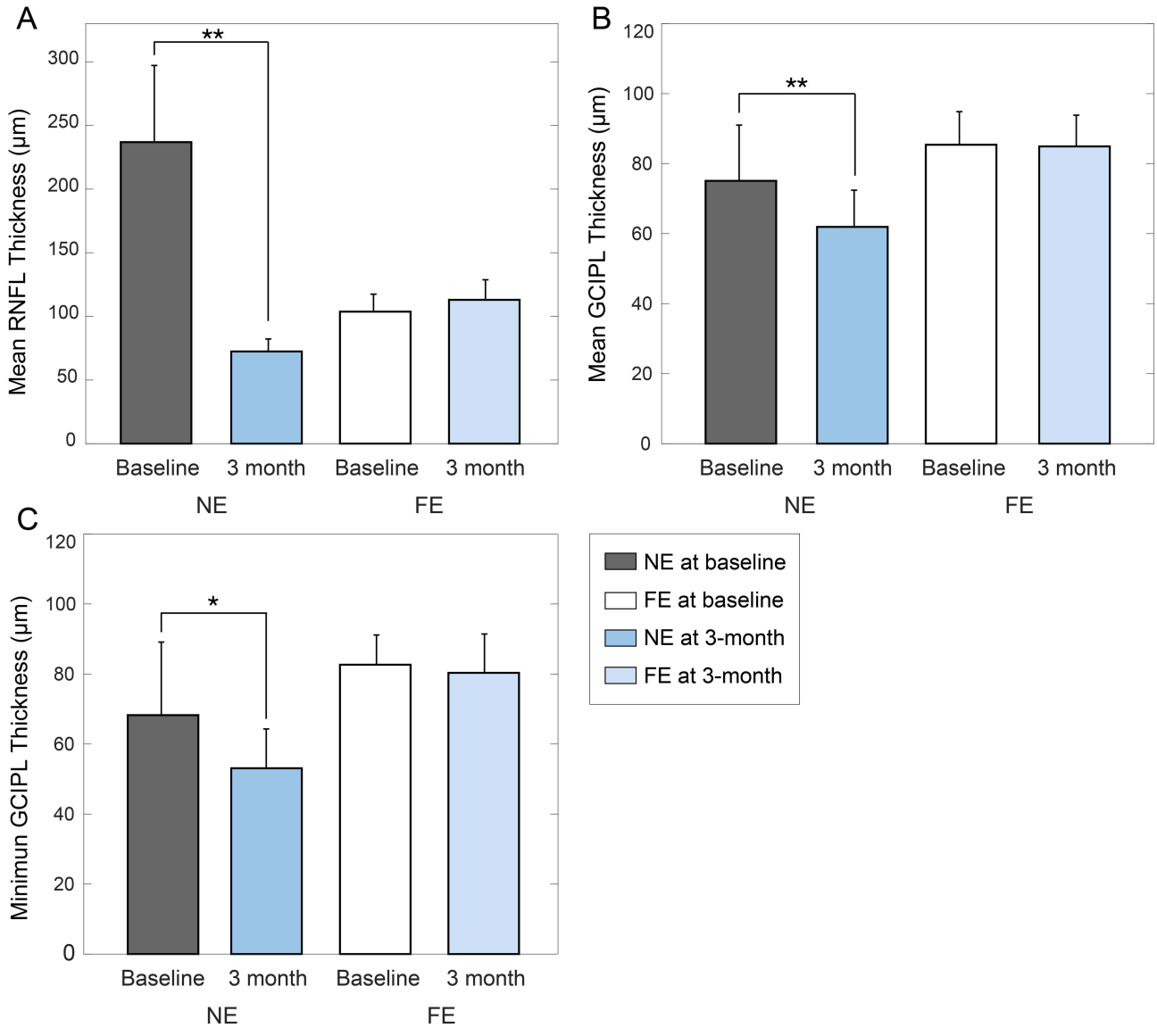

Figure 8 Changes in the mean retinal nerve fiber layer (RNFL) thickness (**A**), mean ganglion cell-inner plexiform layer (GCIPL) thickness (**B**), and minimum GCIPL thickness (**C**) after 3 months in patients with NAION. Solid grey columns represent the NAION eyes (NE) at baseline, hollow columns represent the fellow eyes (FE), blue represents after 3 months of treatment, and error lines represent standard deviation (SD). The results of the paired *t*-test are shown in the figure: *$P < 0.05$, **$P < 0.01$.

permanent neuronal loss within the ganglion cell layer coupled with dendrite deterioration in the inner plexiform layer.[22] The strong correlation between initial GCIPL thickness and three-month visual acuity outcomes further establishes GCIPL as a crucial prognostic indicator.[6,23]

The implementation of OCT-A technology has enabled non-invasive visualization and quantification of microvasculature in both the optic disc and retina across selected layers, offering advantages in assessing hypoperfusion or non-perfusion of the optic nerve head in NAION patients.[24,25] Several studies examining OCT-A in the acute stage of NAION have demonstrated defects in peripapillary microcirculation.[20,26,27] Our investigation revealed increased vessel density in the center-RPC compared to fellow eyes during the acute phase. This dilation may result from mechanical compression and impedance of flow in the radial peripapillary capillaries due to optic nerve edema,[27,28] which correlates with the severity of axonal ischemia.[29] Notably, GCIPL continued to thin despite the presence of dilated peripapillary capillaries, suggesting a potential vicious cycle in neural-vascular interactions during NAION progression.[28,30]

While multifocal electroretinography (mf-ERG) has historically seen limited application in investigating neurodegeneration in NAION eyes, our findings suggest its value as a reliable method for determining the extent of ischemic

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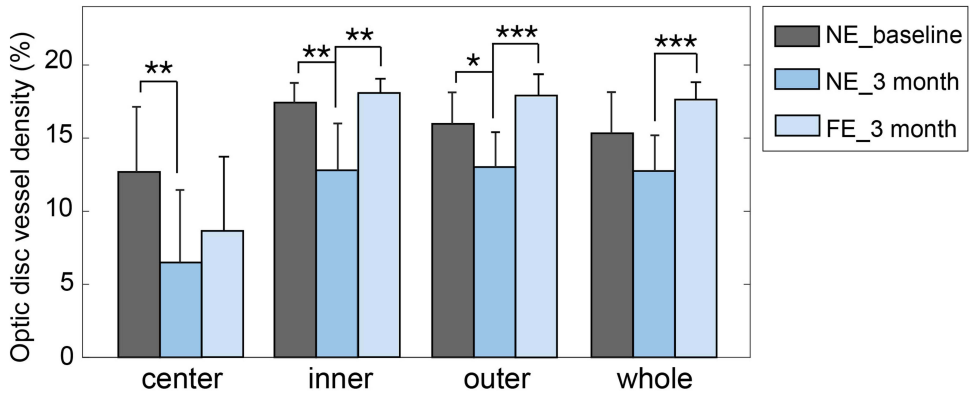

Figure 9 Changes in optic disc vessel density of the NAION eyes (NE) in the superficial capillary layer after 3 months and the differences with the fellow eyes (FE) in patients with NAION. Gray columns represent NE at baseline, blue columns represent after 3 months of treatment, and error lines represent standard deviation (SD). The results of the paired *t*-test are shown in the figure: **P* < 0.01, ***P* < 0.05, ****P* < 0.001.

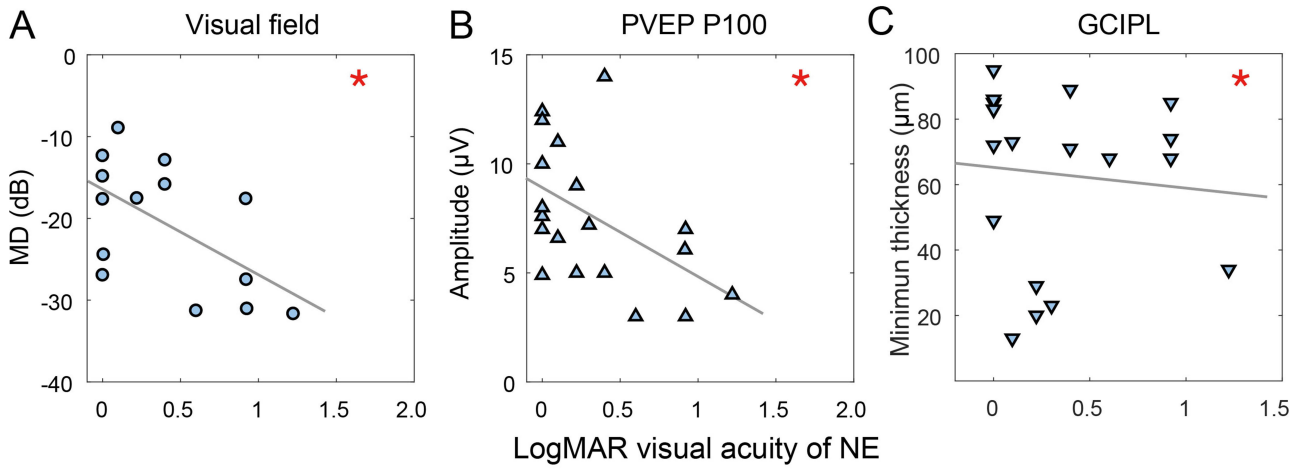

Figure 10 Correlation of logMAR visual acuity of the NAION eyes (NE) at 3 months with its the mean deviation (MD) of the visual field (VF) (**A**), amplitude of pattern visual evoked potentials (PVEP) P100 (**B**), and the minimum ganglion cell-inner plexiform layer (GCIPL) thickness (**C**) at baseline. X-axis represents the logMAR visual acuity of NE, and Y-axis represents the MD of the VF, amplitude of VEP P100 and minimum GCIPL thickness. Each symbol represents each patient, and the gray line represents the best linear fit. MD on VF, P100 amplitude, and the minimum GCIPL thickness of NE at baseline displayed a negative correlation with logMAR visual acuity at 3 months. The results of Spearman correlation test are shown in the figure: **P* < 0.05.

damage to macular elements. Previous research has primarily attributed mf-ERG N1 and P1 components to On and Off bipolar cells, with some N1 contribution from cone photoreceptors.[31] A second, smaller and later response, designated as the optic nerve head component (ONHC) waveform, represents action potential propagation along retinal ganglion cell axons and their myelin acquisition at the translaminar zone.[32] At this point, retinal ganglion cell axonal conduction properties transform from membrane to saltatory conduction.[32] The contribution to the global retinal response from retinal ganglion cells (RGCs) is small, thereby limiting the utility of mf-ERG technique in evaluating axonal and neuronal degeneration. Janáky et al found no characteristic alterations of mf-ERG in eight chronic NAION eyes, suggesting the outer retina remained undamaged.[33] However, their study analyzed only eight patients.[33] In our study, we found the P1 response density of mf-ERG in ring one decreased during the acute phase of NAION and showed significant correlation with GCIPL thickness, indicating contributions from inner retinal components including nerve fiber, RGCs, and inner plexiform layers to mf-ERG waves. Fonseca et al observed that inner retinal contribution was most significant between the prominent troughs and peaks of the mf-ERG response.[34] Wang et al reported localized abnormal mf-ERGs in both acute and chronic phases of Leber hereditary optic neuropathy(LHON) patients, suggesting possible occult maculopathy or previously unknown RGC contributions to first-order mf-ERG.[13] Additionally, Reis et al found decreased mf-ERG response amplitudes correlating with retinal thickness and VA in autosomal dominant optic

atrophy (ADOA) patients, suggesting a retrograde damage mechanism with significant impact on visual function.[14] Our study revealed clear evidence of physiological dysfunction through analysis of early mf-ERG components (N1 and P1), correlating with structural data (GCIPL thickness). Notably, the temporal progression of GCIPL thinning paralleled P1 amplitude reduction in mf-ERG. To our knowledge, no previous literature has reported abnormal mf-ERG in NAION eyes during the early phase. Our findings demonstrate that mf-ERG amplitude analysis serves as a useful objective indicator for monitoring RGC dysfunction and predicting NAION prognosis, while also confirming ganglionic elements' contribution to mf-ERG.

Initial VF mean deviation (MD) showed significant correlation with BCVA at baseline and 3-month follow-up, suggesting its utility as a prognostic indicator. However, we found no correlation between MD and RNFL or GCIPL thickness on OCT, possibly due to our small sample size. Further large-scale studies are needed to better characterize the relationship between neuronal structures and VF.

In functional evaluation, NAION eyes showed decreased amplitude and extended implicit time of VEP P100 compared to unaffected eyes, consistent with previous reports.[10,33,35] BCVA reduction significantly correlated with decreased VEP P100 amplitude, suggesting BCVA changes depend on impaired neural conduction along visual pathway axons.[35] We also found correlation between VEP P100 amplitude and GCIPL thickness, indicating ganglionic elements' contribution to VEP and inner retinal involvement in NAION.[10] Due to peripapillary nerve fiber layer edema, no correlations emerged between VEP P100 and RNFL thickness. Following acute ischemic insult, our findings revealed that both structural alterations and functional deficits extended beyond the optic nerve itself, demonstrating significant deterioration of innermost retinal components with concurrent changes in anatomical and electrophysiological parameters.

In conclusion, our study demonstrates that retinal ganglion cell layer thickness serves as a valuable indicator for objective evaluation of acute optic nerve function in NAION patients. Both VEP amplitude and mf-ERG response density decreases showed significant correlation with retinal ganglion cell layer thickness, possibly secondary to peripapillary axonal degeneration. Additionally, GCL analysis and mf-ERG assessment in the acute phase can serve as monitoring indicators for NAION. Study limitations include small sample size and retrospective design; further research with larger patient cohorts and prospective design is warranted.

Data Sharing Statement

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Disclosure

The authors report no conflicts of interest in this work.

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