ORIGINAL RESEARCH

Impact of 24-Hour Intraocular Pressure on Optic Nerve Fiber Layer Thickness in Patients with Early Diabetic Retinopathy

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ABSTRACT

Background • The optic nerve fiber layer, composed of ganglion cell axons within the ganglion cell layer, undergoes thickness changes due to diabetic retinopathy. However, the relationship between intraocular pressure (IOP) and optic fiber layer thickness remains unclear.

Objective • To investigate the correlation between 24-hour intraocular pressure and optic nerve fiber layer thickness in patients with early diabetic retinopathy.

Methods • This retrospective study collected 353 patients with early diabetic retinopathy from January 2019 to December 2021. They were categorized into the retinopathy group (n = 153) and the control group (n = 200). 24-hour IOP and optic fiber layer thickness were assessed, and the correlation between them was analyzed.

Results • The observation group exhibited significantly higher 24-hour IOP compared to the control group (16.64 ± 2.58 vs. 15.63 ± 2.52 mmHg, $P < .001$). Notably, the thickness of upper, lower, nasal, temporal, and average optic nerve fiber layers in the observation group decreased significantly ($P < .001$). Pearson linear correlation revealed significant negative associations between 24-hour IOP and upper, nasal, temporal, and mean optic nerve fiber layer thickness (R^2 = -0.277, -0.399, -0.344, and -0.489, $P < .05$). The upper, lower, nasal, temporal, and mean optic fiber thickness demonstrated diagnostic value for non-early diabetic retinopathy in type 2 diabetes patients ($P < .05$), with mean optic fiber thickness displaying the highest diagnostic potential (area under the curve: 0.843, 95% Confidence Interval: 0.803-0.884, $P < .001$).

Conclusions • Thinning of the optic nerve fiber layer in early diabetic retinopathy patients holds predictive value for the condition and exhibits a negative correlation with 24-hour intraocular pressure. (*Altern Ther Health Med.* 2023;29(8):297-301).

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INTRODUCTION

Diabetes, a chronic and enduring disease, inflicts damage to blood vessels and the vascular and nervous systems.[1] The prevalence of diabetes stands at approximately 3%, while the associated mortality rate is around 0.25%.[2] The onset of diabetes is attributed to a range of factors, predominantly characterized by hyperglycemia, with the primary pathophysiological mechanism involving relative or absolute insulin deficiency.[1-2] Diabetic retinopathy emerges as a prevalent complication within this context. Research indicates a striking 23.2% incidence of diabetic retinopathy among diabetic patients over a 5-year span. Furthermore, this condition significantly contributes to cases of blindness.

Early detection and diagnosis are pivotal for preventing and treating diabetic retinopathy. Research has elucidated the significant role of intraocular pressure (IOP) in retinopathy progression.[3] The optic nerve fiber layer, a composite of nerve fibers derived from the convergence of ganglion cell axons within the ganglion cell layer, assumes a critical role. Alongside micro-vasculopathy, diabetic retinopathy encompasses alterations in retinal nerve cells, diverse forms of neuronal degeneration, and apoptosis, collectively contributing to fluctuations in optic nerve fiber layer thickness.[4]

Research has suggested alterations in optic nerve fiber thickness among children with type 1 diabetes, potentially linked to cerebral edema.[5] A study conducted in China has underscored the utility of optic nerve fiber layer thickness as a predictive marker for diabetic peripheral neuropathy in individuals with diabetes.[6] However, studies investigating the

relationship between optic nerve fiber layer thickness and intraocular pressure within the context of diabetic retinopathy remain limited.

Understanding the underlying pathophysiological mechanisms can be enhanced by clarifying the relationship between optic nerve fiber layer thickness and intraocular pressure. This comprehension, in turn, facilitates early clinical interventions for diabetic retinopathy, ultimately contributing to the reduction of its incidence.[7] Therefore, this study aimed to explore the impact of 24-hour intraocular pressure on optic nerve fiber layer thickness among patients with early diabetic retinopathy.

MATERIALS AND METHODS

Study Design

A retrospective analysis was employed to gather data from outpatients with early diabetic retinopathy between January 2019 and December 2021 from our hospital's outpatient records. Based on the presence of diabetic retinopathy, these patients were categorized into two groups: the retinopathy group (n = 153) and the control group (n = 200). This study adheres to the principles outlined in the Declaration of Helsinki and has received approval from our hospital's Ethics Committee (Approval No.: 20210174).

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) Diagnosis of Type 2 diabetes mellitus; (2) Disease duration exceeding 10 years; (3) Age range of 18 to 65 years; (4) Comprehensive clinical data available; (5) Corrected visual acuity of ≥0.6; (6) Diopter: equivalent spherical lens ≤2.0; (7) Cup-to-plate ratio <0.6.

Exclusion criteria were as follows: (1) Previous history of cardiovascular and cerebrovascular disorders; (2) Presence of glaucoma; (3) Record of elevated intraocular pressure; (4) High myopia; (5) Past optic nerve-related conditions; (6) History of other secondary ocular disorders; (7) Abnormal ocular development; (8) Prior eye surgery or trauma; (9) Corneal conditions: Patients exhibiting vitreous opacity or lens nuclear hardness > ii.

Observations

(1) Variables recorded: Age, gender, fasting blood glucose levels, disease duration, body mass index, visual acuity. (2) Recorded 24-hour intraocular pressure. (3) Measured thickness of optic nerve fiber layer.

Detection Method

24-hour Intraocular Pressure (IOP). IOP was assessed using a Goldmann tonometer, with measurements taken while patients were seated and under surface anesthesia. The average of three consecutive measurements constituted the final reading. Measurements were taken at 5:00 AM, 7:00 AM, 10:00 AM, 2:00 PM, 6:00 PM, and 10:00 PM, with subsequent calculation of the mean IOP.

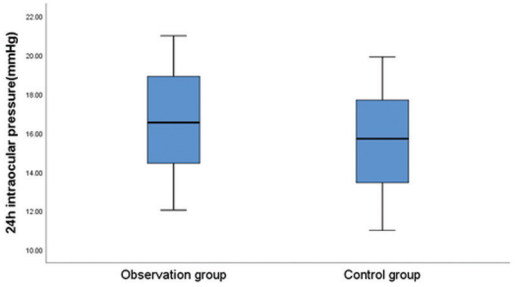
Optic Nerve Fiber Layer Thickness Assessment. Proficient technicians employed the 3D OCT-2000 Visual Papillary Scan Model by Topcon, Japan. The examination centered on the optic papilla, defining a radius of 1.73mm. This model automatically measured the optic nerve fiber layer's upper, lower, nasal, and temporal aspects around the optic papilla, with data systematically recorded.

Table 1. Comparison of General Data between the Two Groups

Project	Observation Group (n = 153)	Control Group (n = 200)	t/χ^2	*P* value
Age	52.56 ± 5.82	52.92 ± 6.07	0.562	.574
Gender(Male)	98 (64.05%)	133 (66.50%)	0.230	.632
FPG(mmol/L)	10.73 ± 1.88	10.92 ± 1.96	0.919	.359
Course of the Disease (Year)	14.38 ± 2.26	14.82 ± 2.75	1.607	.109
BMI(kg/m²)	26.86 ± 3.18	27.04 ± 3.66	0.484	.628
Vision	0.92 ± 0.16	0.95 ± 0.17	1.685	.093

Note: Data presented as mean ± standard deviation or N (%). FPG, fasting plasma glucose; BMI, body mass index.

Figure 1. Comparison of 24-h intraocular pressure between the two groups



Note: The figure illustrates the variation in 24-hour intraocular pressure (IOP) levels between the observation and control groups. Statistical analysis indicates a significant increase in 24-hour IOP in the observation group compared to the control group ($P < .001$). Error bars represent standard deviation.

Statistical Analysis

Data analysis for this study was conducted using SPSS 26.0 (IBM, Armonk, NY, USA). A significance level of $P < .05$ indicated statistical significance. All measurement data conformed to a normal distribution, with results expressed as ($\bar{x} \pm s$) mean ± standard deviation. Counting or categorical data were presented as N (%), and differences in measuring data between groups were analyzed using the chi-square test. The correlation between two measurement variables was assessed using Pearson's linear correlation.

RESULTS

General Data Comparison Between the Two Groups

No significant differences were observed in age, gender, fasting blood glucose, disease duration, body mass index, visual acuity, or other demographic factors between the two groups ($P > .05$), as depicted in Table 1.

Comparison of 24-Hour Intraocular Pressure between the Two Groups

In the observation group, 24-hour IOP was significantly higher compared to the control group (16.64 ± 2.58 vs 15.63 ± 2.52 mmHg, $P < .001$), as illustrated in Figure 1.

Table 2. Comparison of Optic Nerve Fiber Layer Thickness between the Two Groups

Project	Observation Group (n = 153)	Control Group (n = 200)	*t*	*P* value
UP (um)	117.04 ± 15.35	127.16 ± 17.35	5.709	<.001
Down (um)	112.49 ± 13.87	123.91 ± 17.71	6.585	<.001
Nasal Side (um)	70.01 ± 10.45	77.73 ± 10.22	6.961	<.001
Temporal Side(um)	69.10 ± 10.15	77.92 ± 10.20	8.066	<.001
Mean(um)	92.16 ± 6.67	101.68 ± 6.61	13.360	<.001

Note: Data presented as mean ± standard deviation. UP, upper; Down, lower; Nasal: nasal side; Temporal, temporal side.

Table 3. Correlation Analysis between 24-hour IOP and Optic Nerve Fiber Layer Thickness

Project	R^2	*P* value
UP (um)	0.047	.001
Down (um)	0.006	.311
Nasal Side (um)	0.069	<.001
Temporal Side (um)	0.074	<.001
Mean (um)	0.062	<.001

Note: Correlation coefficients (R^2) and associated *P* values are presented. UP, upper; Down, lower; Nasal, nasal side; Temporal, temporal side.

Table 4. Diagnostic Value of Optic Nerve Fiber Layer Thickness in Early Diabetic Retinopathy

Test Result Variable(s)	Area	Std. Error	*P* value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Upper	0.664	0.028	<.001	0.608	0.719
Below	0.685	0.028	<.001	0.631	0.740
Nasal Side	0.689	0.028	<.001	0.634	0.743
Temporal	0.724	0.027	<.001	0.671	0.776
Average	0.843	0.021	<.001	0.803	0.884

Note: Diagnostic performance metrics are presented, including the area under the curve (AUC), standard error (Std. Error), and *P* value. Asymptotic 95% confidence intervals for the AUC are also provided. UP, upper; Below, lower; Nasal, nasal side; Temporal, temporal side.

Comparison of Optic Nerve Fiber Layer Thickness between the Two Groups

In the observation group, the upper, lower, nasal, temporal, and average optic nerve fiber layer thickness exhibited significant reductions compared to the control group ($P < .001$), as depicted in Table 2.

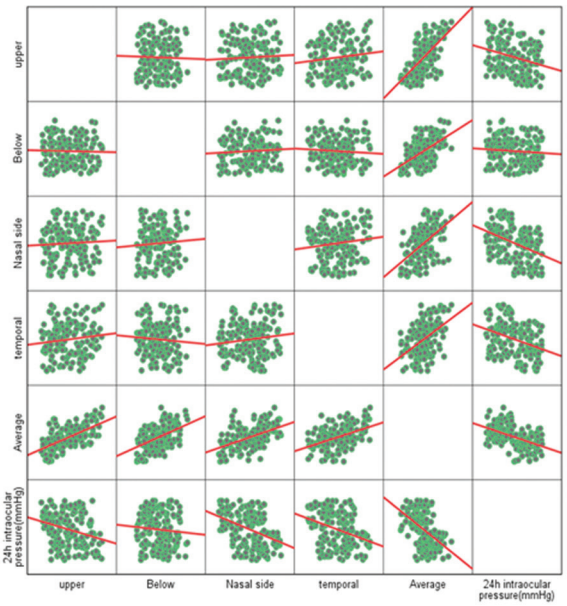
IOP and Optic Fiber Layer Correlation in Early Diabetic Retinopathy

Pearson's linear correlation analysis revealed significant negative correlations between 24-hour IOP and the thickness of the upper, nasal, temporal, and mean optic nerve fiber layers (r = -0.277, -0.399, -0.344, and -0.489, $P < .05$) as illustrated in Table 3 and Figure 2.

Diagnostic Significance of Optic Fiber Layer Thickness in Diabetic Retinopathy

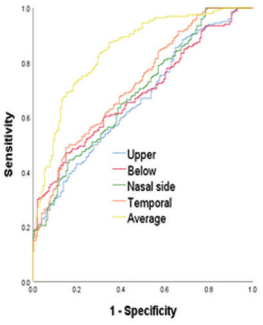
The upper, lower, nasal, temporal, and mean optic fiber thickness demonstrated diagnostic value for differentiating non-early diabetic retinopathy in type 2 diabetes patients ($P < .05$). Particularly, mean optic fiber thickness exhibited the highest diagnostic potential, with an impressive area under the curve of 0.843 (95%CI: 0.803-0.884, $P < .001$), as depicted in Figure 3 and Table 4.

Figure 2. Correlation analysis of 24-h IOP and optic nerve fiber layer thickness in patients with early diabetic retinopathy



Note: The figure depicts the correlation between 24-hour intraocular pressure (IOP) and optic nerve fiber layer thickness in patients with early diabetic retinopathy. Pearson's linear correlation coefficients (r) and associated *P* values are presented for each thickness parameter. Notably, a significant negative correlation is observed between 24-hour IOP and upper, nasal, temporal, and mean optic nerve fiber layer thickness ($P < .05$).

Figure 3. Diagnostic value of optic nerve fiber layer thickness in early diabetic retinopathy



Note: The figure illustrates the diagnostic performance of optic nerve fiber layer thickness for early diabetic retinopathy.

DISCUSSION

Diabetic retinopathy is a prevalent complication of diabetes mellitus, with a 10-year cumulative incidence as high as 19.10% in type 1 and 17.03% in type 2 diabetes mellitus.[8-10] Understanding the mechanism and pathophysiological processes underlying diabetic retinopathy is important for its early prevention and treatment.[11] While previous research has highlighted changes in optic nerve fiber layer thickness and intraocular pressure among diabetic retinopathy patients, the specific relationship between these factors remains unclear. This study was designed to address this gap, revealing a significant increase in 24-hour intraocular pressure alongside a noteworthy decrease in optic fiber layer thickness among

patients with diabetic retinopathy. These findings suggest a negative correlation between the two variables.[12]

The pathogenesis of diabetic retinopathy is rooted in prolonged hyperglycemia among diabetic patients. This condition leads to early damage to retinal microvasculature, resulting in retinal ischemia and hypoxia. These processes induce dysfunctional vascular endothelial cells, impairing the integrity of the blood-retinal barrier, thus leading to microvascular leakage, occlusion, severe ischemia, and eventual initiation of angiogenesis.[13-15] This cascade results in late-stage vitreous hemorrhage, retinal detachment, and subsequent vision loss. Notably, the retina is composed of both vascular and nerve tissue, with an uneven distribution across the neuroretina and vascular retina. The neuroretina holds a larger proportion, whereas the vascular retina occupies a comparatively smaller portion.[16]

The significance of neuroretina in diabetic retinopathy formation has garnered increasing attention. Beyond retinal microvasculopathy, neurological alterations encompass glial activation and nerve cell apoptosis, precipitating damage, and degeneration within the retinal nerve tissue. Prolonged hyperglycemia in diabetic patients is the dominant factor in driving the progression of neuroretinal dysfunction. Remarkably, neurodegenerative transformations in the retina may serve as the primary catalyst for structural shifts in retinal microvessels.[17]

Furthermore, evidence highlights retinal nerve impairment and thinning of optic nerve fibers in diabetes patients even before clinically evident retinopathy emerges. Thus, the optic nerve fiber layer assessment holds the potential to predict early-stage diabetic retinopathy, corroborating the findings of this study. Furthermore, diabetic retinopathy patients commonly exhibit aberrant intraocular pressure, a force generated by the contents of the eyeball interacting with its walls.[18]

In individuals without ocular disorders, intraocular pressure remains within a stable range to uphold the eyeball's anatomical integrity and ensure optimal refraction across the ocular media interface, thus preserving an optimal refractive state.[19] Elevated intraocular pressure is closely linked to glaucoma. This association has been underscored to the extent that a misconception has taken root, equating high intraocular pressure with glaucoma and normal intraocular pressure with immunity to the condition.

The precise mechanism behind elevated IOP in diabetic patients remains uncertain, yet it may be attributed to the following factors: (1) The osmotic gradient induced by heightened blood glucose levels in people with diabetes prompts increased fluid influx into the intraocular space, consequently elevating IOP; (2) Concurrently, the dysfunction of the autonomic nervous system within diabetic patients is also posited as a contributor to intraocular pressure escalation. This increased intraocular pressure eventually exacerbates the impairment of retinal microvessels, culminating in retinal ischemia and hypoxia. These conditions further induce vascular endothelial cell dysfunction, ultimately contributing to damage and degeneration of the retinal nerve tissue.

The findings of this study have revealed a significant negative correlation between 24-hour IOP and optic nerve fiber layer thickness among individuals with early diabetic retinopathy. These findings are consistent with previous studies.[20,21] These results suggest that elevated intraocular pressure could contribute to retinal and optic nerve impairment in diabetic patients. The management of intraocular pressure might offer benefits in retarding the progression of diabetic retinopathy.[22]

Study Limitations and Contribution

It is important to acknowledge certain limitations within this study. Firstly, the retrospective design might introduce inherent biases and confounding variables that could influence the observed outcomes. Secondly, the sample size, although sufficient for the study objectives, might limit the generalizability of the findings to broader populations. Additionally, the study does not establish whether reduction of IOP leads to symptom amelioration in diabetic retinopathy patients. The absence of long-term follow-up could hinder a comprehensive understanding of the dynamic relationship between intraocular pressure and optic nerve fiber layer thickness over time.

Despite these limitations, the current study contributes valuable insights into the correlation between these variables in early diabetic retinopathy. It unravels the negative correlation between 24-hour IOP and optic nerve fiber layer thickness in early diabetic retinopathy. These findings could guide future research towards interventions to optimise intraocular pressure to mitigate diabetic retinopathy progression.

CONCLUSION

This study highlights the intricate interplay between 24-hour intraocular pressure and optic nerve fiber layer thickness in early diabetic retinopathy. The observed significant negative correlation highlights the potential role of elevated intraocular pressure in retinal and optic nerve damage among diabetic patients. These findings emphasize the importance of monitoring and managing intraocular pressure as a potential avenue for delaying the progression of diabetic retinopathy. However, the retrospective nature and limited sample size of the present study suggest avenues for further multicenter randomized controlled trials to explain the long-term implications and clinical strategies for optimizing intraocular pressure control in diabetic retinopathy management.

DATA AVAILABILITY
The data used to support this study is available from the corresponding author upon request.

CONFLICTS OF INTEREST
The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS
Kai Liao and Xuehao Cui contributed equally to this work.

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