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Impact of Hyperglycemia on Tear Film and Meibomian Gland Dysfunction: A Cross-Sectional Study

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Purpose: Elevated blood glucose levels may disrupt tear film and meibomian gland function, contributing to dry eye disease (DED) and meibomian gland dysfunction (MGD). This study aimed to explore the relationship between hyperglycemia and DED parameters.
Methods: A cross-sectional study at Chifeng Chaoju Eye Hospital (June–August 2024) included 56 participants with DED symptoms. Tear meniscus height (TMH), non-invasive tear film breakup time (FNIBUT, ANIBUT), bulbar redness, and meibomian gland atrophy (U-LAMG, L-LAMG) were assessed using a non-invasive ocular surface analyzer. Fasting blood glucose levels stratified patients into high (≥7 mmol/l) and normal (<7 mmol/l) groups, and their association with DED parameters was analyzed.
Results: Among 56 patients (mean age 52.5 ± 18.0 years), those with elevated glucose levels (n=28) had more severe DED symptoms (OSDI, $p = 0.046$), lower TMH, FNIBUT, ANIBUT, and higher bulbar redness scores (all $p < 0.05$). In contrast, lower glucose levels were associated with greater U-LAMG and L-LAMG atrophy ($p < 0.05$). Glucose positively correlated with intraocular pressure (IOP), redness, U-LAMG, and L-LAMG but negatively correlated with TMH, FNIBUT, and ANIBUT (all $p < 0.05$).
Conclusion: Hyperglycemia is linked to impaired tear film stability, meibomian gland function, and DED symptoms. Ocular surface disorders in individuals with diabetes may be prevented by effective glycemic control.
Keywords: hyperglycemia, dry eye disease, meibomian gland dysfunction, tear meniscus height, non-invasive tear film breakup time

Introduction

Hyperglycemia, a condition marked by elevated blood glucose levels, is a key feature of diabetes mellitus and has long been associated with numerous systemic complications, particularly diabetic retinopathy, the leading global cause of blindness among working aged population.[1] Emerging research, however, suggests that hyperglycemia may also affect the ocular surface health.[2–5] The tear film, which plays a vital role in maintaining the health of the cornea and conjunctiva, consists of multiple layers, including an outer lipid layer that helps prevent evaporation and shields the eye from external irritants.[6] This lipid layer primarily derives from the meibomian glands, which secrete a blend of fatty acids and wax esters essential for tear film stability.[7]

There is growing evidence that hyperglycemia disrupts the function of the meibomian glands, leading to changes in the quality and composition of the lipid layer in the tear film.[8,9] These disruptions can result in ocular surface disorders such as dry eye disease (DED), meibomian gland dysfunction (MGD), and blepharitis,[10,11] which manifest through symptoms like eye irritation, dryness, burning, and blurred vision. Additionally, chronic alterations in the tear film due to hyperglycemia may promote inflammation and damage to the cornea and conjunctiva, potentially leading to long-term visual impairment[12–14] Study by Zhang et al and others suggest that hyperglycemia alters lipid profiles, leading to

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increased meibum viscosity and gland obstruction, resulting in tear film instability and inflammation.[15] However, most research in this area has focused on dyslipidemia and its impact on MGD, with limited investigation into how hyperglycemia independently influences the ocular surface measurements. Recent studies have shown a significant correlation between blood glucose levels and intraocular pressure (IOP), with diabetes and hyperglycemia increasing IOP and the risk of glaucoma, while dry eye is common among high IOP patients, often due to multiple medications.[16,17] This study aims to explore the potential impact of hyperglycemia on the tear film and MGD, focusing on how elevated blood glucose levels may influence lipid layer composition and ocular surface health. By investigating the relationship between hyperglycemia and tear film integrity, the research will contribute to a better understanding of how metabolic imbalances can predispose individuals to ocular surface disorders such as DED and MGD.

Methods

This cross-sectional study was conducted in Chifeng Chaoju Eye Hospital, between June 2024 and August 2024. It adhered to the principles of the Declaration of Helsinki and received approval from the Institutional Review Board (IRB) of Chifeng Chaoju Eye Hospital (CFKYLL-2024-02). Informed consent was obtained from all participants. The inclusion criteria were: (1) participants aged ≥ 18 years and ≤ 70 years; (2) Patients reported symptoms of ocular discomfort, including foreign body sensation, dryness, blurred vision, pain, itching, redness, sensitivity to light, tearing, and frequent blinking; (3) Participants had an ocular surface disease index (OSDI) score of 13 or higher, a tear break-up time (BUT) of 5 seconds or less, and Schirmer I test results (without anesthesia) showing 5 mm or less of tear production in 5 minutes; (4) There were notable abnormalities in the quality and expressibility of the meibomian gland secretions. Glaucoma was an exclusion criterion in this study to avoid confounding effects on intraocular pressure (IOP) and other ocular parameters.

DED and MGD assessments were conducted using the non-invasive ocular surface analyzer (OSA), which measured bulbar redness score (Jenvis scale), tear meniscus height (TMH), first and average non-invasive tear film breakup time (F-NIBUT and A-NIBUT), and meibomian gland analysis (U-LAMG and L-LAMG). Tear film stability was automatically detected by the Placido disc for NIBUT, while TMH was manually measured. The lipid layer was evaluated against the Guillon interferometric pattern. Meibomian gland dropout was analyzed via infrared imaging, yielding U-LAMG and L-LAMG values between 0% (no dropout) and 100% (complete gland loss). If only one eye of the subject meets the inclusion criteria, that eye will be included; if both eyes meet the criteria, the right eye will be included for analysis. To maintain measurement consistency, all assessments were conducted in the same room under controlled temperature and airflow conditions. All assessments were conducted in a room with controlled environmental conditions, but an environmental chamber was not used. The mean temperature (22°C ± 1°C) and humidity (50% ± 5%) were maintained throughout the measurements.

IOP was measured using a non-contact tonometer (Topcon CT-800, Topcon Corporation, Tokyo, Japan).

Measurement of glucose levels after an overnight fast (≥ 8 hours). Serum glucose testing involves drawing venous blood via venipuncture, using a sterile needle and glycolysis-inhibiting tubes. Blood glucose levels were measured in-house using a glucose oxidase-based assay with a standardized kit (Roche Diagnostics, Basel, Switzerland) to ensure consistency across all samples.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0 (IBM Corporation, Armonk, NY). Sample size calculation was conducted using the PASS software, assuming a 95% confidence interval, 80% power, and a 10% dropout rate, which resulted in an estimated sample size of total 37 participants. Two groups of participants were formed stratified by fasting blood glucose levels, ie glucose < 7 mmol/L and glucose≥ 7 mmol/L, and matched for age and sex to minimize potential confounding effect. Differences in DED parameters based on serum glucose levels were assessed using Student's *t*-test for parametric data or the Mann–Whitney *U*-test for nonparametric data. Correlations between DED and dyslipidemia were analyzed using Pearson's correlation for parametric data or Spearman's rho for nonparametric data. Continuous variables were presented as mean ± standard deviation (SD) with interquartile ranges (IQRs), while

categorical variables were expressed as frequencies (n) and percentages (%). All statistical tests were two-sided, with a significance level of $p < 0.05$.

Results

A total of 56 patients, 21 (37.5%) men and 35 (62.5%) women with a mean age of 52.5 ± 18.0 were included in the study. Glucose abnormalities levels were found in the respective numbers of patients: 28 (50%) patients with glucose ≥ 7 mmol/l; 28 (50%) patients with glucose < 7 mmol/l. More details on the characteristics of the analyzed population are outlined in Table 1.

The relationship between serum glucose levels and DED is outlined in Table 2. Regarding DED symptoms, a marginally significant trend in OSDI scores was observed, where patients with elevated glucose levels (≥ 7 mmol/l) reported more severe DED symptoms ($p = 0.046$). Regarding DED signs, patients with elevated glucose levels also reported significantly lower TMH, FNIBUT, ANIBUT, and bulbar redness score (all $p < 0.05$), while those with lower glucose levels (< 7 mmol/l) showed significantly lower U-LAMG and L-LAMG (all $p < 0.05$). However, there was no significant difference in IOP between high and low glucose levels ($p = 0.349$).

Regarding correlations (Figure 1A-1D, and Figure 2A-2D), significant positive correlations were found between glucose and IOP ($r = 0.038$, $p = 0.011$), bulbar redness score ($r = 0.698$, $p < 0.011$), U-LAMG ($r = 0.687$, $p < 0.001$), and L-LAMG ($r = 0.695$, $p < 0.001$). Of note, glucose was negative associated with TMH ($r = -0.509$, $p < 0.001$), FIBUT (r =

Table 1 Characteristics of the Study Population [Demographics, mean ± SD, IQR, or n (%)]

Characteristics	N = 56
Age (years)	52.50±18.00
Sex, male/female	21 (37.50)/35 (62.50)
Height (cm)	161.00±11.00
Weight (g)	138.91±21.53
Systolic blood pressure (mmHg)	130.00±20.00
Diastolic blood pressure (mmHg)	82.00±10.00
Glucose (mmol/L)	7.25±3.10
Visual acuity	0.50±0.50
Intraocular pressure (mmHg)	14.00±4.00

Table 2 Characteristics of Subjects Divided by Glucose Levels

	Glucose < 7 mmol/L (n = 28)	Glucose ≥ 7 mmol/L (n = 28)	p
Age (years)	51.32±16.28	53.21±17.13	0.67
Gender (female, %)	17 (60.71)	18 (64.28)	0.78
IOP (mmHg)	14.00 (3.00)	14.00 (4.00)	0.349
TMH (mm)	0.22 (0.07)	0.15 (0.04)	<0.001
FNIBUT (s)	9.66±1.34	2.86±1.13	<0.001
ANIBUT (s)	14.68±1.74	7.30±2.36	<0.001
Ocular redness analysis score	1.68±0.40	1.50±0.28	<0.001
Upper meibomian glands atrophy score	0.40±0.40	1.68±0.40	<0.001
Lower meibomian glands atrophy score	0.30±0.57	1.60±0.40	<0.001
OSDI score	29.75±13.14	36.86±12.65	0.046

Abbreviations: IOP, intraocular pressure; FNIBUT, first non-invasive breakup time; ANIBUT, average non-invasive breakup time; TMH, tear meniscus height; OSDI, ocular surface disease index.

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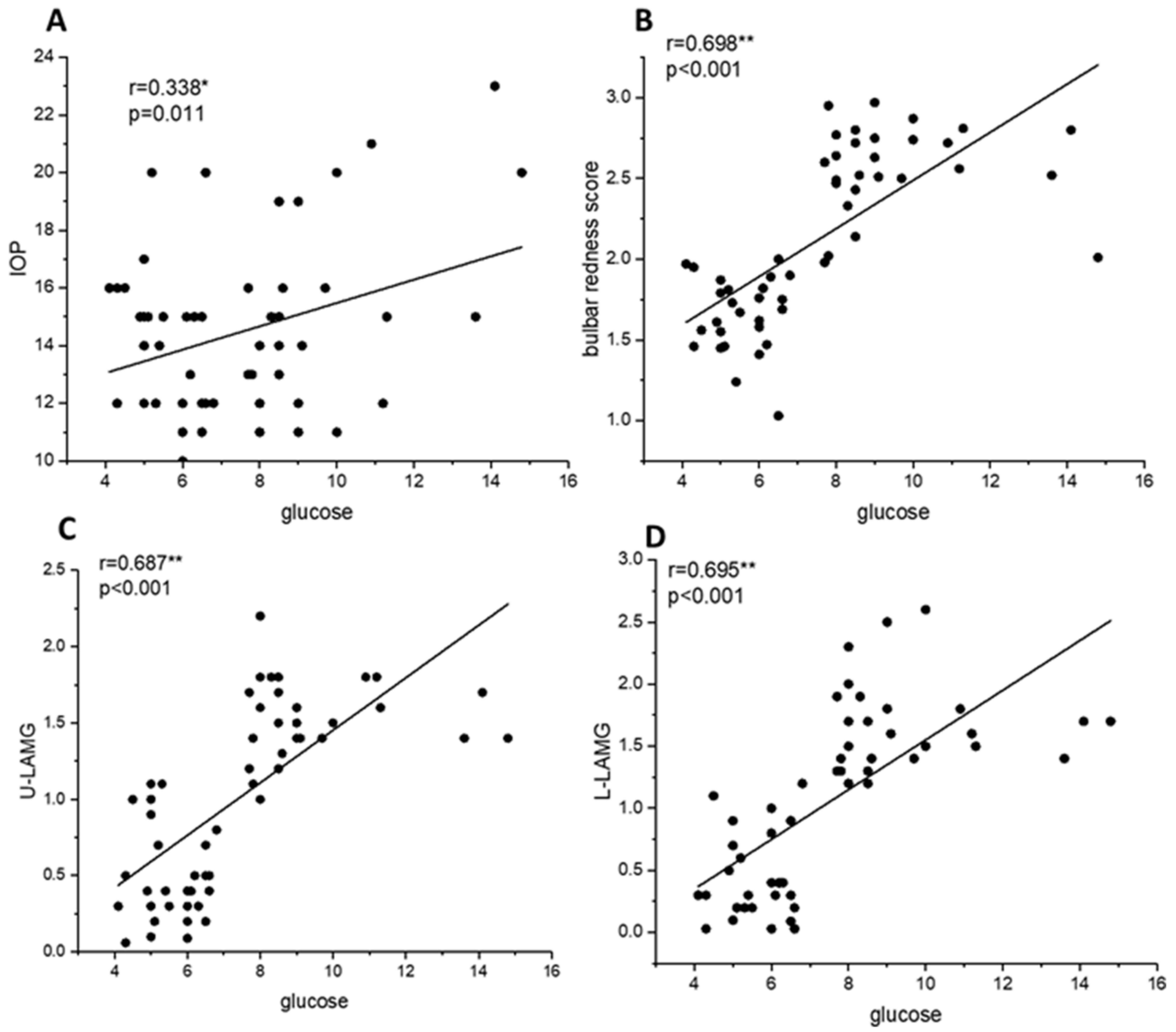

Figure 1 The correlation between glucose level and (**A**) intraocular pressure (IOP); (**B**) bulbar redness score; (**C**) upper meibomian gland atrophy (U-LAMG); (**D**) lower meibomian gland atrophy (L-LAMG). *, $p < 0.05$; **, $p < 0.001$.

−0.746, $p < 0.001$), and ANIBUT ($r = -0.740$, $p < 0.001$), while higher glucose levels showed no significant negative correlation with and OSDI score ($r = 0.191$, $p = 0.157$).

Discussion

The present study comprehensively examined the relationship between serum glucose levels and DED symptoms and signs. Our main findings demonstrated that elevated glucose levels (≥ 7 mmol/l) were significantly associated with more severe DED symptoms, as reflected by OSDI scores, as well as several key clinical signs, including TMH, non-invasive tear film breakup time (FNIBUT, ANIBUT), and increased bulbar redness score. These findings suggest that elevated glucose levels are associated with compromised tear quality and ocular surface dysfunction. In contrast, lower glucose levels (< 7 mmol/l) were associated with reduced upper and lower lid meibomian gland dysfunction, but no significant difference in IOP was observed between the groups. This indicates that while glucose levels affect tear film stability and meibomian gland function, IOP may not be directly impacted by glucose fluctuations in this context. These findings

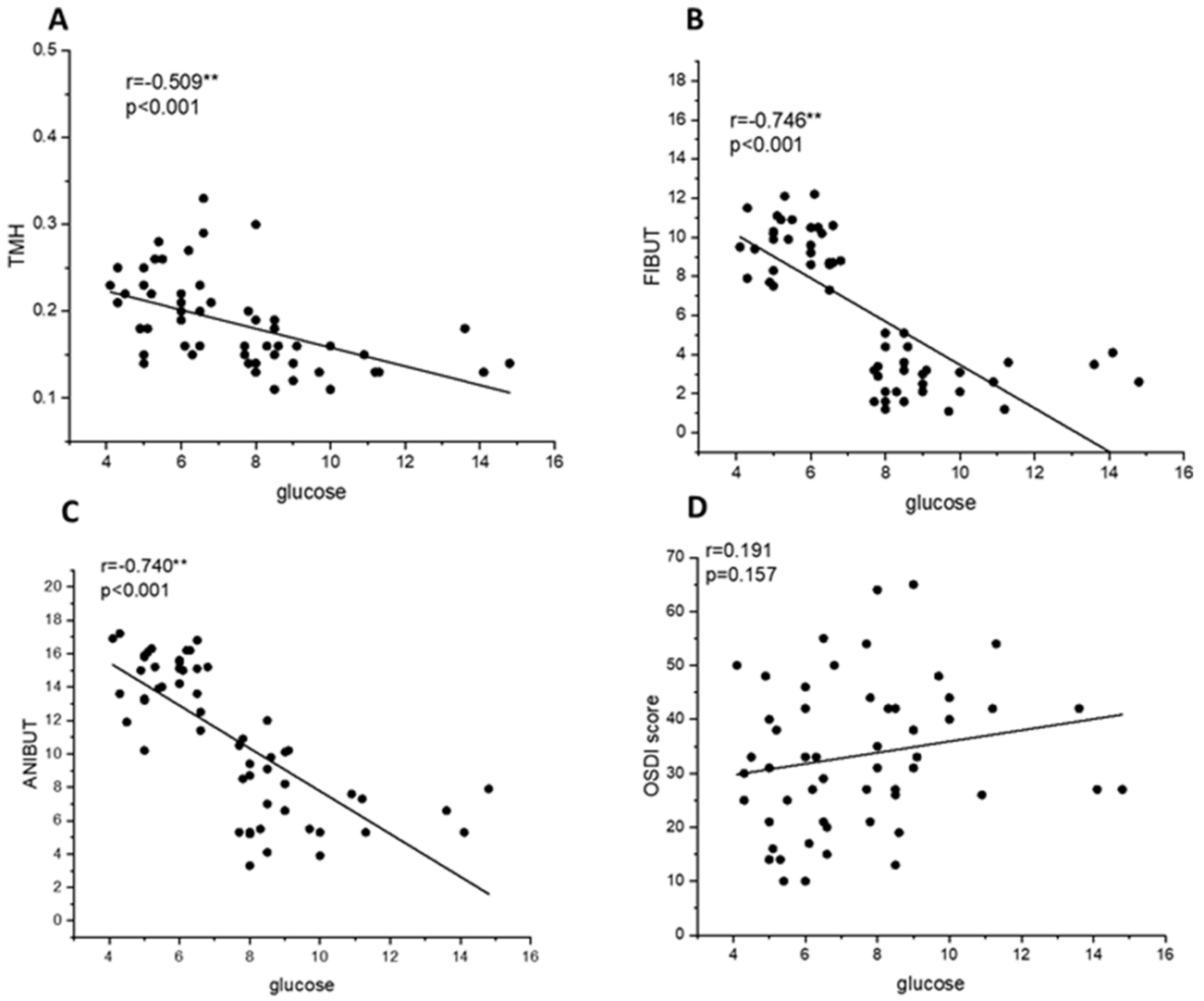

Figure 2 The correlation between glucose level and (**A**) tear meniscus height (TMH); (**B**) first non-invasive tear film breakup time (FNIBUT); (**C**) average non-invasive tear film breakup time (ANIBUT); (**D**) ocular surface disease index (OSDI). **, $p < 0.001$.

highlight the potential role of glucose metabolism in the pathophysiology of DED, with hyperglycemia potentially exacerbating ocular surface dysfunction.

Our results are consistent with previous studies linking hyperglycemia to dry eye symptoms and signs.[18] Prior research has shown that individuals with diabetes, characterized by elevated serum glucose levels, are at a higher risk for developing DED, potentially due to compromised corneal nerves, impaired tear production, and changes in tear film stability.[19–21] Persons with diabetes and dry eye exhibited notably higher corneal fluorescein and conjunctival lissamine green staining scores.[10] Similarly, studies have reported reductions in tear film break-up time and tear volume in individuals with elevated glucose,[22] which aligns with our findings of reduced FNIBUT and TMH in patients with higher glucose levels. However, we observed no significant association between serum glucose and intraocular pressure, contrasting with some studies that reported elevated IOP in individuals with diabetes.[23]

The pathophysiological link between type I diabetes and DED is believed to be partially due to antigen cross-reactivity, which can trigger autoimmune-mediated destruction of the lacrimal glands.[24,25] In individuals with diabetes, poorer glycemic control and the presence of microvascular complications have been linked to increased severity of DED symptoms and clinical signs.[26–28] Additionally, peripheral neuropathy, the most common complication of diabetes mellitus,[29] contributes to corneal nerve damage and reduces neurotrophic support, exacerbating DED.[30,31] The loss of

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corneal nerves in diabetes not only diminishes corneal sensitivity but also impairs the neural regulation of tear production, further increasing the risk of corneal neurotrophic keratopathy. This impaired corneal sensitivity may also lead to an under-reporting of dry eye symptoms, as patients may be less aware of discomfort, masking the true burden of the disease.[25] Furthermore, diabetic-related inflammation and oxidative stress may worsen ocular surface dysfunction, adding another layer of complexity to the relationship between diabetes and DED.

The strengths of this study include a well-defined cohort with detailed clinical assessment of both subjective symptoms and objective signs of DED, as well as a comprehensive analysis of the relationship between serum glucose levels and various DED parameters. However, several limitations should be acknowledged. First, the study sample was relatively small, which may limit the generalizability of the findings. Additionally, the cross-sectional design precludes the establishment of causality between glucose levels and DED. Future longitudinal studies are needed to confirm these associations and explore the long-term effects of glucose control on DED outcomes. Furthermore, while our study focused on serum glucose, other factors such as insulin resistance and systemic inflammation were not evaluated, which may also contribute to the observed associations. HbA1c, a key marker of long-term glycemic control, was not included due to logistical constraints in the outpatient setting, limiting our understanding of glycemic fluctuations and their impact on DED and MGD. Additionally, screen time, a known risk factor for DED, was not assessed due to the lack of reliable tools, potentially introducing residual confounding. Lastly, as a single-center study, the generalizability of our findings is limited. Future studies should include HbA1c, screen time, and larger, more diverse populations to validate and extend these findings.

Conclusion

In conclusion, our study demonstrates a significant association between elevated serum glucose levels and both subjective and objective markers of DED, suggesting that hyperglycemia may exacerbate dry eye symptoms and ocular surface dysfunction. These findings underscore the importance of glucose control in patients with or at risk of DED, and highlight the need for further research into the underlying mechanisms linking glucose metabolism to ocular surface health.

Data Sharing Statement

The data presented in this study are available on reasonable request from the corresponding author. The data are not publicly available due to restrictions with their containing information that could compromise the privacy of research participants.

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Chifeng Chaoju Eye Hospital (Approval ID: 20240010; Approval date: 14 June 2024).

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Disclosure

The authors report no conflicts of interest in this work.

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