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Comparing 24-hour IOP fluctuation slope curve between newly diagnosed ocular hypertension and primary open-angle glaucoma

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ABSTRACT

Objective To compare the 24-hour intraocular pressure (IOP) fluctuation slope curve between newly diagnosed patients with ocular hypertension (OHT) and primary open-angle glaucoma (POAG).

Methods and analysis Newly diagnosed and untreated OHT and POAG patients who underwent 24-hour IOP monitoring were consecutively enrolled in the study. IOP measurements were taken every 2 hours from 8:00 to 6:00 hours the following day using an iCare PRO tonometer. Patients maintained their daily routines, with IOP measured in a seated position during the day and supine at night. The 24-hour IOP fluctuation indices, including peak, trough and overall fluctuation, were calculated. Differences in the 24-hour IOP fluctuation slope curves over time between groups were analysed using a generalised additive mixed model.

Results 46 patients with OHT and 41 with POAG were included. From 2:00 to 10:00 hours, mean IOP increased by 0.69 mm Hg every 2 hours in the POAG group (p<0.0001) and by 0.40 mm Hg in the OHT group (p<0.0001). After 10:00, the IOP showed a downward trend, decreasing by 0.31 mm Hg in the POAG group (p<0.0001) and by 0.17 mm Hg in the OHT group (p=0.0003) every 2 hours. The rate of slope change in the upward phase differed significantly between the groups (0.30 mm Hg per 2 hours; p=0.02), as did the rate in the downward phase (0.14 mm Hg per 2 hours; p for interaction=0.04). Multivariate models showed that each 1 mm Hg increase in circadian and diurnal IOP fluctuation was associated with a 27% and 21% higher likelihood of POAG presence, respectively.

Conclusion The 24-hour IOP slope curve differed between POAG and OHT, with a steeper slope observed in the POAG group. However, the study is limited by potential confounding factors, reliance on a single 24-hour measurement period and the need for further longitudinal studies to validate these findings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Some patients with ocular hypertension (OHT) experience progression to primary open-angle glaucoma (POAG). Previous studies found that intraocular pressure (IOP) fluctuation is recognised as the risk factor for glaucoma progression.

WHAT THIS STUDY ADDS

⇒ Our study explored whether there is a difference between the OHT and POAG groups in terms of the slope of 24-hour IOP curve, which reflects the speed of IOP changes.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Clinicians and researchers should consider the speed of IOP changes when predicting which OHT patients are likely to progress to POAG. The slope of the 24-hour IOP curve may be an important risk factor for glaucoma progression.

INTRODUCTION

Patients presenting with high intraocular pressure (IOP) yet without characteristic glaucomatous optic disc changes and visual field (VF) loss are diagnosed with ocular hypertension (OHT). Elevated IOP is the only characteristic that distinguishes OHT from normal individuals.[1] According to previous research, partial OHT patients have the tendency to progress to primary open-angle glaucoma (POAG) during follow-up while others do not. The Ocular Hypertension Treatment Study (OHTS) has demonstrated that the 5-year cumulative probability of untreated OHT patients developing glaucoma was 9.5%.[2] Moreover, the 20-year cumulative incidence of unilateral or bilateral glaucoma was 45.6% in all OHT participants, 49.3% in the observation group and 41.9% in the medication group.[3] As emphasised by Weinreb *et al*, both the incidence of the disease and the lifetime risk of visual impairment should be carefully considered. It has been estimated that the 15-year risk of progression from OHT to blindness in untreated patients ranged from 1.5% to 10.5%.[4] Additionally, a prospective study by Grippo and Weinreb found that 33% of patients with OHT developed

glaucoma during an average follow-up period of 4.3±3.8 years.[5] Notably, some risk factors remain unknown that may potentially explain who in the OHT tends to progress into POAG.

IOP fluctuation is considered to be more important than one-time measurements for ocular health as IOP is a dynamic physiological parameter.[6] In practice, single IOP measurement during office hours provides insufficient information when discussing OHT progression.[7] Research has shown that 67.2% of peak IOP values occur out of clinic hours, meanwhile, significant diurnal/nocturnal IOP fluctuations are recognised as major risk factors for glaucoma progression.[7–9] Therefore, 24-hour IOP monitoring plays a crucial role in the diagnosis, treatment and follow-up of glaucoma patients.

In 24-hour IOP monitoring, multiple IOP measurements are required to observe IOP variations using parameters such as maximum and minimum IOP, IOP fluctuations (maximum IOP value minus minimum IOP value) and SD. However, these indices have certain limitations as they do not reflect the speed and direction of IOP changes. For instance, when IOP fluctuates from the minimum to maximum values by the same magnitude, the resulting IOP curve differs significantly between a short 2-hour interval and a longer 10-hour interval. During a 10-hour interval, the IOP curve appears smoother and flatter compared with a steeper curve during a 2-hour interval. Current parameters do not adequately describe the rate of change in the 24-hour IOP fluctuation slope curve, which is critical in understanding IOP dynamics. A steeper slope reflects a more rapid change of the IOP over a given time, which also reflects the amplitude of pressure change on the optic nerve per unit time.

In this study, the generalised additive mixed model (GAMM) was applied to fit 24-hour IOP slope curves for both OHT and POAG groups. The objective of this investigation is to compare the 24-hour IOP fluctuation between patients diagnosed with POAG and OHT, specifically investigating differences in the slope of the 24-hour IOP curve. Furthermore, we aim to explore the potential association between the steepness or flatness of the slope curve and its relevance as a risk indicator for the presence of POAG.

MATERIALS AND METHODS

Clinical data

The inclusion criteria were age ≥18 years and newly diagnosed POAG or OHT. POAG was defined as follows: (1) normal anterior chamber and open angles on gonioscopy; (2) untreated IOP >21 mm Hg (measured at least once in 24 hours) in either eye and (3) characteristic glaucomatous optic disc damage and VF defects. OHT was defined as follows: (1) untreated IOP >21 mm Hg (measured at least once in 24 hours) in either eye and (2) absence of clinical evidence indicating optic nerve damage, VF defect or other pathology.[5]

Exclusion criteria were as follows: (1) previous or current use of antiglaucoma medication and systemic or topical steroids; (2) any condition preventing reliable IOP measurement such as corneal pathology; (3) other possible causes of elevated IOP, such as diabetes; (4) suspected primary angle-closure glaucoma; (5) intraocular surgery or laser surgery, or severe ocular trauma at any time; (6) inadequate visualisation of the fundus, due to conjunctivitis, keratitis, uveitis; (7) progressive retinal or optic nerve diseases other than glaucoma and (8) secondary (eg, pseudoexfoliation syndrome), pigmentary or traumatic glaucoma.

All participants underwent a complete ophthalmic examination, including best-corrected visual acuity (logarithmic (logMAR) visual acuity chart), anterior segment examination with a slit-lamp (BQ900, Haag-Streit, Bern, Switzerland), gonioscopy (Goldmann one-mirror lens, Haag-Streit, Bern, Switzerland), IOP (NT510, Non-Contact tonometer, Nidek, Gamagori, Japan), fundus photography (CR-DGi Non-mydriatic retinal camera, Canon, Tokyo, Japan), central corneal thickness (CCT) and axial length (Lenstar biometer, LS900, Haag-Streit, Switzerland) and VF testing (Humphrey 750i visual field analyzer, Carl Zeiss, Dublin, California, USA).

Glaucoma diagnosis

Optic disc damage was characterised by the presence of any two or more of the following criteria: a cup-to-disc (C/D) ratio of 0.6 or greater, localised rim loss, disc haemorrhage or a C/D asymmetry of 0.2 or more, adjusted for optic disc size considerations.[10] A typical glaucomatous VF defect was identified in at least two reliable standard 24–2 VF examinations, with reliability defined as fixation losses under 20%, and false-positive and false-negative rates below 33%. VF defects were confirmed when at least two of the following conditions were met: a cluster of three or more depressed non-edge points in the pattern deviation plot at a significance level of $p<0.05$, with at least one point depressed at $p<0.01$ on two consecutive tests; a glaucomatous hemifield test result outside normal limits and a pattern SD occurring in less than 5% of normal fields.[10] Open angles were determined to be present if the posterior trabecular meshwork was visible over at least 180° of the angle on static gonioscopy, and no peripheral anterior synechiae were detected through indentation gonioscopy. The final diagnosis was made by a senior grader (SL) based on digital fundus photographs of the optic nerve and additional testing (including silt-lamp, gonioscopy and VF).

24-hour IOP measurement

The 24-hour IOP measurement is part of the standard tests for suspected POAG in China. POAG suspects were defined as a maximum untreated IOP >21 mm Hg on two consecutive visits in either eye, C/D ratio ≥0.6 and asymmetry in the VCDR of no less than 0.2. Patients were admitted to the hospital for 24-hour IOP monitoring using an iCare PRO tonometer (iCare Finland Oy, Vantaa, Finland). The IOPs of both eyes were measured every 2 hours from 8:00 to 6:00 hours the next day—that

is, from 8:00 to 20:00 hours (diurnal IOP) and from 22:00 to 6:00 hours (nocturnal IOP). iCare Pro tonometer simultaneously recorded six reliable measurements. The built-in software automatically discarded the highest and lowest values, and IOP was calculated based on four measurements.[11] All IOPs were measured by well-trained clinicians.

We encouraged patients to resume their daily routine during this study and allowed them to sleep between IOP measurements. The 24-hour IOP rhythm was measured at a habitual body position—that is, seated during the day and supine at night.

The calculation of 24-hour IOP parameters

For each group, the mean IOP for 24 hours was calculated without adjusting for CCT. The circadian fluctuation was calculated by subtracting the trough IOP from the peak IOP; diurnal and nocturnal fluctuations were recorded as daytime IOP variations measured from 8:00 to 20:00 hours, and night-time IOP variations from 20:00 to 6:00 hours, respectively. Peak IOP and trough IOP were noted as the highest and the lowest values among the 12 IOP values in 24 hours and during the diurnal and nocturnal periods. One additional parameter was also calculated: abnormal-IOP frequency, which is the cumulative frequency of abnormal IOP points (IOP>21 mm Hg).

Statistical analysis

For patients with unilateral or bilateral OHT or POAG, only the affected or right eye was included in the statistical analysis. Statistical analyses were performed using the commercially available SPSS V.22.0 (IBM). First, the continuous variables were described as means and SD. The two groups were compared using the independent-sample t-test and Mann-Whitney statistical test. The categorical variables were described as frequencies and constituent ratios and were analysed using the χ^2 test. Second, to avoid the collinearity between independent variables, we used different models and subdivided them into 24 hours and diurnal/nocturnal parameters in each model while adjusting for fixed covariates of age, sex, CCT and frequency of IOP >21 mm Hg. Each multivariate linear model was performed stepwise. Differences were considered statistically significant at p values of ≤0.05.

The difference in change rate of the 24-hour IOP fluctuation slope curve between groups was compared using a GAMM, with the trough IOP as baseline. The change rate of 24-hour IOP fluctuation slope curve in both the OHT group and the POAG group was also analysed using GAMM. GAMM is a flexible statistical approach that allows for the modelling of non-linear relationships between the dependent and independent variables while accounting for random effects. This is particularly useful in our study for capturing the intricate diurnal variations in IOP. GAMM extends the traditional linear mixed models by incorporating smoothing functions, enabling more accurate modelling of non-linear trends in the data. In our analysis, we used GAMM to estimate the IOP fluctuation slope and identify key inflexion points, such as the trough at 2:00 hours and the inflexion point around 10:00 hours. The model also accounts for random effects, such as interindividual variability, ensuring that the results are robust and generalisable. All statistical analyses were performed by using Empower (R) (www. empowerstats. com; X&Y Solutions, Boston, Massachusetts, USA) and R software V.3.6.1 (http://www.r-project.org). A two-tailed p<0.05 was considered statistically significant.

RESULTS

Altogether, 102 POAG suspects from 5 centres (Beijing, Shijiazhuang, Handan, Fushun and Xingtai) were included in this study; 53 and 49 patients with non-glaucoma and glaucoma, respectively, were initially diagnosed. After 24-hour IOP measurements, 46 and 41 eyes were diagnosed with OHT and POAG, respectively (figure 1).

Demographics and ophthalmic characteristics

Demographic and ophthalmic characteristics of the patients are shown in table 1. The groups differed significantly in sex (p=0.01) and age (p<0.001). A higher percentage of older males were seen in patients with POAG. The OHT group had significantly thicker CCT and greater abnormal IOP fluctuation frequency (p<0.001).

In addition, POAG group had significantly higher 24-hour and diurnal IOP fluctuation (p=0.04 and p=0.03, respectively); lower 24 hours, diurnal, nocturnal trough IOP (p=0.01, p=0.04 and p=0.01, respectively); lower nocturnal peak IOP (p=0.01). No statistical differences were observed in 24-hour and diurnal peak IOP, and nocturnal fluctuation between the two groups.

IOP fluctuation and the risk of POAG

We further investigated the association between IOP fluctuations and POAG. We present the univariate regression analysis of factors associated with different diagnoses in online supplemental table. Table 2 shows multivariate analysis of IOP fluctuation as possible factors associated with POAG after adjusting for age, sex, CCT and abnormal IOP frequency.

In model I, adjustment was made for age, sex, CCT and abnormal IOP frequency to explore the relationship between 24-hour IOP fluctuations and the risk of POAG. Compared with the OHT group, every 1 mm Hg increase in IOP circadian fluctuation increased the risk of POAG by 27% (OR=1.27, p=0.001) (table 2). Besides, diurnal and nocturnal fluctuations were analysed in model II. In comparison with the OHT group, risk of POAG went up by 21% with each 1 mm Hg increase in the diurnal fluctuation of IOP (OR=1.21, p=0.001) (table 2).

Difference in change rate of the 24-hour IOP fluctuation between OHT and POAG

In both the OHT and POAG groups, the increase in IOP followed an inverted 'U'-shaped curve with a trough IOP

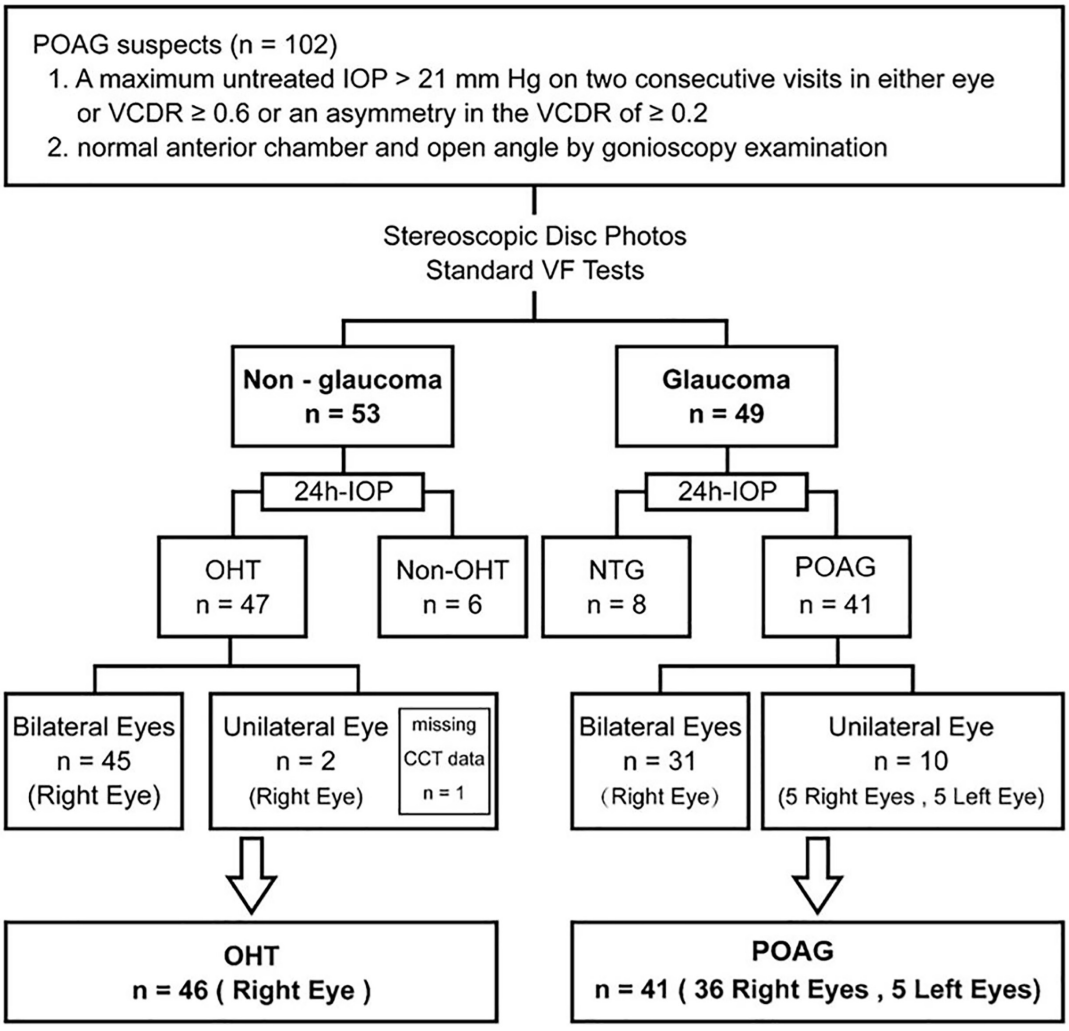

Figure 1 Participant selection and reasons for exclusion. CCT, central corneal thickness; IOP, intraocular pressure; NTG, normal-tension glaucoma; OHT, ocular hypertension; POAG, primary open-angle glaucoma; VCDR, vertical cup/disc ratio; VF, visual field.

at 2:00 hours (set as the baseline) and an inflexion point at approximately 10:00 hours. From 2:00 to 10:00 hours, IOP was positively correlated with the time, while after 10:00 hours, there was a negative correlation. Compared with that of the OHT group, the POAG group had a steeper ascent and descent in the inverted 'U' curve (figure 2).

From 2:00 to 10:00 hours, the increment rate over time in the OHT group was 0.40 mm Hg per 2 hours (95% CI 0.23, 0.56; p<0.0001) compared with 0.69 mm Hg (95% CI 0.50, 0.88; p<0.0001) in the POAG group. In addition, IOP increased significantly faster in the POAG group by 0.30 mm Hg per 2 hours (95% CI 0.04, 0.55; p for interaction=0.02) after adjusted for age, sex and CCT (table 3).

After the inflexion point at 10:00 hours, the decrement rate over time in the OHT group was 0.17 mm Hg per 2 hours (95% CI −0.26 to −0.08; p=0.0003), compared with 0.31 mm Hg per 2 hours (95% CI −0.41 to −0.20; p<0.0001) in the POAG group. There was a significantly faster decrease in terms of IOP in the POAG group by 0.14 mm Hg (95% CI −0.29 to −0.004; p for interaction=0.04) after adjusted for age, sex and CCT (table 3).

DISCUSSION

To our knowledge, this is the first study to describe the changes in the slope curve of 24-hour IOP fluctuation in POAG and OHT. As demonstrated in previous research, the difference between maximum and minimum values was generally applied to describe fluctuation of 24-hour IOP. Yet, the time duration from maximum to minimum IOP values are in fact of greater importance when discussing IOP fluctuation. For example, the conversion between maximum and minimum values in 2 hours is evidently different from that in 10 hours, as the latter possesses a flatter curve. Hence, in order to describe the steepness and flatness of the slope curve of 24-hour IOP fluctuation, we introduce the new index 'time-varying curve'.

Our results showed an inverted 'U' shape pattern of the 24-hour IOP fluctuation slope curve in both POAG and OHT, with IOP peaking between 10:00 and 12:00

Table 1 Demographics and ophthalmic characteristics of study population (N=87)

Characteristics	OHT (n=46)	POAG (n=41)	P value
Age	37.39±19.83	58.51±14.56	<0.001
Gender (male%)	20 (43.5)	25 (71.4)	0.01
CCT	571.52±35.16	545.24±32.67	<0.001
Mean IOP	22.99±2.76	21.16±5.41	0.162
Abnormal-IOP frequency	8.61±2.94	5.37±2.91	<0.001
IOP fluctuation, mm Hg			
Circadian fluctuation	10.33±4.26	12.48±5.18	0.04
Diurnal fluctuation	8.04±3.97	10.11±4.24	0.03
Nocturnal fluctuation	7.25±3.73	8.09±4.83	0.39
Peak and trough IOP, mm Hg			
Circadian peak IOP	28.22±3.81	28.18±6.78	0.97
Circadian trough IOP	17.90±2.92	15.70±4.87	0.01
Diurnal peak	27.68±3.79	27.83±6.67	0.91
Diurnal trough	19.65±3.19	17.72±5.24	0.04
Nocturnal peak	25.92±3.81	24.31±7.05	0.01
Nocturnal trough	18.67±3.19	16.23±5.13	0.01

Results in table: mean±SD.
Mean IOP: mean value of 24-hour intraocular pressure.
CCT, central cornea thickness; IOP, intraocular pressure; n, number; OHT, ocular hypertension; POAG, primary open-angle glaucoma.

hours. Additionally, IOP fluctuation slope curve in POAG was steeper than that in OHT. Multivariate analysis associated a steeper 24-hour IOP fluctuation slope with the presence of POAG as a potential risk factor. The distribution times of trough and peak IOP in this study are comparable to those reported by the Handan Eye Study (HES), which also examined adults over 18 years old from Northern China with similar lifestyles and dietary habits. The HES described the 24-hour variation in IOP (measured at six time points in our study) in newly diagnosed but untreated POAG patients within a population-based cohort. Consistent with our observations, 76.5% of the subjects in the HES experienced peak IOP in the morning (6:00–10:00 hours while 70.2% experienced the minimum IOP at night-time (22:00–2:00 hours).[10] However, unlike our hospital-based study, over 80% of HES subjects had peak IOPs below 21 mm Hg.[10]

Furthermore, our results suggest a significantly faster IOP variation speed in the POAG group compared with the OHT group. Unlike the intuitive fluctuation values commonly used in clinical practice, this finding indicates that the more intensive and consistent IOP changes experienced by POAG patients throughout the day may lead to earlier damage. These findings could help in accurately quantifying and identifying critical IOP fluctuations that contribute to disease progression in OHT patients.

In our study, we applied the GAMM to fit 24-hour IOP curves for both OHT and POAG groups. The GAMM

Table 2 Multivariable regression analysis of factors of fluctuation associated with different diagnosis

Outcome	Model I OR (95% CI)	Model I P value	Model II OR (95% CI)	Model II P value
Age	1.09 (1.04, 1.14)	<0.001	1.08 (1.04, 1.13)	0.001
Gender	0.15 (0.33, 0.71)	0.02	0.15 (0.03, 0.69)	0.01
Abnormal-IOP frequency	0.62 (0.47, 0.82)	0.001	0.66 (0.51, 0.85)	0.001
Circadian fluctuation, mm Hg	1.27 (1.04, 1.54)	0.02	–	–
Diurnal fluctuation, mm Hg	–	–	1.21 (1.01, 1.44)	0.04
Nocturnal fluctuation, mm Hg	–	–	–	–

Model I adjusted for age, gender, CCT, abnormal-IOP frequency, circadian fluctuation.
Model II adjusted for age, gender, CCT, abnormal-IOP frequency, diurnal fluctuation, nocturnal fluctuation.
CCT, central cornea thickness; IOP, intraocular pressure.

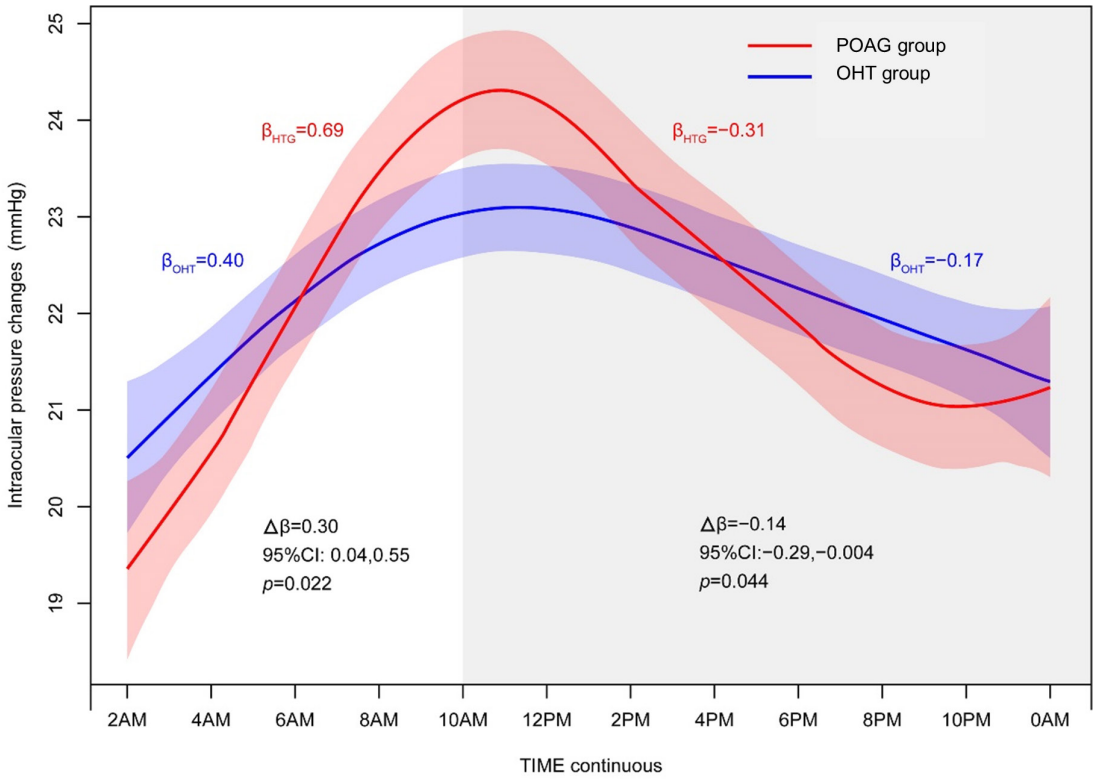

Figure 2 Relationship between the time-varying pattern (TVP) in 24-hour IOP and clinical grouping (OHT vs POAG) in the generalised additive mixed model. The TVP in 24-hour IOP in the OHT and POAG groups followed an inverted 'U' curve with the trough IOP at 2:00 hours (set as the baseline for analysis). From 2:00 hours (trough) onward, the IOP increase showed an upward pattern. It reached an increasing peak at 10:00 and 12:00 hours, reaching close to the plateau period and then showed a downward pattern after 12:00 hours. The slope of the IOP curve in the POAG group (red) was steeper than that in the OHT group (blue). IOP, intraocular pressure; OHT, ocular hypertension; POAG, primary open-angle glaucoma.

was then used to model the changes in IOP fluctuations over time. This approach captured differences in mean IOP trajectories between the POAG and OHT groups, accounting for both overall group trends and individual variability. Unlike general linear models, which typically fit group mean IOP over time, GAMM allows for a more detailed analysis by incorporating individual deviations from baseline IOP and assessing how changes in IOP fluctuations over time are associated with the presence of POAG or OHT.[12 13] Additionally, individual differences before and after specific time points were offset within the mixed model framework. Potential confounders were also controlled for in the GAMM.

Previous studies have explored risk factors for the progression from OHT to POAG. The OHTS indicated that high IOP is an important risk factor for progression

Table 3 Relationship between the time-varying slope in 24-hour IOP (per 2 hours) and clinical grouping at 2:00–10:00 and10:00–2:00 hours from a generalised additive mixed model (OHT vs POAG)

	Non-adjusted		Adjusted*	
	β (95% CI)	P value	β (95% CI)	P value
2:00–10:00 hours				
TVP^{OHT} (per 2 hours)	0.38 (0.22, 0.53)	<0.0001	0.40 (0.23, 0.56)	<0.0001
TVP^{POAG} (per 2 hours)	0.68 (0.50, 0.86)	<0.0001	0.69 (0.50, 0.88)	<0.0001
TVP×group (OHT vs POAG)	0.30 (0.06, 0.55)	0.02	0.30 (0.04, 0.55)	0.02
10:00–02:00 hours				
TVP^{OHT} (per 2 hours)	−0.17 (−0.26, 0.09)	<0.0001	−0.17 (−0.26, −0.08)	0.0003
TVP^{POAG} (per 2 hours)	−0.30 (−0.41, 0.20)	<0.0001	−0.31 (−0.41, −0.20)	<0.0001
TVP×group (OHT vs POAG)	−0.13 (−0.26, 0.01)	0.06	−0.14 (−0.29, −0.004)	0.04

*Adjusted for age, sex and central corneal thickness.
IOP, intraocular pressure; OHT, ocular hypertension; POAG, primary open-angle glaucoma; TVP, time-varying pattern.

to POAG, and lowering IOP through medication led to reduced progression.[14] In addition to IOP, baseline age, C/D, pattern SD and CCT were identified as risk factors for progression to POAG.[2 15 16] Our multivariate regression analysis similarly found that participants in the POAG group were older, more likely to be male and exhibited more circadian or diurnal OP fluctuation compared with those in the OHT group, even after adjusting for the frequency of abnormal IOP measurements. These findings align with previous research on risk factors for POAG progression.

Understanding the progression from OHT to POAG may be more closely associated with IOP, particularly 24-hour IOP fluctuation, than with other risk factors. In this study, the results showed that IOP fluctuation in POAG was greater than that in OHT. The IOP fluctuation indices (eg, circadian and diurnal fluctuations) were associated with POAG diagnosis. As circadian and diurnal fluctuations increased by 1 mm Hg, the risk of developing POAG in untreated OHT patients increased by 27% and 21%, respectively. According to the Advanced Glaucoma Intervention Study, every 1 mm Hg increase in long-term IOP variation increased the risk of progressive VF loss by 31%.[17] Additionally, Asrani *et al*[12] noted that the risk ratios of short-term and long-term IOP fluctuations for glaucoma progression were 5.69 and 5.76, respectively, after controlling for baseline IOP during office hours, age, race and sex. These findings suggest that even small increases in IOP fluctuations could be critically important for glaucoma progression.

Recent advancements in contact lens tonometry provide a non-invasive method for continuous 24-hour IOP monitoring. The Triggerfish contact lens sensors (CLS) (Sensimed, Lausanne, Switzerland) record corneal dimensional changes corresponding to IOP variations.[18] Studies have shown that continuous 24-hour IOP monitoring with the CLS reveals a nocturnal acrophase in both healthy subjects and glaucoma patients, suggesting that circadian IOP patterns should be evaluated in clinical practice for better glaucoma management.[19 20] Additionally, 24-hour IOP fluctuations assessed by the CLS can serve as a risk factor for POAG progression, aiding in early treatment adjustments.[21] However, the Triggerfish outputs data in millivolt equivalents rather than mm Hg, complicating clinical.

A novel CLS system developed by the Hong Kong University outputs continuous IOP curves in mm Hg. This system has demonstrated good sensing capability in detecting IOP changes and features an IOP-signal gauged model to minimise errors.[22] Its safety and tolerability for continuous 24-hour use in adults have been deemed acceptable.[23] Recent studies on this novel CLS device in normal Chinese subjects showed stable 24-hour IOP outputs, with comparable mean levels between day and night, and variations positively correlated with age and male sex.[24]

There are some limitations to this study. First, we could not completely exclude other confounding factors regarding individual lifestyle that can alter IOP or circadian rhythms.[25 26] Despite adjusting for confounding factors such as age, sex and CCT, these factors may present as biased in the real-world setting. Second, IOP measurements were obtained over a single 24-hour period. Similar IOP profiles were observed in both the POAG and OHT groups; thus, it would be useful to determine if the changes in IOP were reproducible on different days. To evaluate the repeatability of IOP fluctuation changes over time in 24-hour IOP and its influencing factors, future studies are warranted for measurements of 24-hour IOP for at least 3 days, recording the participants' activity or posture in each measurement period. Interestingly, our data from another independent randomised controlled trial (yet to be published) shows that, after matching for confounding factors such as age and sex in the OHT and POAG groups, the 24-hour IOP variation pattern also presents an inverted U-shape in both groups, similar to this study. Additionally, the slope of IOP variation is significantly steeper in the POAG group compared with the OHT group. Third, this was a hospital-based study in Northern China, and the results may not be directly comparable to those in other regions or populations. Fourth, the cross-sectional design has limited value in evaluating causal effects. Future longitudinal studies are needed to further establish a causal relationship between IOP fluctuation changes over time and OHT or POAG diagnosis.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and approval was obtained from Beijing Tongren Hospital's Ethical Committee (https://www.chictr.org.cn/; identifier: ChiCTR2300073216). Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available on reasonable request.

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