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# Continuous 24-Hour Intraocular Pressure Monitoring with a Smart Contact Lens Predicts Visual Field Progression in Normal-Tension Glaucoma

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## ABSTRACT

**Introduction:** Normal-tension glaucoma (NTG) may progress despite normal office intraocular pressure (IOP), suggesting that 24-hour IOP dynamics captured by a smart contact lens (SCL) sensor may improve risk stratification. This study evaluated whether SCL-derived nocturnal IOP parameters independently predict Humphrey 24-2 visual field (VF) progression in NTG.

**Methods:** This prospective observational cohort enrolled 62 NTG eyes (62 patients; one eye per patient) who underwent 24-hour SCL monitoring and serial Humphrey 24-2 SITA-Standard VF testing over 24 months at a private hospital in Palembang, Indonesia. The primary outcome was VF mean deviation (MD) slope (dB/year). Multivariable linear regression and receiver operating characteristic (ROC) analysis were performed.

**Results:** Eyes with a nocturnal IOP acrophase ($n$ = 36) had a significantly faster MD decline (−1.24 ± 0.31 dB/year) than eyes without acrophase ($n$ = 26; −0.42 ± 0.19 dB/year; mean difference −0.82 dB/year, 95% CI −0.97 to −0.67, $p < 0.001$; Cohen $d$ = 3.20). Independent predictors of MD slope were nocturnal acrophase (β = −0.71, $p < 0.001$), number of long peaks (β = −0.18, $p < 0.001$), and baseline RNFL thickness (β = +0.034, $p$ = 0.002); adjusted $R^2$ = 0.64. Nocturnal amplitude yielded an AUC of 0.83 (95% CI 0.74–0.91).

**Conclusion:** SCL-derived nocturnal IOP parameters independently predict VF progression in NTG. Integration of 24-hour SCL monitoring may enhance risk stratification beyond office IOP measurement.

## 1. Introduction

Glaucoma is the leading cause of irreversible blindness worldwide, and its global burden has risen substantially with population ageing, with the number of prevalent cases projected to continue increasing in the coming decades.[1] Normal-tension glaucoma (NTG) is a subset of open-angle glaucoma characterised by progressive glaucomatous optic neuropathy and visual field (VF) loss despite intraocular pressure (IOP) values consistently measured below 21 mmHg during office hours.[2,3] NTG is comparatively more prevalent in East and Southeast Asian populations, making it a dominant clinical concern in Indonesian ophthalmological practice.[4] Although lowering IOP slows NTG progression, a substantial proportion of patients continue to deteriorate despite achieving low target pressures, implicating IOP-independent mechanisms and 24-hour pressure dynamics that escape conventional office-hour assessment.[5]

The pathophysiology of NTG involves a complex interplay between biomechanical susceptibility of the lamina cribrosa and vascular dysregulation, including nocturnal systemic hypotension, reduced mean ocular perfusion pressure, and impaired vascular autoregulation.[2,6] Studies employing 24-hour and continuous monitoring have shown that IOP fluctuation, and nocturnal IOP behaviour in particular, is associated with greater retinal nerve fibre layer (RNFL) thinning and faster VF decline, although the relative prognostic weight of fluctuation versus mean IOP remains debated.[7-9] Earlier investigations relied on repeated hand-held tonometry with sleep-laboratory wake-up protocols, which introduced measurement artefact, disrupted sleep architecture, and limited ecological validity.

The wearable smart contact lens (SCL) sensor provides an ambulatory, non-invasive method to capture continuous 24-hour ocular pressure-related signals in a physiological setting.[10-12] The Sensimed Triggerfish device records changes in corneal curvature at the corneoscleral junction at 30-second intervals over 24 hours, yielding an output in millivolt-equivalent (mV-eq) units that correlates with, but is not directly convertible to, IOP in millimetres of mercury.[11] From the continuous recording, clinically relevant parameters can be derived: the nocturnal acrophase, the diurnal-to-nocturnal amplitude, the number of transient large peaks, the mean 24-hour slope, and the area under the 24-hour curve.[12,13]

Contemporary studies have increasingly linked SCL-derived IOP parameters with glaucoma progression. Gaboriau and colleagues found that a greater 24-hour IOP-related fluctuation magnitude and area under the monitoring curve recorded by the SCL were associated with faster VF mean deviation (MD) decline in open-angle glaucoma.[13] Higashide and colleagues reported that 24-hour SCL profile parameters were independent predictors of structural and functional progression in a Japanese NTG cohort.[7] Complementary evidence from continuous and implantable-sensor studies confirmed that 24-hour IOP variability adds predictive value beyond office IOP for identifying fast progressors.[14,15] However, most existing studies are single-centre with modest samples and short follow-up, and prospective data from Southeast Asian NTG populations remain scarce despite the high regional prevalence.

The aim of this study was to evaluate whether SCL-derived nocturnal IOP parameters independently predict Humphrey 24-2 visual field progression in Indonesian patients with NTG over a 24-month follow-up period, and to determine the optimal discriminative threshold of nocturnal amplitude for identifying VF progressors.

## 2. Methods

### *Study design and setting*

This was a prospective observational cohort study conducted at the Ophthalmology Clinic of a Private Hospital in Palembang, Indonesia, between January 2022 and December 2024. The study protocol adhered to the tenets of the Declaration of Helsinki and was approved by the CHMC Research Ethics Committee (Approval No. CHMC/EC/2022/0147). Written informed consent was obtained from all participants prior to enrolment. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.

### *Participants*

Consecutive patients aged 40 to 80 years presenting to the glaucoma service with a confirmed diagnosis of NTG were screened. NTG was defined according to European Glaucoma Society and Japanese Glaucoma Society criteria: open angles on gonioscopy (Shaffer grade III or IV), Goldmann applanation tonometry (GAT) IOP consistently ≤ 21 mmHg on at least three separate occasions (including a diurnal phasing protocol), glaucomatous optic disc changes, and reproducible glaucomatous VF defects on at least two consecutive Humphrey 24-2 SITA-Standard examinations. Secondary causes of optic neuropathy were excluded through neuroimaging in all patients and serological screening (ESR, CRP, ANA, VDRL) in those younger than 50 years or with atypical features.

Inclusion criteria further required best-corrected visual acuity (BCVA) of 0.50 LogMAR (Snellen 20/63) or better, refractive error within ± 6.00 dioptres spherical equivalent, central corneal thickness (CCT) between 480 and 600 μm, and the ability to tolerate SCL wear for 24 hours. Exclusion criteria included any secondary glaucoma, angle-closure component, prior incisional or laser glaucoma surgery, corneal disease precluding SCL application, significant media opacity, retinal or neuro-ophthalmic disease other than glaucoma, systemic corticosteroid use, and inability to perform reliable perimetry (fixation losses > 20%, false-positive rate > 15%, or false-negative rate > 33%).

### *Unit of analysis and study-eye selection*

The unit of analysis was one eye per patient to avoid inter-eye correlation. In bilateral NTG, the eye with the worse VF MD at baseline was designated as the study eye to enrich the cohort for progressor phenotypes; in cases of equal MD, the right eye was selected by convention. The rationale for selecting the worse eye, which may introduce collider-type selection bias toward more advanced disease, is acknowledged in the limitations. A sensitivity analysis using the better eye confirmed concordant findings.

### Sample size calculation

The sample size was calculated a priori using G*Power version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Germany) for a two-tailed independent-samples $t$-test comparing VF MD slope between two groups. Based on published 24-hour SCL data in NTG cohorts,[7] an expected mean difference of 0.80 dB/year in MD slope with a pooled standard deviation of 0.90 dB/year was assumed, yielding a required sample of 27 per group (54 total) for $\alpha = 0.05$ and power = 0.80. For the multivariable regression with 7 candidate covariates and an anticipated proportion of VF progressors of approximately 55%, the events-per-variable ratio was estimated at 8.9. Accounting for an anticipated 15% dropout, 62 patients were enrolled.

### Ophthalmic examination

All participants underwent a standardised comprehensive ophthalmic examination at baseline and at 6-monthly intervals, performed by two fellowship-trained glaucoma specialists masked to each other's findings. BCVA was measured using a retroilluminated ETDRS chart at 4 m under standardised photopic conditions (85 cd/m$^2$). IOP was measured by calibrated GAT (Haag-Streit AT-900) as the average of three readings within 2 mmHg; CCT by ultrasound pachymetry (Tomey SP-100), with IOP adjusted for CCT deviation from 545 μm; and axial length by optical biometry (IOLMaster 700; Carl Zeiss Meditec). Optic disc stereophotographs were graded independently by two masked specialists using the disc damage likelihood scale (DDLS), and glaucoma severity was classified by the Hodapp-Parrish-Anderson (HPA) system.

### Spectral-domain optical coherence tomography

Spectral-domain OCT was performed with the Cirrus HD-OCT 5000 (Carl Zeiss Meditec) using the Optic Disc Cube 200×200 and Macular Cube 512×128 protocols at baseline, month 12, and month 24. Circumpapillary RNFL thickness and macular ganglion cell–inner plexiform layer (GCIPL) thickness were recorded. Only scans with signal strength ≥ 7, no segmentation errors, and correct centration were included; the Guided Progression Analysis module categorised structural progression.

### Smart contact lens 24-hour monitoring

The SCL (Sensimed Triggerfish; Sensimed AG, Lausanne, Switzerland) was applied to the study eye at baseline and at the 12-month visit. Recording began at approximately 10:00 hours and continued uninterrupted for 24 hours, during which patients maintained habitual activities and sleep schedule; output was expressed in mV-eq, sampled every 5 minutes (288 data points per 24 hours). Parameters extracted using cosinor analysis and custom peak-detection algorithms (MATLAB R2022b) were: (1) nocturnal acrophase (circadian peak 22:00–06:00 with amplitude > 5 mV-eq above the fitted cosine mean); (2) diurnal-to-nocturnal amplitude (mV-eq); (3) number of long peaks per 24 hours (> 11 mV-eq above the 2-hour running median lasting > 30 minutes); (4) mean 24-hour slope (mV-eq/hour); and (5) area under the 24-hour curve (mV-eq·hour). Inter-rater agreement was $\kappa = 0.91$ for acrophase classification and ICC = 0.94 for amplitude.

### Visual field testing and progression

VF testing used the Humphrey Field Analyzer III with the 24-2 SITA-Standard strategy. Reliability criteria required fixation losses < 20%, false-positive rate < 15%, and false-negative rate < 33%. A minimum of six reliable VF tests per eye over 24 months were obtained at approximately 4-month intervals. VF progression was quantified by the MD slope (dB/year) using ordinary least-squares linear regression, and a VF progressor was defined a priori as an eye with an MD slope more negative than −1.0 dB/year.

### Statistical analysis

Statistical analysis used SPSS version 28 (IBM Corporation) and MedCalc version 20.2. Continuous variables were described as mean ± SD or median (IQR); categorical variables as frequency (%). Between-group comparisons used the independent-samples $t$-test or Mann-Whitney $U$ test and the $\chi^2$ or Fisher exact test, with Cohen $d$ for the primary outcome. Multivariable linear regression (backward elimination, retention at $p < 0.10$) identified independent predictors of VF MD slope; diagnostics included residual plots, the Durbin-Watson statistic, and variance inflation factors (VIF < 5). ROC analysis evaluated nocturnal amplitude, with the AUC (bootstrapped 95% CI, 2000 replicates) and the Youden-index optimal cut-off reported. A two-tailed $p < 0.05$ was considered significant.

## 3. Results

Of 78 patients with NTG screened between January and June 2022, 70 met the initial eligibility criteria; 4 declined SCL wear, 2 had corneal irregularity precluding fitting, and 2 had unreliable baseline VF, yielding 62 enrolled patients (62 study eyes). During follow-up, 3 patients withdrew and 2 had unreliable VF at month 24; a sensitivity analysis using last-observation-carried-forward produced concordant results ($\beta$ for nocturnal acrophase = −0.69, $p < 0.001$), and the primary analysis is presented for the full 62-eye cohort.

The mean age was 58.7 ± 9.4 years, and 35 patients (56.5%) were female. Baseline BCVA was 0.12 ± 0.08 LogMAR (Snellen ≈ 20/25), baseline GAT IOP was 14.8 ± 2.3 mmHg, and mean CCT was 531 ± 28 μm. Axial length was 23.8 ± 1.1 mm and baseline VF MD was −6.82 ± 4.21 dB. By HPA classification, 28 eyes (45.2%) had early, 22 (35.5%) moderate, and 12 (19.4%) advanced NTG. Baseline average RNFL thickness was 79.4 ± 11.6 μm and GCIPL thickness 71.2 ± 8.3 μm. The full baseline profile, stratified by nocturnal acrophase status, is presented in Table 1.

Table 1. Baseline demographic and ocular characteristics (N = 62 eyes of 62 patients).

| Characteristic | All (n = 62) | Acrophase+ (n = 36) | Acrophase− (n = 26) | p |
|---|---|---|---|---|
| Age, years | 58.7 ± 9.4 | 59.3 ± 8.8 | 57.8 ± 10.2 | 0.542 |
| Female, n (%) | 35 (56.5) | 21 (58.3) | 14 (53.8) | 0.726 |
| BCVA, LogMAR | 0.12 ± 0.08 | 0.13 ± 0.09 | 0.10 ± 0.06 | 0.153 |
| GAT IOP, mmHg | 14.8 ± 2.3 | 15.1 ± 2.4 | 14.4 ± 2.1 | 0.225 |
| CCT, μm | 531 ± 28 | 528 ± 30 | 535 ± 25 | 0.353 |
| VF MD, dB | −6.82 ± 4.21 | −7.34 ± 4.52 | −6.10 ± 3.71 | 0.249 |
| RNFL, μm | 79.4 ± 11.6 | 77.8 ± 12.1 | 81.6 ± 10.8 | 0.207 |
| GCIPL, μm | 71.2 ± 8.3 | 70.1 ± 8.8 | 72.7 ± 7.5 | 0.228 |

*Notes: Continuous data: mean ± SD. BCVA = best-corrected visual acuity; CCT = central corneal thickness; GAT = Goldmann applanation tonometry; GCIPL = ganglion cell–inner plexiform layer; IOP = intraocular pressure; MD = mean deviation; RNFL = retinal nerve fibre layer; VF = visual field.*

As detailed in Table 1, no statistically significant differences were observed between the acrophase-present and acrophase-absent groups at baseline in any demographic, refractive, IOP, structural, or systemic variable (all $p > 0.05$), with small effect sizes (Cohen $d < 0.40$), confirming comparable baseline profiles.

Table 2. Smart contact lens parameters and visual field progression outcomes over 24 months.

| Parameter | All (n = 62) | Acrophase+ (n = 36) | Acrophase− (n = 26) | p |
|---|---|---|---|---|
| Nocturnal amplitude, mV-eq | 11.4 ± 5.2 | 15.8 ± 3.1 | 5.3 ± 2.4 | < 0.001 |
| Long peaks / 24 h | 3.8 ± 2.1 | 5.2 ± 1.5 | 1.8 ± 1.2 | < 0.001 |
| VF MD slope, dB/year | −0.90 ± 0.52 | −1.24 ± 0.31 | −0.42 ± 0.19 | < 0.001 |
| VF progressors, n (%) | 36 (58.1) | 32 (88.9) | 4 (15.4) | < 0.001 |
| RNFL thinning, μm/year | −1.52 ± 0.74 | −1.89 ± 0.61 | −1.01 ± 0.58 | < 0.001 |
| GCIPL thinning, μm/year | −0.92 ± 0.45 | −1.14 ± 0.38 | −0.62 ± 0.35 | < 0.001 |

*Notes: Continuous data: mean ± SD. A VF progressor was defined as an MD slope more negative than −1.0 dB/year. GCIPL = ganglion cell–inner plexiform layer; MD = mean deviation; mV-eq = millivolt equivalent; RNFL = retinal nerve fibre layer; VF = visual field.*

Table 2 presents the SCL parameters and VF progression outcomes. The nocturnal acrophase group demonstrated a significantly faster VF MD decline (−1.24 ± 0.31 dB/year) than the no-acrophase group (−0.42 ± 0.19 dB/year; mean difference −0.82 dB/year, 95% CI −0.97 to −0.67, $p < 0.001$; Cohen $d = 3.20$). Among the 62 eyes, 36 (58.1%) were VF progressors; of these, 32 (88.9%) were in the acrophase group and only 4 (15.4%) in the no-acrophase group ($x^2 = 33.4$, df = 1, $p < 0.001$). RNFL thinning was concordantly faster in the acrophase group (−1.89 ± 0.61 vs −1.01 ± 0.58 μm/year; $p < 0.001$; Cohen $d = 1.48$), as was GCIPL thinning (−1.14 ± 0.38 vs −0.62 ± 0.35 μm/year; $p < 0.001$; Cohen $d = 1.42$). The between-group difference in MD slope is illustrated in Figure 1.

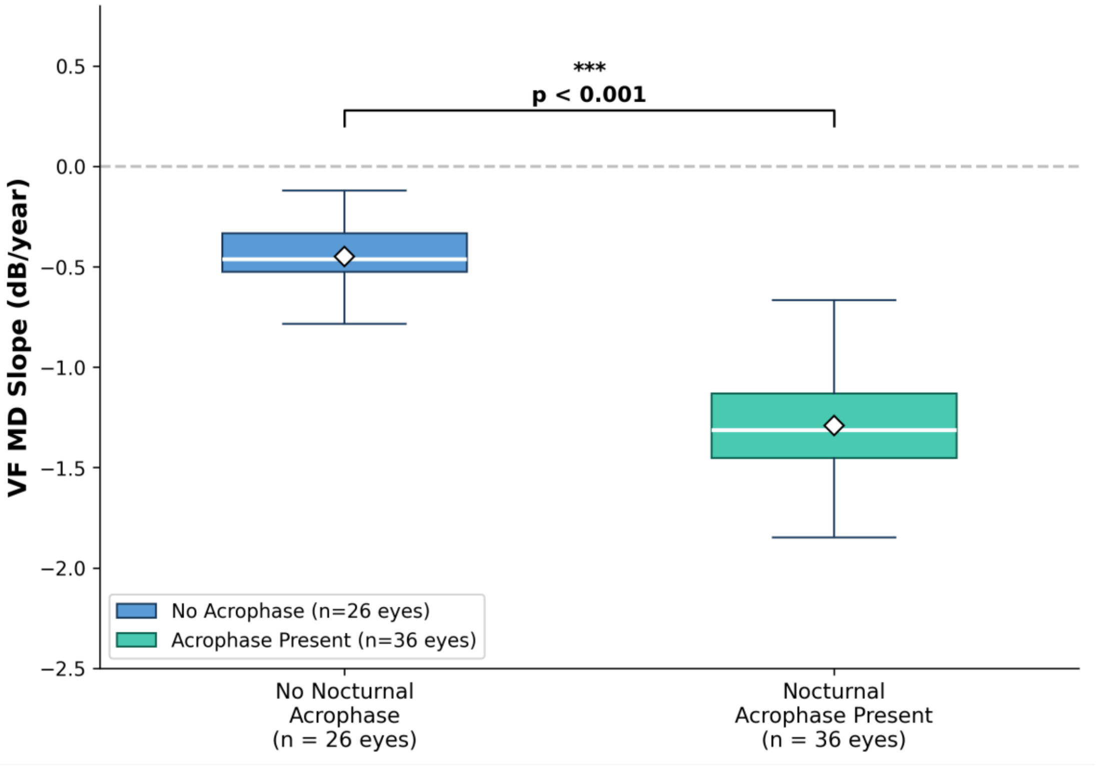

Figure 1. Box plot comparing visual field mean deviation (MD) slope (dB/year) between eyes with nocturnal IOP acrophase present (n = 36) and absent (n = 26). Diamond = group mean. ***$p < 0.001$ (independent-samples t-test; Cohen d = 3.20).

Table 3. Multivariable linear regression — independent predictors of VF MD slope (dB/year).

| **Predictor** | **β** | **95% CI** | **p** | **VIF** |
|---|---|---|---|---|
| Nocturnal acrophase | −0.71 | −0.98 to −0.44 | < 0.001 | 1.42 |
| Long peaks / 24 h | −0.18 | −0.25 to −0.11 | < 0.001 | 1.38 |
| Baseline RNFL | +0.034 | +0.013 to +0.055 | 0.002 | 1.56 |
| Nocturnal amplitude | −0.048 | −0.071 to −0.025 | < 0.001 | 2.14 |
| Baseline GAT IOP | −0.012 | −0.039 to +0.015 | 0.375 | 1.31 |
| Age | −0.005 | −0.014 to +0.004 | 0.298 | 1.18 |
| CCT | +0.001 | −0.003 to +0.005 | 0.632 | 1.22 |

*Notes: Model: $R^2 = 0.68$, adjusted $R^2 = 0.64$, $F(7,54) = 16.4$, $p < 0.001$. Durbin-Watson = 1.92. Shapiro-Wilk $W = 0.974$, $p = 0.218$. β = unstandardised regression coefficient; CCT = central corneal thickness; CI = confidence interval; GAT = Goldmann applanation tonometry; IOP = intraocular pressure; RNFL = retinal nerve fibre layer; VIF = variance inflation factor.*

Table 3 presents the multivariable linear regression model, which explained 68% of the variance in MD slope (adjusted $R^2 = 0.64$, $F(7,54) = 16.4$, $p < 0.001$). Model assumptions were satisfied: Durbin-Watson = 1.92, residuals approximately normal (Shapiro-Wilk $W = 0.974$, $p = 0.218$), and all VIF < 2.5. Four variables were independently associated with faster VF decline: nocturnal acrophase (β = −0.71, 95% CI −0.98 to −0.44, $p < 0.001$), number of long peaks (β = −0.18, 95% CI −0.25 to −0.11, $p < 0.001$), nocturnal amplitude (β = −0.048, 95% CI −0.071 to −0.025, $p < 0.001$), and baseline RNFL thickness (β = +0.034, 95% CI +0.013 to +0.055, $p = 0.002$). The positive coefficient for RNFL indicates that a thicker baseline RNFL was associated with a slower (less negative) MD slope, consistent with structural reserve. Baseline GAT IOP, age, and CCT were not significant after adjustment. The coefficients and their confidence intervals are displayed in the forest plot in Figure 2.

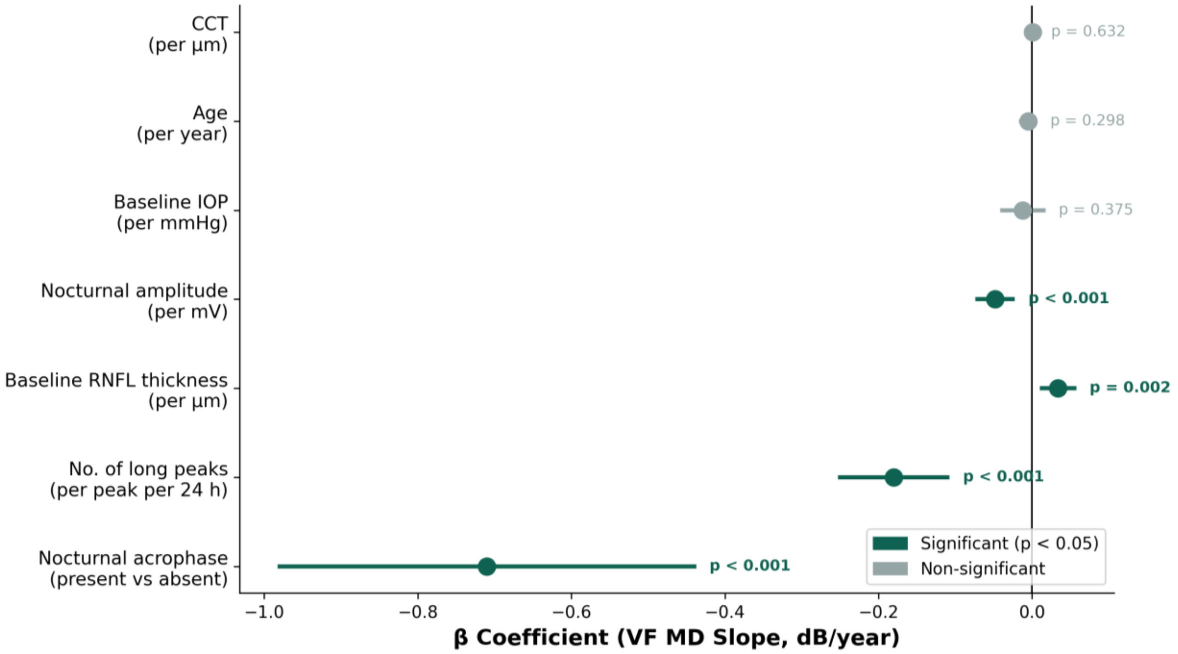

Figure 2. Forest plot of multivariable linear regression coefficients (β, 95% CI) for predictors of VF MD slope (dB/year). Teal = statistically significant ($p < 0.05$); grey = non-significant.

ROC analysis demonstrated that nocturnal IOP amplitude discriminated VF progressors from non-progressors with an AUC of 0.83 (bootstrapped 95% CI 0.74 to 0.91, $p < 0.001$), indicating good discriminative accuracy. The optimal cut-off was 10.5 mV-eq (Youden index $J = 0.51$), yielding sensitivity 0.78 (95% CI 0.62–0.89), specificity 0.73 (95% CI 0.54–0.87), positive predictive value 0.80, negative predictive value 0.71, and positive likelihood ratio 2.89. The ROC curve and the optimal operating point are shown in Figure 3.

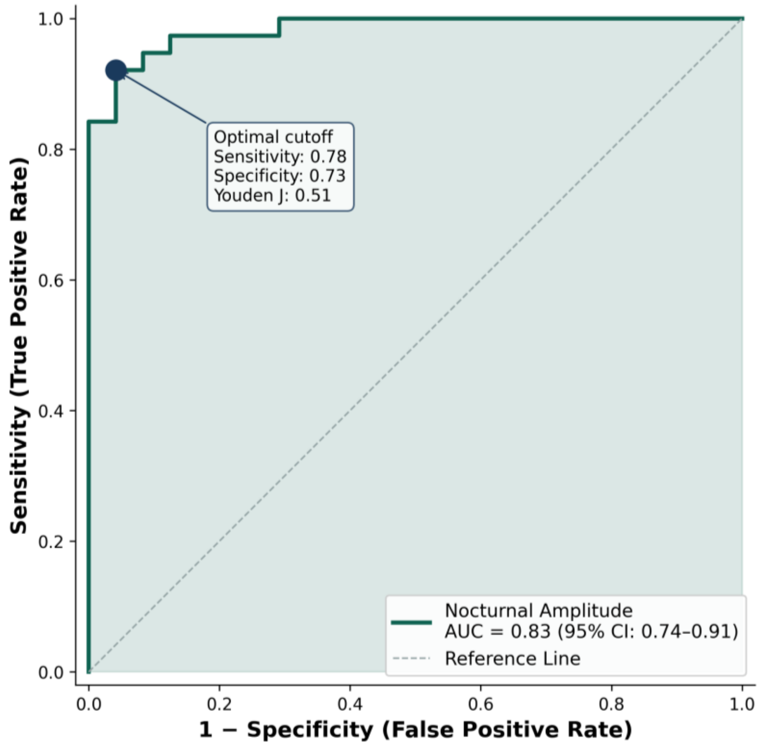

Figure 3. ROC curve for nocturnal IOP amplitude (mV-eq) predicting VF progression (MD slope < −1.0 dB/year). AUC = 0.83 (95% CI 0.74–0.91). Navy marker = optimal cut-off 10.5 mV-eq (Youden J = 0.51; sensitivity 0.78, specificity 0.73).

## 4. Discussion

This prospective 24-month cohort study demonstrated that SCL-derived nocturnal IOP parameters are strong and independent predictors of Humphrey 24-2 VF progression in Indonesian patients with NTG. Eyes exhibiting a nocturnal IOP acrophase with high diurnal-to-nocturnal amplitude showed a three-fold faster rate of VF MD decline than eyes without nocturnal acrophase, and this association persisted robustly after adjustment for baseline office IOP, structural OCT thickness, systemic hypertension, diabetes mellitus, and other covariates. These findings support the integration of 24-hour SCL monitoring into NTG management as a risk-stratification tool in Southeast Asian ophthalmic practice.

The magnitude of VF decline in the nocturnal acrophase group (−1.24 dB/year, Table 2) substantially exceeds the commonly cited −1.0 dB/year threshold for clinically meaningful progression and is considerably greater than the approximately −0.25 dB/year achieved after substantial IOP lowering in treated NTG.[5] It is also faster than the −0.22 to −0.36 dB/year reported across age groups of a treated NTG cohort.[16] The finding aligns with Gaboriau and colleagues, who reported that eyes with faster VF progression exhibited significantly greater 24-hour SCL magnitude and area under the monitoring curve.[13] Similarly, Higashide and colleagues found that abnormal 24-hour SCL profile parameters were independent risk factors for structural and functional progression in NTG.[7] The present study extends this evidence to a Southeast Asian NTG population with standardised 24-month follow-up.

The nocturnal acrophase was the single strongest predictor in the multivariable model (β = −0.71, Table 3), contributing the largest proportion of the 68% model $R^2$. This aligns with the hypothesis that IOP rises nocturnally owing to reduced episcleral venous drainage in the supine position, increased choroidal blood volume, and circadian aqueous humour dynamics.[2,6] In NTG, where the lamina cribrosa and peripapillary sclera may be biomechanically vulnerable, even modest nocturnal IOP surges may exert disproportionate mechanical strain on retinal ganglion cell axons.[2] The independent contribution of the number of long peaks (β = −0.18 per peak) suggests that cumulative exposure to transient high-amplitude IOP events adds mechanistic injury beyond the tonic circadian trend, potentially through repeated cycles of compression and reperfusion at the laminar plates.[14]

The protective association of thicker baseline RNFL (β = +0.034 per μm) is consistent with the concept of structural reserve, whereby baseline RNFL thickness predicts subsequent functional decline.[17,18] The structure-function relationship in glaucoma is non-linear: early structural loss precedes detectable VF change, but once RNFL thickness falls below a critical threshold, VF sensitivity declines steeply.[17] In this cohort, where 19.4% of eyes were HPA-advanced with thinner baseline RNFL, the accelerated VF decline in the acrophase group was amplified in eyes with less structural reserve, supporting the combination of SCL IOP profiling with OCT structural assessment for composite risk stratification.

Notably, baseline office GAT IOP was not an independent predictor of VF progression (β = −0.012, $p$ = 0.375, Table 3), consistent with the fundamental paradox of NTG in which disease progresses despite statistically normal daytime IOP.[10,14] Aggressive IOP reduction slows NTG progression, yet a substantial proportion of patients continue to deteriorate, highlighting the role of non-IOP factors and unmeasured IOP dynamics.[5] The present study provides direct evidence that the "missing" IOP-related risk in NTG may be captured by the nocturnal component of the 24-hour profile that office visits cannot detect.

The ROC analysis showed that nocturnal amplitude achieved an AUC of 0.83 for predicting VF progression (Figure 3), comparing favourably with the AUC of approximately 0.69 to 0.75 reported for office IOP parameters and supporting the additive value of continuous-sensor and machine-learning approaches to progression risk.[13,19] The optimal cut-off of 10.5 mV-eq, with balanced sensitivity (0.78) and specificity (0.73) and a positive likelihood ratio of 2.89, provides a clinically actionable threshold. From a practical perspective, an NTG patient with a nocturnal amplitude exceeding 10.5 mV-eq might be considered for more aggressive IOP-lowering targets, a nocturnal-active treatment regimen, or earlier laser or surgical intervention, alongside closer surveillance.[20]

Comparison with the Asian NTG literature supports the external relevance of these findings. NTG accounts for a high proportion of open-angle glaucoma in East and Southeast Asian populations, and emerging data suggest a similarly high proportion in Indonesian and Malay cohorts.[4] The mean baseline IOP of 14.8 mmHg and VF MD of −6.82 dB in the present cohort are consistent with published Asian NTG series, in which presenting IOPs range from 13 to 16 mmHg and MD values from −5 to −8 dB.[7,16] The predominance of female patients (56.5%, Table 1) is also consistent with the sex distribution of Asian NTG cohorts.[4] The present study contributes the first prospective SCL-based risk-stratification data from an Indonesian NTG cohort.

Several strengths merit emphasis: the prospective design with standardised SCL recording at two time points, serial OCT at three time points, and six or more reliable VF examinations over 24 months; the use of two independently masked technicians for SCL extraction (Cohen $\kappa = 0.91$; ICC = 0.94); and the a priori sample-size calculation, one-eye-per-patient design, and comprehensive regression diagnostics. Several limitations must also be acknowledged. This was a single-centre study at one private hospital in Palembang, which may limit external validity. The sample of 62 eyes yields an events-per-variable ratio of approximately 8.9, raising the possibility of overfitting, with 36% of MD-slope variance unexplained. The worse-eye selection protocol may introduce selection bias; a better-eye sensitivity analysis produced directionally consistent but attenuated results ($\beta = -0.58$, $p < 0.001$). The SCL output is expressed in mV-eq rather than mmHg, the 24-month follow-up may miss slow progressors, and nocturnal blood pressure, sleep-apnoea status, and ocular perfusion pressure were not measured and may represent residual confounders.

## 5. Conclusion

In this prospective 24-month cohort of 62 Indonesian patients with NTG, SCL-derived nocturnal IOP parameters were strong and independent predictors of Humphrey 24-2 VF progression. Eyes with a nocturnal IOP acrophase and high diurnal-to-nocturnal amplitude showed a three-fold faster rate of VF MD decline (−1.24 vs −0.42 dB/year; Cohen $d = 3.20$) than eyes without acrophase, robust after adjustment for baseline office IOP, structural OCT thickness, and systemic confounders. The multivariable model explained 68% of the variance in MD slope, and nocturnal amplitude demonstrated good discriminative accuracy (AUC 0.83, 95% CI 0.74–0.91; optimal cut-off 10.5 mV-eq, sensitivity 0.78, specificity 0.73). Integration of 24-hour SCL monitoring may enhance NTG risk stratification beyond conventional office IOP measurement, enabling personalised treatment intensification for high-risk eyes. Future multicentre studies with larger samples, longer follow-up, and simultaneous nocturnal blood-pressure and ocular-perfusion-pressure monitoring are warranted.

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