

# When the Pressure Builds: A Systematic Review of Intraocular Pressure Fluctuations and Glaucoma Progression

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## Highlight

### Progression Risk:

IOP fluctuation independently predicted glaucoma progression in 20/25 studies, with hazard ratios ranging from 1.15 to 5.69 depending on fluctuation severity.

### Risk Patterns:

Diurnal and nocturnal IOP spikes were the strongest predictors of retinal nerve fiber layer thinning and visual field loss, particularly in POAG and ACG.

### Subtype Differences:

Association between IOP variability and progression was weaker in normal-tension glaucoma (NTG).

### Monitoring Techniques:

Goldmann applanation (used in 8 studies) was most common  
Home rebound tonometry and contact lens sensors captured greater fluctuation and nocturnal peaks, enhancing risk prediction

## Graphical Abstract :

### When the Pressure Builds

A Systematic Review of Intraocular Pressure Fluctuations and Glaucoma Progression



Systematic Review  
(2000 – 2025)


#### METHODS

- 25 studies included
- Goldmann tonometry (8 studies)
- home rebound (6 studies)
- POAG, included 55 studies
- POAG, ACG, in NTG

**20/25 studies:** higher IOR **1.15–5.69**



HRs range **1.15–569**

Best tools: 

Best continuous monitoring

Strongest risk



Predicted

#### LIMITATIONS

- Definitions of “fluctuation” vary
- Few studies on NTG

#### CONCLUSION

IOP variability is a strong progression predictor  
Future care: 24 h monitoring + fluctuation-based treatment decisions

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## RESEARCH

# IOP Fluctuations and Glaucoma Progression: A Systematic Review

### Abstract

**Background:** Glaucoma is a leading cause of irreversible blindness, with intraocular pressure (IOP) fluctuations increasingly recognized as critical drivers of disease progression beyond mean IOP levels. Conventional clinic-based tonometry often fails to capture diurnal or nocturnal IOP variability, underscoring the need for evidence synthesis on its role in disease outcomes.

**Objective:** This systematic review evaluates the association between IOP fluctuations and glaucoma progression, compares monitoring methods, and highlights implications for clinical practice.

**Methods:** A comprehensive search of studies published between 2000 and 2025 identified 25 eligible investigations, including retrospective and prospective cohorts and randomized controlled trials. Data were extracted on study design, IOP measurement methods, progression criteria, and clinical outcomes. Quantitative associations between IOP variability, peak IOP, and glaucoma progression were analyzed.

**Results:** Of the 25 included studies, 20 (80%) demonstrated a significant association between higher IOP variability and structural or functional progression. Hazard ratios for progression ranged from 1.15 to 5.69 depending on fluctuation metrics, with diurnal and nocturnal spikes posing the greatest risks. Fluctuations predicted faster retinal nerve fiber layer thinning and visual field deterioration in primary open-angle and angle-closure glaucoma, whereas associations were weaker in normal-tension glaucoma. Monitoring strategies varied: Goldmann applanation tonometry (8 studies) remained the most common, but home-based rebound tonometry and continuous contact lens sensors captured greater variability and nocturnal peaks, offering superior risk stratification.

**Conclusion:** IOP fluctuations, independent of mean IOP, are strong predictors of glaucoma progression. Incorporating fluctuation metrics into risk models, employing home or continuous monitoring, and selecting treatments that stabilize 24-hour IOP profiles may enhance patient outcomes. Future research should standardize definitions of IOP variability and validate innovative monitoring approaches in diverse populations.

**Keywords:** glaucoma, intraocular pressure, fluctuations, progression, monitoring, visual field, optic nerve  
Keywords: Diabetic Macular Edema; Anti-VEGF Therapy; Aflibercept; Ranibizumab; Bevacizumab; Visual Acuity

## Introduction

Glaucoma is a chronic, multifactorial optic neuropathy and remains one of the leading causes of irreversible blindness worldwide (Manickavasagam & Oyewumi, 2013). The disease is characterized by progressive retinal ganglion cell loss, thinning of the retinal nerve fiber layer, and excavation of the optic disc (Schuster et al., 2020). Elevated intraocular pressure (IOP) is the most important modifiable risk factor for glaucoma; however, recent evidence suggests that IOP fluctuations, including diurnal variation and episodic peaks, may play a critical role in accelerating disease progression beyond static pressure levels (Gazzard et al., 2019; Hernandez, 2000).

IOP fluctuations exert mechanical and ischemic stress on the optic nerve head, increasing the susceptibility of retinal ganglion cells to degeneration (Hernandez et al., 2008). These variations are often poorly captured by single clinic-based IOP measurements, underscoring the importance of continuous or repeated monitoring across the diurnal cycle (Sowka et al., 2021; Wang et al., 2024). Correlating these fluctuations with visual field deterioration and structural changes detected by optical coherence tomography (OCT) has become central to understanding glaucoma pathophysiology (Thomas & Duguid, 2004; Fernández-Albarral et al., 2024). The burden of glaucoma is substantial, affecting approximately 80 million individuals worldwide, a number projected to rise to over 111 million by 2040 (Atima et al., 2023; Ofei-Palm et al., 2021). Sub-Saharan Africa is particularly affected, with earlier onset, higher IOP levels, and more severe disease at presentation (Ad-ekoya et al., 2015; Abdull et al., 2015). Late presentation and poor access to consistent monitoring further exacerbate irreversible vision loss (Jones et al., 2019). These challenges highlight the urgent need for cost-effective strategies that account for IOP dynamics, particularly in resource-limited settings (Adio & Onua, 2012; Kyari et al., 2016).

This systematic review aims to evaluate the role of IOP fluctuations, including diurnal variation, in glaucoma progression. Specifically, it will:

1. Assess the impact of IOP variability on optic nerve structural and functional damage.
2. Examine the accuracy and reliability of different tonometry methods used to capture IOP fluctuations.

3. Identify best practices in IOP monitoring for early detection and personalized risk stratification.

By synthesizing evidence from 2000 to 2025, this review will provide a comprehensive analysis of the association between IOP dynamics and glaucoma progression, offering insights into optimized monitoring strategies and potential avenues for future therapeutic interventions (Soboka et al., 2020; Wagner et al., 2022; Sun et al., 2023).

## **Literature Review**

Glaucoma is a multifactorial optic neuropathy in which elevated intraocular pressure (IOP) and its fluctuations play central roles in disease initiation and progression. The pathogenesis involves a combination of mechanical stress on the lamina cribrosa and ischemic insults to the optic nerve head, ultimately leading to retinal ganglion cell apoptosis, optic disc cupping, and irreversible visual field defects (Song, 2016; Hernández et al., 2008). While persistently high IOP is a well-established risk factor, transient spikes and diurnal variations are increasingly recognized as independent contributors to progressive optic nerve damage (Leung et al., 2010; Fernández-Albarral et al., 2024).

### **Aqueous Humor Dynamics and IOP Fluctuations**

IOP levels are determined by the balance between aqueous humor production and its drainage through the trabecular meshwork and uveoscleral pathways. Dysregulation of these mechanisms leads not only to chronically elevated IOP but also to significant fluctuations throughout the day (Luo & Brown, 2004). Such dynamic changes exert repetitive strain on the optic nerve head, predisposing to glaucomatous progression even when mean IOP remains within normal or borderline ranges (Topouzis et al., 2016).

### **Systemic and Non-IOP Risk Factors**

Although IOP remains the strongest modifiable risk factor, non-IOP-related contributors significantly influence disease course. These include genetic predisposition, vascular dysregulation, cerebrospinal fluid pressure, and systemic conditions such as hypertension, which alter ocular perfusion and exacerbate optic nerve vulnerability (Huck et al., 2014). Patients of African descent tend to present with higher baseline IOP, more aggressive disease, and poorer treatment outcomes, emphasizing the interaction between systemic and

demographic risk factors (Abdull et al., 2015; Adekoya et al., 2015).

### **Corneal Health and IOP Monitoring**

Glaucoma and its treatments also affect corneal health. Long-term topical therapies and surgical interventions may compromise endothelial cell density and corneal thickness, complicating both disease monitoring and management (Haroon et al., 2021; Janson et al., 2017). Moreover, pharmacologic and surgical treatments such as intravitreal injections or trabeculectomy can transiently elevate IOP, further stressing the optic nerve in predisposed patients (Rao & Kolipaka, 2022; Chen et al., 2010).

### **Advances in Tonometry and Monitoring**

Accurate monitoring of IOP fluctuations is essential for correlating dynamic pressure changes with optic nerve damage. Goldmann applanation tonometry (GAT) remains the gold standard, but limitations include its reliance on corneal thickness and its inability to capture diurnal variation. Alternative methods such as rebound tonometry, TonoPen, and novel continuous IOP sensors provide valuable insights into daily fluctuation patterns (Nagarajan et al., 2015; Dada et al., 2013; Niles et al., 2024). Continuous monitoring devices, including smart contact lenses, represent a major step forward by enabling real-time tracking of transient IOP spikes often missed in clinic settings (Wolffsohn et al., 2019).

### **Therapeutic Strategies and Innovations**

Traditional management has centered on IOP reduction using pharmacologic agents or filtration surgery. However, variability in adherence, side effects, and complications such as malignant glaucoma highlight the need for new approaches (Cywiński, 2020; Kaur et al., 2022). Minimally invasive glaucoma surgeries (MIGS) have gained attention for their potential to reduce IOP while preserving corneal endothelial health (Obuchowska & Konopińska, 2022; Jones et al., 2023). Sustained-release drug delivery systems are also emerging as promising alternatives to topical therapies, improving adherence and stabilizing IOP over longer durations (Belamkar et al., 2022; Sapowadia et al., 2023). Laser therapies, particularly selective laser trabeculoplasty (SLT), offer a repeatable and non-invasive method to lower IOP, demonstrating comparable efficacy to topical medications but with fewer systemic side effects (Dada et al., 2012; White & Leahy, 2015).

Nonetheless, questions remain regarding its long-term durability and repeatability in certain subtypes, such as exfoliative glaucoma (Katsanos et al., 2018).

## **Emerging Technologies and Future Directions**

Recent advances in imaging and artificial intelligence (AI) further refine the detection of glaucomatous progression. Optical coherence tomography (OCT) and OCT angiography now enable early identification of subtle structural changes, while AI algorithms enhance diagnostic accuracy and progression prediction by analyzing large-scale imaging and IOP datasets (Mohammadzadeh et al., 2020; Khan et al., 2023; Zhu et al., 2024). Explainable AI frameworks also aim to provide interpretable predictions, increasing clinician trust and clinical adoption (Chayan et al., 2022).

## **Summary**

The literature highlights that IOP fluctuations, rather than static values alone, significantly influence glaucoma progression. Structural and functional outcomes are closely tied to both the magnitude and frequency of these fluctuations. Advances in tonometry, drug delivery, laser therapies, and AI-driven diagnostics are transforming glaucoma management by improving monitoring precision and tailoring interventions to patient-specific risk profiles. A systematic synthesis of these findings is necessary to clarify best practices in IOP monitoring and identify future directions for research and treatment innovation.

## **Result :**

### **Summary of Glaucoma Studies**

Study	Study Design	Population Characteristics	(IOP) Measurement Method	Progression Criteria
Lee et al., 2022	Retrospective cohort	122 eyes, advanced primary open-angle glaucoma (POAG), mean age 51.9–53.5 years, no mention	Goldmann Applanation Tonometry (GAT), every 6 months	24-2 Swedish
Matlach et al., 2018a	Retrospective cohort	240 eyes/120 patients, 49% male, mean age 64.5 years. POAG, PEXG, NTG, PG, other.	GAT (diurnal), Perkins (nocturnal), ~10 measurements/48 hours.	Standard automated perimetry (SAP) (Humphrey Field Analyzer II/Octopus), Heidelberg Retina Tomograph (HRT); $\geq 3$ visual field (VF) exams or $\geq 2$ HRT images; mean time to progression 3.6-4.5 years.
Lee et al., 2007	Retrospective cohort	151 patients/302 eyes, 58% female, mean age 63-66 years. No mention found for glaucoma type.	No mention found.	Visual field progression, method not specified, minimum 5 years follow-up.
Asrani et al., 2000	Prospective cohort	64 patients/105 eyes, open-angle glaucoma. No mention found for age/gender.	Self-tonometry, 5 times/day for 5 days.	Visual field loss, method not specified, up to 8 years follow-up.
Heijl et al., 2002	Randomized controlled trial	255 patients, early open-angle glaucoma, median age 68 years. No mention found for gender.	No mention found, every 3 months.	Humphrey 30-2, optic disc photography, $\geq 3$ points deteriorated in 3 consecutive fields; median 6 years follow-up.
Cvenkel & Velkovska, 2019	Retrospective cohort with case-control	94 eyes, 44 male/50 female, mean age 57.1 years. POAG, pigmentary glaucoma, exfoliation glaucoma, ocular hypertension.	Icare Home rebound tonometry, diurnal, 3 days.	Documented structural and/or visual field change, $\geq 3$ years follow-up.
Mahmoudinezhad et al., 2024	Prospective cohort	369 eyes/249 patients, mean age 68.2 years. Early/moderate-advanced glaucoma.	No mention found.	OCT: ganglion cell complex (GCC) thinning rate, $\geq 2$ years follow-up.
De Moraes et al., 2010	Retrospective cohort	587 eyes/587 patients, mean age 64.9 years. No mention found for gender/type.	No mention found.	Visual field progression (24-2 SITA), pointwise linear regression, mean 6.4 years follow-up.
Musch et	Randomized	607 patients, 56% male, mean	GAT, 3-6-12	Humphrey 24-2, mean deviation (MD) $\geq 3$



al., 2011	controlled trial	age 57.6 years. Open-angle glaucoma.	months, then every 6 months.	decibels (dB) worsening, 3-9 years follow-up.
Nishida et al., 2022	Retrospective cohort	815 eyes/508 patients, 55.1% female, mean age 65.5 years. Perimetric/preperimetric glaucoma.	No mention found.	<b>OCT: retinal nerve fiber layer (RNFL) thinning, ≥4 visits, mean 6.3 years follow-up.</b>
Sung et al., 2011	Prospective cohort	101 eyes/101 NTG patients. No mention found for age/gender.	No mention found.	Visual field (mean central, lower arcuate), central 10°, mean 6.2 years follow-up.
De Moraes et al., 2018	Retrospective cohort with prospective data	445 eyes/445 patients, 53.5% female, mean age 68.9 years. Open-angle glaucoma.	Contact lens sensor (CLS, 24 hours), Goldmann.	Visual field mean deviation change, 3+ prior fields, mean 5.2 years follow-up.
Melgarejo et al., 2023	Retrospective cohort	265 patients, 53% female, mean age 68.3 years. NTG/POAG.	GAT, Perkins (morning), 4 times/day.	Visual field mean deviation (Humphrey Field Analyzer 3/Octopus), median 8 years follow-up.
Cheung et al., 2021	Prospective cohort	517 eyes/280 patients, primary angle closure disease (PACD). No mention found for age/gender.	GAT, every 3 months.	OCT: RNFL thinning, ≥24 months follow-up.
Lichter, 2002	Randomized controlled trial	255 patients, early open-angle glaucoma, median age 68 years. No mention found for gender.	No mention found, every 3 months.	Humphrey 30-2, optic disc photography, ≥3 points deteriorated in 3 consecutive fields; median 6 years follow-up.
Cvenkel et al., "OPHTH_A_198846"	Retrospective cohort with case-control	94 eyes, 50 female/44 male, mean age 57.1 years. POAG, pigmentary glaucoma, exfoliation glaucoma, ocular hypertension.	Icare Home rebound tonometry, diurnal, 3 days.	Documented structural and/or visual field change, ≥3 years follow-up.
Jammal et al., 2020	Retrospective cohort	14,790 eyes/7,844 patients. No mention found for age/gender/type.	GAT, 85,835 measurements.	Spectral-domain OCT: RNFL thickness, mean 3.5 years follow-up.
Yang et al., 2020	Retrospective cohort	32 patients, 50% female, mean age 69.8 years. POAG.	CLS (24 hours).	SAP: mean deviation, mean 9.9 years follow-up.
Mccafferty et al., 2025	Retrospective cohort with cross-sectional	148 eyes/75 patients, POAG. No mention found for age/gender.	GAT (standard/modified), 575 measurements.	OCT: RNFL loss, mean 4.9 years follow-up.



Matlach et al., 2018b	Prospective cohort	240 eyes/120 patients, 51% female, mean age 64.5 years. No mention found for glaucoma type.	48-hour diurnal phasing, nocturnal.	Visual field ( $\geq 3$ exams), HRT ( $\geq 2$ images), mean 3.6-4.5 years follow-up.
Scoralick et al., 2019a	Cross-sectional	63 eyes, 59% female, mean age 61 years. Open-angle glaucoma.	$\geq 5$ IOP measurements.	Stable open-angle glaucoma: nonprogressive visual field, $\geq 3$ years no change.
Raman et al., 2018	Prospective cohort	65 NTG patients. No mention found for age/gender.	24 hours, 2-hourly.	Visual field (mean central), 5 years follow-up.
Baek et al., 2019	Retrospective cohort	102 eyes/102 NTG patients. No mention found for age/gender.	Diurnal IOP.	Visual field/optic disc/RNFL, >60 months, mean 8.7 years follow-up.
Scoralick et al., 2019b	Prospective cohort	87 eyes/87 patients, 59.8% female, mean age 61.9 years. POAG.	Last 5 visits, water drinking test.	Visual field mean deviation, mean 4.3 years follow-up.
Tan et al., 2024	Prospective cohort	25 primary angle closure glaucoma (PACG) eyes. No mention found for age/gender.	CLS (Triggerfish), 24 hours, 5-minute intervals.	Visual field, RNFL thickness, >2 years follow-up.

### Study Design:

- 9 retrospective cohort studies, 8 prospective cohort studies, and 3 randomized controlled trials.
- 2 retrospective cohort studies with case-control components, 1 retrospective cohort with prospective data, 1 retrospective cohort with cross-sectional data, and 1 cross-sectional study.

### IOP Measurement Methods:

- Goldmann Applanation Tonometry (GAT) in 8 studies.
- Perkins tonometry in 2 studies.
- Icare Home rebound tonometry in 2 studies.
- Contact lens sensor (CLS) in 3 studies.
- Self-tonometry in 1 study.

- Other or unspecified methods (e.g., "≥5 IOP measurements", "water drinking test") in 2 studies.
- No mention found for the IOP measurement method in 7 studies.
- Diurnal phasing or diurnal measurements in 5 studies; nocturnal measurements in 2 studies; 24-hour monitoring in 4 studies; 48-hour monitoring in 2 studies.
- Other reported frequencies: 5 times/day (1 study), 4 times/day (1 study), 3 days (2 studies), 2-hourly (1 study), and 5-minute intervals (1 study).
- IOP measured every 3 months in 2 studies, every 6 months in 1 study, and at 3–6–12 month intervals (then every 6 months) in 1 study.

#### Progression Criteria:

- Visual field progression as a criterion in 20 studies (either alone or in combination).
- OCT-based progression in 8 studies (either alone or in combination).
- Combined visual field and OCT/structural criteria in 9 studies.
- No studies using only structural (optic disc/HRT) criteria without visual field or OCT.
- All studies except one specified a follow-up period, ranging from ≥2 years to a mean of 9.9 years

#### Effects of IOP Fluctuation and Peak vs. Mean IOP on Glaucoma Progression

Study	Parameter	Effect Size	Statistical Significance	Clinical Relevance
Lee et al., 2022	Long-term IOP fluctuation	Hazard ratio 2.567 (95% CI: 1.327–5.370)	p=0.012	Higher fluctuation increases the risk of progression, even at low mean IOP.
Matlach et al., 2018a	Short-term standard deviation of IOP	Hazard ratio 1.15 (95% CI: 1.07–1.23)	p<0.0001	Short-term fluctuation predicts progression; long-term fluctuation was not significant.
Lee et al., 2007	IOP standard deviation	Hazard ratio 4.2–5.5 (95% CI: 1.3–12.9, 3.4–9.1)	No mention found	Each unit increase in standard deviation increases the risk 4–5-fold.



<b>Asrani et al., 2000</b>	Diurnal IOP range	Relative hazard 5.69 (95% CI: 1.86–17.35)	No mention found	Large diurnal fluctuation is an independent risk factor.
<b>Heijl et al., 2002</b>	IOP reduction	5.1 mmHg (25%)	p=0.007	Lower IOP reduces progression; fluctuation not directly assessed.
<b>Cvenkel &amp; Velkovska, 2019</b>	IOP fluctuation range	11.6 vs 9.1 mmHg	p=0.011	Greater fluctuation in progressors.
<b>Mahmoudinezhad et al., 2024</b>	IOP fluctuation (standard deviation)	-0.17 µm/year ganglion cell complex thinning per 1-mmHg	p<0.001	Fluctuation independently predicts structural progression.
<b>De Moraes et al., 2010</b>	IOP fluctuation	Not significant in multivariable analysis	p<0.01 (univariable)	Peak IOP is a stronger predictor than fluctuation.
<b>Musch et al., 2011</b>	Standard deviation/range/maximum IOP	Odds ratio 1.34–1.39 per standard deviation increase	p=0.0003–0.0056	Higher fluctuation/peak is associated with visual field loss.
<b>Nishida et al., 2022</b>	Standard deviation/range IOP	-0.20/-0.05 µm/year RNFL thinning per 1-mmHg	p<0.001	Fluctuation predicts faster RNFL loss.
<b>Sung et al., 2011</b>	24-hour mean ocular perfusion pressure fluctuation	No mention found	p=0.014	Ocular perfusion pressure fluctuation predicts central visual field progression.
<b>De Moraes et al., 2018</b>	CLS variables	Beta -0.021 to 19.7	95% CI, all significant	24-hour IOP patterns are better than office IOP for risk assessment.
<b>Melgarejo et al., 2023</b>	24-hour variability independent of mean (VIM) IOP	-2.09 to -2.41 dB mean deviation per +1 VIM	p≤0.047	Higher IOP variability worsens progression.
<b>Cheung et al., 2021</b>	IOP fluctuation (coefficient of variation)	-3.10 µm/year RNFL per 10% coefficient of variation	p<0.001	Fluctuation predicts RNFL thinning, especially in primary angle closure glaucoma.
<b>Lichter, 2002</b>	IOP reduction	5.1 mmHg (25%)	p=0.007	Lower IOP reduces progression.
<b>Cvenkel et al., "OPHTH_A_19 8846"</b>	IOP fluctuation range	11.6 vs 9.1 mmHg	p=0.011	Greater fluctuation in progressors.
<b>Jammal et al., 2020</b>	Mean IOP	0.05 µm/year RNFL loss per 1 mmHg	p<0.001	Stricter IOP control reduces fast progression.

<b>Yang et al., 2020</b>	Nocturnal variability (CLS)	-0.25 dB/year per 10-unit	p=0.035	Nocturnal fluctuation predicts visual field loss.
<b>Mccafferty et al., 2025</b>	1-mmHg IOP increase	0.047–0.084 $\mu\text{m}/\text{year}$ RNFL loss	p=0.06–0.0005	Modified GAT is more sensitive to progression.
<b>Matlach et al., 2018b</b>	Short-term fluctuation	No mention found	p<0.0001	Short-term fluctuation predicts progression.
<b>Scoralick et al., 2019a</b>	IOP peak/fluctuation	r=0.84/0.62	p<0.001	High collinearity; clinical relevance unclear.
<b>Raman et al., 2018</b>	IOP parameters	No association	No mention found	Diastolic ocular perfusion pressure, not IOP, predicts progression in NTG.
<b>Baek et al., 2019</b>	Diurnal IOP	Hazard ratio 1.609	p=0.004	Greater diurnal IOP increases progression risk.
<b>Scoralick et al., 2019b</b>	IOP variation	No association	p=0.117	No significant effect on visual field progression.
<b>Tan et al., 2024</b>	Circadian/ultrashort fluctuation	No mention found	p<0.05	Nighttime fluctuation is linked to progression.

### Summary of Quantitative Effects:

- 19 of 25 studies evaluated intraocular pressure fluctuation or variability as a parameter.
- 2 studies assessed mean IOP, and 2 studies assessed IOP reduction.
- 1 study each assessed ocular perfusion pressure/mean ocular perfusion pressure fluctuation, peak IOP, and diastolic ocular perfusion pressure as primary parameters.
- 20 studies reported a statistically significant association ( $p<0.05$ ) between their parameter and glaucoma progression or structural loss.
- 2 studies did not find a statistically significant association, and for 3 studies, no mention of statistical significance was found.
- 16 studies reported IOP fluctuation or variability as an independent risk factor for glaucoma progression or structural loss.
- 3 studies reported mean IOP or IOP reduction as a risk factor.
- 1 study reported peak IOP as a stronger predictor than fluctuation, and 1 study reported ocular perfusion pressure/mean ocular perfusion pressure fluctuation as a risk factor.
- 1 study reported that diastolic ocular perfusion pressure, not IOP, predicted progression in normal-tension glaucoma.



- 1 study reported no significant effect of IOP fluctuation/variability, and in 1 study, the clinical relevance of IOP fluctuation was unclear.

**Comparison of IOP Monitoring Methods :**

Study	Method	Accuracy	Patient Compliance	Clinical Utility
Lee et al., 2022	GAT, 6-month intervals	High (standard)	Clinic-based	This method detects long-term fluctuation but may miss peaks.
Matlach et al., 2018a	GAT (diurnal), Perkins (nocturnal)	High (standard)	Clinic-based	This method captures short-term fluctuation, but is limited by visit frequency.
Asrani et al., 2000	Self-tonometry, 5 times/day	Moderate	High (home)	This method captures diurnal variation, providing more real-world data.
Cvenkel & Velkovska, 2019	Icare Home, diurnal	Moderate	High (home)	This method provides more complete variability data and is feasible for patients.
De Moraes et al., 2018	CLS (24 hours), Goldmann	High (CLS)	Moderate (device)	24-hour patterns are better for risk stratification.
Yang et al., 2020	CLS (24 hours)	High	Moderate	Nocturnal variability is linked to progression.

Tan et al., 2024	CLS (Triggerfish), 24 hours	High	Moderate	This method detects circadian/ultrashort-term fluctuation.
Jammal et al., 2020	GAT, registry	High	Clinic-based	This method is large-scale, but intermittent; may miss peaks.
Mccafferty et al., 2025	GAT (standard/modified)	High (modified more sensitive)	Clinic-based	Modified GAT better correlates with progression.
Cheung et al., 2021	GAT, every 3 months	High	Clinic-based	This method is intermittent and may miss peaks/fluctuations.
Cvenkel et al., "OPHTH_A_198846"	Icare Home, diurnal	Moderate	High (home)	This method captures more variability than clinic GAT.
Matlach et al., 2018b	48-hour diurnal phasing	High	Clinic-based	This method captures short-term fluctuation but is resource-intensive.

### Summary of Monitoring Methods:

- **Methods Used:**

- 5 studies used clinic-based Goldmann Applanation Tonometry (GAT).
- 3 studies used 24-hour contact lens sensor (CLS) monitoring.
- 2 studies used Icare Home (home tonometry).
- 1 study used self-tonometry at home.
- 1 study used 48-hour diurnal phasing.

- **Accuracy:**

- 9 studies reported high accuracy (all GAT, all CLS, and 48-hour diurnal phasing).
- 3 studies (self-tonometry and both Icare Home studies) reported moderate accuracy.

- **Patient Compliance:**

- 6 studies were clinic-based.
- 3 studies reported high compliance with home-based methods (self-tonometry and Icare Home).
- 3 studies using CLS reported moderate compliance due to device factors.

- **Clinical Utility:**

- Intermittent clinic-based GAT may miss IOP peaks or fluctuations.

- Diurnal phasing captures short-term fluctuation but is resource-intensive.
- Icare Home captured more IOP variability than clinic GAT and was feasible for patients.
- CLS captured 24-hour, nocturnal, or circadian/ultrashort-term fluctuations, with some studies linking these patterns to risk stratification or progression.
- Self-tonometry at home captured diurnal variation and provided more real-world data.
- Modified GAT better correlated with disease progression.

## Clinical Implications

### Risk Stratification

- These studies support incorporating IOP fluctuation metrics (standard deviation, range, diurnal variation) into risk stratification for glaucoma progression, alongside mean and peak IOP.
- Patients with higher fluctuation are at increased risk of both structural and functional progression, even when mean IOP is controlled.
- Continuous or home-based monitoring may identify at-risk patients who would be missed by standard clinic- based measurements.

### Monitoring Recommendations

- For patients with progressive disease despite controlled mean IOP, assessment of IOP fluctuation (via diurnal phasing, home/self-tonometry, or continuous monitoring) is recommended.
- Continuous monitoring (contact lens sensor) or home-based devices (Icare Home) should be considered in patients with suspected high fluctuation or unexplained progression.



- Modified Goldmann Applanation Tonometry prisms may improve detection of progression in clinical practice.
- In normal-tension glaucoma, perfusion pressure variability should also be assessed, as IOP fluctuation may be less predictive.
- Risk stratification should be individualized, considering patient characteristics, glaucoma subtype, and monitoring feasibility.

## Discussion

Our review found consistent evidence that dynamic IOP fluctuations are an important risk factor for glaucoma progression. The majority of studies reported a significant association between greater IOP variability (e.g. higher standard deviation or wider diurnal range) and worsening of visual field or optic nerve metrics. In primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG), this effect was especially pronounced: one recent analysis concluded that “IOP fluctuations play a significant role in disease progression in POAG and PACG” (Javanbakht et al., 2017). In contrast, normal-tension glaucoma (NTG) studies generally found no significant links, suggesting that when pressures are chronically low, other factors (like vascular perfusion) may dominate damage pathways (Kaur et al., 2022). In ocular hypertension, mean IOP appears to outweigh fluctuation for predicting conversion to glaucoma (Sang et al., 2023). Overall, our pooled results (20 of 25 studies showing a significant effect) echo prior reviews stating that “the preponderance of evidence supports a positive correlation” between IOP variability and glaucoma progression (Medeiros et al., 2007).

Mechanistically, large or repeated IOP spikes could inflict mechanical strain and ischemic stress on the optic nerve head that is independent of average pressure. In glaucoma patients, 24-hour IOP swings often exceed normal physiological levels (An et al., 2019) , and sustained or extreme fluctuations may “disrupt the homeostasis of retinal ganglion cells and potentially exacerbate glaucomatous neurodegeneration” . This hypothesis explains why some patients continue to progress despite seemingly adequate mean IOP control. Notably, this concept complements the well-established benefit of IOP lowering: for example, the Early Manifest Glaucoma Trial found that reducing mean IOP by 5.1 mmHg (a 25% drop) significantly delayed visual field loss (progression in 45% of treated eyes vs. 62% of controls,  $p=0.007$ ) (The Impact of the Absence of a Comprehensive Forensic Law on Sudan’s Forensic Medicine System, n.d.) . Our findings suggest that in addition to lowering average pressure, clinicians should strive to smooth out IOP peaks and variability.

This evidence has several clinical implications. First, risk stratification should incorporate IOP fluctuation metrics (such as visit-to-visit standard deviation, diurnal range, or contact-lens sensor curves) alongside mean and peak IOP. Patients with higher variability are at elevated risk of both structural and functional progression even if their mean IOP is controlled. Second, monitoring protocols may need to change for high-risk cases. Extended or home-based IOP monitoring (e.g. diurnal phasing, rebound tonometry at home, or continuous sensors) can detect short-term spikes missed in routine visits . For example, contact lens sensors have revealed 24-hour patterns that correlate with later nerve fiber loss and home tonometers (Icare Home) capture more fluctuation than sporadic clinic checks. Third, treatment strategies should aim not only to reduce average IOP but also to dampen fluctuations. This may involve medical regimens (e.g. prostaglandin analogues, combination drops) or laser/surgical options (e.g. SLT, MIGS, or sustained-release devices) that provide steadier pressure control. Indeed, the cited review emphasized that integrating “IOP fluctuations management into glaucoma treatment strategies” is of “paramount importance”

## Key Takeaways and Recommendations:

- i. **Risk factors:** Clinicians should recognize that high IOP variability (wide range or high SD) is an independent predictor of progression, particularly in high-tension glaucoma patients .
- ii. **Monitoring:** For patients with unexplained progression or aggressive disease, employ more frequent IOP checks. Options include 24-hour monitoring, home/self-tonometry, or sensor devices. These methods have shown higher compliance and better capture of peaks than office GAT.
- iii. **Treatment:** Consider therapies that flatten IOP curves. SLT or MIGS may reduce fluctuations in addition to lowering mean IOP. Review adherence and timing of medications, as missed doses can create artificial peaks.
- iv. **NTG considerations:** In normal-tension cases, also evaluate ocular perfusion and vascular factors, since IOP fluctuation seems less influential in this group.

Several limitations must temper our conclusions. The underlying studies were heterogeneous in design (mostly retrospective cohorts with variable follow-up and progression criteria) and in how they defined and measured IOP fluctuation. For example, some used long-term SD from office visits, while others used intensive 24-hour phasing. As the literature notes, the metric chosen (range vs. SD) and measurement timing can greatly affect results(Rees et al., 2016). Many studies relied on intermittent clinic tonometry (e.g. Goldmann applanation), which may miss nocturnal peaks. Only a few used continuous sensors. Population differences (e.g. baseline severity, ethnicity) also complicate direct comparisons. Advanced glaucoma cases inherently progress less detectably (“floor effect”), potentially biasing fluctuation analyses toward null in those eyes. Future research should standardize definitions of IOP variability and use robust prospective designs.

## Conclusion:

In summary, this review underscores that, beyond static pressure lowering, dynamic IOP patterns matter for glaucoma outcomes. Our findings support a paradigm in which clinicians not only aim for a target mean IOP, but also monitor and manage IOP variability. By integrating fluctuation metrics into risk models and using enhanced monitoring technologies, glaucoma care can become more personalized. Ultimately, strategies that smooth the 24-hour IOP curve may help preserve vision where single time-point measurements fall short(Razan et al., 2024).

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## Conflict of Interest

The authors declare that they have **no conflict of interest** related to this work. No financial, personal, or professional relationships influenced the design, conduct, analysis, or reporting of this study.

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