

Review Article

Advances in Glaucoma Diagnosis: From Conventional Clinical Assessment to Multimodal Imaging and Artificial Intelligence

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ABSTRACT

Glaucoma is a group of progressive optic neuropathies characterized by retinal ganglion cell loss, optic nerve head damage and corresponding visual field impairment. Its early course is frequently asymptomatic, allowing structural injury to progress before patients recognize functional loss. The thesis underlying this review identifies glaucoma as a major cause of irreversible blindness and emphasizes the complementary roles of intraocular pressure (IOP) measurement, gonioscopy, fundus examination, visual-field testing and optical coherence tomography (OCT), while highlighting automated fundus-image analysis and artificial intelligence (AI) as emerging diagnostic tools. Current evidence supports a shift from single-test assessment toward integrated structural, functional and risk-based evaluation. Fundus photography enables scalable assessment of the optic disc, cup-to-disc ratio (CDR) and retinal nerve fiber layer (RNFL) changes; OCT provides reproducible quantitative measurements of RNFL, ganglion-cell complex and optic nerve head parameters; and visual-field testing captures the functional consequence of disease. AI and deep learning can assist with image classification, segmentation and progression analysis, with recent meta-analyses demonstrating high diagnostic performance for fundus photography and OCT, although performance is generally lower in external validation than in internal datasets. Vision-transformer and multimodal approaches are particularly promising because they can model long-range relationships and combine heterogeneous ophthalmic information. Nevertheless, AI cannot substitute for clinical examination, especially in atypical disease, myopia, media opacity and angle-closure mechanisms. This review discusses conventional and emerging diagnostic approaches, discusses their strengths and limitations, and proposes a practical multimodal diagnostic pathway for earlier and more reproducible glaucoma detection.

Keywords: Glaucoma; Intraocular Pressure; Optic Nerve Head; Cup-To-Disc Ratio; Retinal Nerve Fiber Layer; Optical Coherence Tomography; Visual Field; Fundus Photography; Artificial Intelligence.

Introduction

Glaucoma is not a single disease but a heterogeneous group of optic neuropathies that share characteristic

structural injury of the optic nerve and retinal ganglion cells with corresponding functional visual-field loss. It is a major cause of irreversible blindness. A global systematic review estimated glaucoma prevalence at

3.54% among people aged 40–80 years and projected the number of affected individuals to increase from 64.3 million in 2013 to 111.8 million by 2040, with substantial differences between regions and glaucoma subtypes [1]. More recent global eye-health reporting continues to identify glaucoma among the major causes of blindness and emphasizes the importance of timely detection and access to eye care [2].

The clinical importance of glaucoma arises from the mismatch between disease biology and symptom awareness. Primary open-angle glaucoma (POAG), the most common form, often progresses gradually without pain. Peripheral visual-field loss may be compensated for by the fellow eye and may remain unnoticed until substantial damage has occurred. By contrast, angle-closure disease may produce an acute rise in IOP with severe ocular pain, blurred vision, halos, headache, nausea and vomiting and requires urgent assessment [3,4].

The submitted thesis emphasizes the 'silent thief of sight' concept and reviews the transition from conventional diagnosis to automated retinal-image analysis. Its central diagnostic theme is appropriate: glaucoma should be assessed using complementary evidence rather than a single numerical threshold. IOP is a major modifiable risk factor, but glaucoma may occur at statistically normal pressures; therefore, optic nerve structure and visual function remain essential [5]. *The submitted project specifically emphasizes automated fundus analysis, CDR evaluation, OCT and emerging AI/ViT approaches.*

This review reorganizes and updates the thesis material into a publication-oriented narrative. Particular attention is given to advances in imaging, automated CDR and optic-disc analysis, OCT/OCTA, AI-based detection, multimodal fusion and Vision Transformer (ViT) architectures. The goal is not to propose an unvalidated diagnostic algorithm, but to summarize where current evidence supports clinical use and where additional validation remains necessary.

Glaucoma: Pathobiology and Clinical Phenotypes

Aqueous humor is produced by the ciliary body and normally exits predominantly through the trabecular meshwork and Schlemm's canal, with an additional uveoscleral route. Increased resistance to aqueous outflow can raise IOP, producing mechanical and biomechanical stress on the optic nerve head. However, vascular susceptibility, laminar and connective-tissue properties, age-related changes, genetic factors and neurodegenerative mechanisms also contribute to retinal ganglion cell vulnerability [5,6]. Consequently, IOP should be viewed as a major

risk factor and therapeutic target rather than a stand-alone diagnostic criterion.

Clinically, glaucoma can be classified as open-angle or angle-closure, and each may be primary or secondary. POAG is characterized by an anatomically open anterior chamber angle with progressive optic neuropathy. Normal-tension glaucoma demonstrates glaucomatous structural and functional damage despite IOP values that do not appear elevated. Angle-closure glaucoma results from crowding or closure of the drainage angle and may be chronic or acute. Secondary glaucomas may arise from corticosteroid exposure, trauma, inflammation, pseudoexfoliation, pigment dispersion, lens-related mechanisms and other ocular or systemic disorders [3,4].

The structural phenotype includes enlargement or deformation of the optic cup, focal or diffuse neuroretinal-rim thinning, RNFL defects and progressive loss of retinal ganglion cells. The functional phenotype includes localized visual-field defects that may progress with time. Structural and functional measures do not always change synchronously; therefore, discordance between OCT, fundus examination and perimetry should prompt clinical review rather than automatic classification.

Risk Factors and the Need for Early Detection

Age is a major determinant of glaucoma prevalence. Family history is important, and ancestry and anatomical characteristics influence the distribution of POAG and angle-closure disease [1,3]. Other clinically relevant risk factors include elevated IOP, thin central corneal thickness, myopia, diabetes, vascular disease, prior ocular trauma and prolonged corticosteroid exposure. Risk should be interpreted in combination rather than as an isolated checklist.

Because established optic-nerve injury cannot simply be reversed, diagnosis aims to identify disease before extensive functional loss and to establish a baseline against which future change can be measured. The World Health Organization has noted that glaucoma is often asymptomatic early and that appropriately targeted eye examinations are important for protecting visual function [2]. A population-wide strategy based only on one test is unlikely to be sufficient; clinical risk stratification and access to comprehensive eye examinations remain important.

Conventional Diagnostic Approach

Intraocular pressure measurement

Tonometry quantifies IOP and remains central to glaucoma assessment because lowering IOP is the only established modifiable intervention shown to reduce the risk of progression. However, IOP fluctuates over time and may be influenced by corneal biomechanics and measurement technique. Some individuals with elevated IOP do not develop glaucomatous damage, whereas normal-tension glaucoma demonstrates that optic neuropathy can occur without conventionally high IOP [5,7]. Thus, IOP is best interpreted alongside structural and functional findings.

Gonioscopy and anterior-segment assessment

Gonioscopy directly evaluates the iridocorneal angle and is indispensable when angle closure is suspected. It distinguishes open-angle from angle-closure mechanisms and can identify secondary causes. In patients at risk of acute angle closure, recognition of a narrow or occludable angle has immediate clinical implications.

Fundus and optic-disc examination

Fundus examination provides a direct view of the optic nerve head, retinal vessels and posterior pole. Classical glaucomatous findings include neuroretinal-rim thinning, increased cupping, disc hemorrhage and RNFL defects. The cup-to-disc ratio is useful but should not be interpreted in isolation because disc size, anatomical variation and image quality affect its meaning. Computer-aided analysis can reduce inter-observer variability by standardizing segmentation and feature extraction [8].

Visual-field testing

Automated perimetry measures functional visual loss and remains an essential component of diagnosis and progression assessment. Structural damage can precede clearly demonstrable field loss, while field testing is affected by learning effects, fatigue, fixation and test variability. Repeated testing is therefore often required to establish a reliable trajectory. Recent work also suggests that increasing the number of early visual-field observations can improve identification of very slow progression [9].

Optical coherence tomography

OCT provides high-resolution cross-sectional retinal imaging and quantitative measurements of RNFL thickness, ganglion-cell complex/ganglion-cell-innerplexiform-layer parameters and optic nerve head morphology. OCT is particularly valuable for detecting structural damage and documenting change over time. A 2026 systematic review and network meta-analysis

identified average and inferior RNFL parameters, macular ganglion-cell loss-volume measures, inferotemporal GC IPL, rim area and CDR among informative parameters for early glaucoma detection [10].

OCT angiography and vascular assessment

OCT angiography (OCTA) provides non-invasive visualization of retinal and optic-nerve-head microvascular networks without dye injection. Reduced vessel density and altered perfusion patterns have been investigated as complementary biomarkers. OCTA should currently be regarded as an adjunct rather than a replacement for established structural and functional tests, because acquisition artifacts, segmentation errors and disease-related vascular confounding remain relevant.

Automated Fundus Analysis and Cup-To-Disc Ratio

Digital fundus photography is attractive for screening because it is non-invasive, relatively inexpensive and scalable. Automated systems can localize the optic disc, segment the optic cup and disc, estimate CDR and detect RNFL or rim abnormalities. Earlier computer-aided systems depended on hand-crafted features and conventional classifiers; deep learning subsequently enabled end-to-end feature learning from images [8,11].

The thesis emphasizes CDR-based analysis of preprocessed fundus photographs and describes automated image processing as a low-cost approach. For a publication-oriented interpretation, however, the numerical success estimate reported in the thesis should not be presented as a validated clinical accuracy unless supported by a reproducible dataset, reference standard, independent test set and statistical confidence intervals. In clinical practice, CDR is one feature among several and is not sufficient by itself to establish glaucoma.

Deep learning has substantially expanded automated fundus analysis. In a 2018 study, Li et al. developed a deep learning system for glaucomatous optic neuropathy from color fundus photographs, demonstrating the feasibility of automated image-based detection [12]. A separate deep-learning study using 1,542 fundus photographs reported an AUROC of 0.94 on its test dataset for a convolutional neural network, illustrating the high performance achievable in curated datasets [13]. These results are encouraging but do not guarantee equivalent performance in different cameras, ethnic populations, disease spectra or primary-care environments.

Artificial Intelligence in Glaucoma Diagnosis

From machine learning to deep learning

Machine-learning approaches can use structured variables such as IOP, OCT measurements, visual-field indices and demographic information. Deep-learning systems, particularly convolutional neural networks (CNNs), learn image representations directly from fundus or OCT data. Applications include optic-disc/cup segmentation, glaucoma classification, RNFL and ganglion-cell analysis, visual-field interpretation and progression prediction [14].

A 2025 systematic review and meta-analysis of 48 studies reported pooled sensitivity and specificity of 0.92 and 0.93 for glaucoma detection from fundus photographs, with an AUROC of 0.90. For OCT, pooled sensitivity and specificity were 0.90 and 0.87, respectively, with an AUROC of 0.86. The same review found that progression-prediction performance was less robust and that internal validation generally produced higher performance than external validation [15].

AI using OCT

OCT is well suited to AI because it produces large quantities of standardized, quantitative image data. A 2024 systematic review and meta-analysis of 20 studies and 51 models found pooled sensitivity of 0.91 and specificity of 0.90 for AI-based glaucoma detection from spectral-domain OCT, with a pooled AUC of 0.95 [16]. These findings support AI as a potentially useful decision-support layer, while also demonstrating why model validation must be separated from clinical implementation.

AI can also assist in progression assessment. Huang et al. developed a self-supervised ViT approach using macular OCT to detect and predict clinically significant visual-field progression [17]. Mandal et al. similarly investigated deep learning to distinguish glaucoma progression from age-related changes in serial OCT scans [18]. Such work moves the field beyond static classification toward longitudinal risk assessment.

Explainability and clinical integration

High accuracy alone is insufficient for clinical adoption. Ophthalmologists need to understand which anatomical regions or measurements influence an AI output and whether the model is behaving consistently across devices and populations. Explainable AI methods, saliency maps, attention visualization and structured feature attribution can support review, but

explanations should not be assumed to prove biological causality. A 2026 review identified explainability, multimodal data and integration with routine ophthalmic assessment as important themes in AI-enabled glaucoma diagnosis [19].

Vision Transformers and Multimodal Diagnosis

CNNs learn local spatial patterns through convolutional operations. Vision Transformers instead divide an image into patches and use self-attention to model relationships among distant image regions. This ability to capture long-range contextual information is relevant to glaucoma because clinically meaningful patterns may involve relationships between the optic disc, peripapillary retina and other retinal regions.

The thesis proposes a hybrid-fusion Vision Transformer concept integrating fundus photography, OCT and visual-field information. The rationale is consistent with contemporary clinical practice: fundus imaging provides a top-down structural view; OCT supplies quantitative cross-sectional information; and visual-field testing captures function. A multimodal model can potentially reduce the limitations of any one modality. However, many published datasets remain single-modality, and heterogeneous multimodal datasets require careful alignment of patient identity, visit timing, device characteristics and diagnostic labels.

Recent evidence suggests that multimodal AI can be valuable, but the key challenge is not simply increasing model complexity. Models must be trained and externally validated on representative populations, including different ethnic groups, age ranges, degrees of myopia, image-quality levels and glaucoma severities. Data leakage between training and test images from the same patient or visit can substantially inflate performance if not controlled.

Limitations and Challenges of AI-Based Diagnosis

The most important limitation is generalizability. A model trained on high-quality images from a tertiary glaucoma clinic may perform differently in community screening, where images are lower quality and disease prevalence is different. Spectrum bias can arise when normal controls and advanced glaucoma cases are easier to separate than mild disease and healthy aging.

Myopia presents another challenge because disc tilt, peripapillary atrophy and altered retinal anatomy can mimic or obscure glaucomatous changes. Media opacity, small pupils, poor fixation and camera differences can reduce image quality. OCT interpretation may also be affected by segmentation

errors and normative databases that do not represent every population.

Clinical labels are another source of uncertainty. Glaucoma diagnosis is not always binary and can

depend on longitudinal evidence. A model trained against a single clinician label may reproduce that label's limitations. Reference standards should ideally incorporate specialist examination, structural imaging, functional testing and follow-up where appropriate.

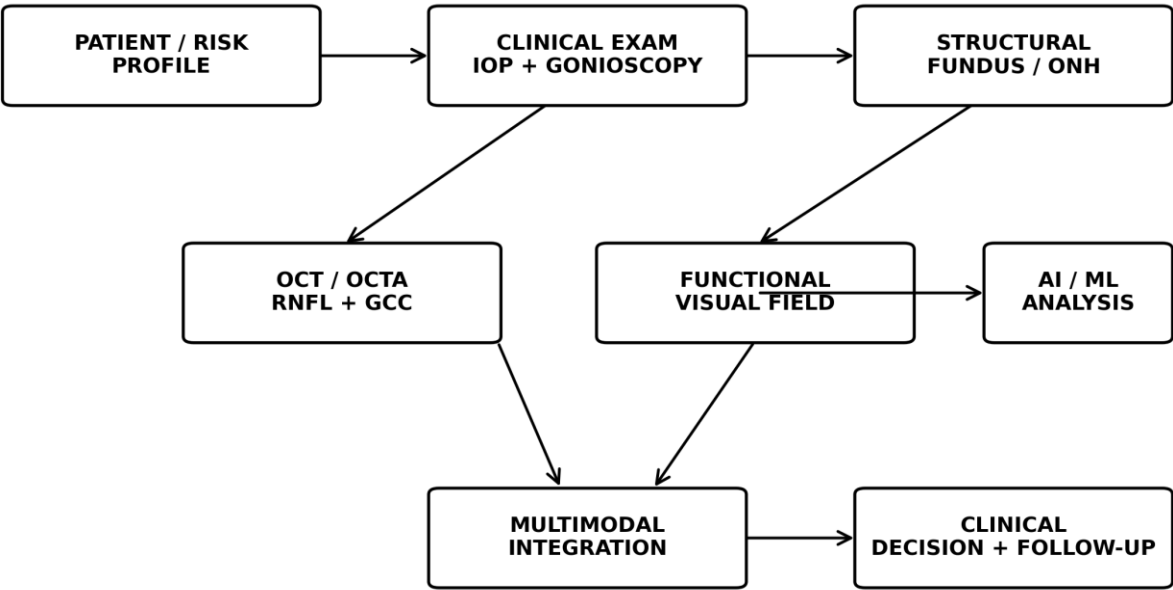


Figure 1: Integrated modern workflow for glaucoma diagnosis. The pathway combines risk assessment, clinical examination, structural imaging, functional testing and AI-assisted interpretation. AI outputs should remain decision-support information within comprehensive ophthalmic care.

Comparison of Diagnostic Modalities

Table 1: Comparison of diagnostic modalities.

Modality	Primary information	Major strengths	Important limitations
Tonometry	IOP	Fast, quantitative, essential for risk and treatment monitoring	IOP variability; glaucoma may occur at normal IOP
Gonioscopy	Anterior chamber angle	Defines angle status and mechanism	Requires skill and contact lens examination
Fundus photography	Optic disc, cup, RNFL	Scalable, documentable, suitable for AI	Image quality and anatomical variation; CDR alone is insufficient
Visual field	Functional loss	Directly measures visual function and progression	Patient-dependent; learning and test variability
OCT	RNFL, GCC/GCIPL, ONH	High-resolution quantitative structural assessment	Device/segmentation artifacts; myopia can complicate interpretation
OCTA	Microvascular features	Non-invasive vascular information	Artifacts and evolving evidence base
AI / deep learning	Pattern recognition across images/data	Automation, consistency, scalability, multimodal potential	Dataset shift, bias, explainability, external validation and workflow integration

Table 2: Representative Evidence for AI-Assisted Glaucoma Diagnosis.

Evidence area	Study / evidence	Reported finding	Clinical interpretation
Fundus photography	Deep-learning meta-analysis [15]	Pooled sensitivity 0.92; specificity 0.93; AUROC 0.90	Strong diagnostic signal in studied datasets; external validation remains essential
SD-OCT	Systematic review/meta-analysis [16]	Pooled sensitivity 0.91; specificity 0.90; AUC 0.95	Supports OCT-AI as decision support for structural detection
Macular OCT + ViT	Huang et al. [17]	Detected and predicted visual-field progression	Shows potential for longitudinal prediction, not merely classification
Serial OCT progression	Mandal et al. [18]	Deep learning distinguished progression from age-related change	Potential to support longitudinal monitoring
Fundus AI systems	Recent clinical evaluation [20]	Combined systems achieved AUC 0.903 in a retrospective cohort	Performance requires prospective and broader validation

Finally, AI implementation raises issues of privacy, cybersecurity, informed use, regulatory oversight and responsibility for errors. A model that is accurate on average can still produce clinically important false-negative or false-positive results. Accordingly, AI should be framed as an adjunct to, rather than a replacement for, qualified clinical assessment.

Emerging Directions in Glaucoma Diagnosis

Future diagnostic systems are likely to integrate multimodal longitudinal data rather than classify a single image. Potential inputs include fundus photographs, OCT/OCTA, visual fields, IOP trajectories, medication history, age, refractive status and other clinical variables. Self-supervised learning may reduce dependence on expensive manual labels, while transformer architectures may facilitate fusion of imaging and structured clinical information.

Portable imaging and teleophthalmology may expand access in areas with limited specialist availability. Recent evidence on portable glaucoma diagnostic devices indicates growing interest in technologies that can move testing beyond conventional hospital-based equipment [21]. Such tools are particularly relevant to screening pathways, although referral mechanisms and confirmatory examinations remain necessary.

The diagnostic objective should also shift from 'glaucoma versus no glaucoma' toward clinically useful questions: Is there evidence of glaucomatous optic neuropathy? Is structural damage progressing? Is functional loss progressing? What is the patient's risk of future deterioration? Which findings are discordant and require specialist review? AI systems designed

around these questions may provide greater clinical value than isolated image classification.

Therapeutic advances also reinforce the need for better diagnosis. Current treatment remains centered on IOP reduction using topical agents, laser procedures and surgery, while minimally invasive glaucoma surgery, sustained drug delivery, neuroprotective approaches and gene-based strategies remain active areas of investigation. Better diagnostic phenotyping may eventually support more individualized treatment selection.

Practical Clinical Diagnostic Algorithm

A practical diagnostic pathway derived from the thesis and current evidence can be summarized as follows: (1) identify risk factors and symptoms; (2) perform comprehensive ocular examination and IOP measurement; (3) assess the anterior chamber angle when indicated; (4) examine and document the optic nerve head and fundus; (5) obtain OCT measurements of RNFL and macular ganglion-cell parameters; (6) perform reliable visual-field testing when appropriate; (7) use OCTA or other adjunctive imaging when it provides clinically relevant additional information; (8) use AI as a supportive second reader or triage tool where validated; and (9) establish a baseline and monitor structural and functional change over time.

For suspected acute angle closure, the priority is urgent clinical assessment rather than automated screening. For suspected early or pre-perimetric glaucoma, discordant structural and functional findings should be interpreted longitudinally. In all settings, a diagnostic label should reflect the total clinical evidence rather

than a single AI probability, CDR value or IOP measurement.

Discussion

The thesis appropriately emphasizes that glaucoma detection is moving from subjective examination toward quantitative imaging and automated analysis. The strongest current evidence supports a complementary model. Conventional examination remains necessary because it defines the clinical context and identifies mechanisms that may not be captured by posterior-segment image classifiers. Fundus photography offers scalability; OCT provides quantitative structural biomarkers; visual fields provide functional confirmation and progression assessment; and AI can integrate patterns that may be difficult to quantify manually.

The evidence also argues against presenting AI performance as equivalent to clinical effectiveness. Meta-analytic diagnostic performance is often derived from retrospective datasets with substantial heterogeneity. Internal validation can overestimate real-world performance, and external validation across devices, sites and populations is still needed [15,16]. Consequently, the most defensible near-term role for AI is decision support, triage and longitudinal monitoring in settings where the system has been appropriately validated.

The thesis's focus on CDR is historically and practically relevant, but modern glaucoma diagnosis is more nuanced. CDR is influenced by disc size and normal anatomical variation. RNFL and ganglion-cell measurements, optic-nerve-head morphology and visual-field defects provide complementary evidence. The emergence of ViTs and multimodal fusion offers an opportunity to combine these signals, but complexity should not be mistaken for clinical superiority. A simpler, externally validated model may be more useful than a sophisticated model that lacks transparency or robustness.

Overall, the field is progressing toward earlier, quantitative and increasingly automated detection. The most important research priorities are representative datasets, prospective multicenter validation, longitudinal outcome studies, explainability, standardized reporting and integration into real clinical workflows. These priorities are particularly important for low-resource settings, where scalable imaging and AI-assisted referral could potentially extend specialist expertise, provided confirmatory pathways are available.

Conclusion

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Glaucoma remains a major cause of irreversible vision loss because optic-nerve damage can progress silently before patients recognize functional impairment. The diagnostic landscape has evolved from reliance on IOP and subjective optic-disc assessment toward a complementary framework involving gonioscopy, fundus photography, visual-field testing, OCT/OCTA and longitudinal analysis. Automated fundus analysis and AI-based interpretation offer promising opportunities for scalable screening and decision support, while recent meta-analyses demonstrate strong diagnostic performance for deep learning applied to fundus photographs and OCT. Vision Transformers and multimodal fusion may further improve the integration of structural and functional information.

However, AI should not be interpreted as a replacement for comprehensive ophthalmic assessment. Generalizability, dataset bias, image artifacts, clinical labeling, explainability and external validation remain important barriers. The most clinically appropriate direction is therefore an integrated pathway in which validated AI augments—not replaces—expert examination and longitudinal monitoring. Earlier identification of structural change, reliable confirmation of functional loss and timely intervention remain the central objectives of glaucoma care.

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Conflict of Interest

None declared.

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