

Artificial Intelligence in Ophthalmology: A study on different AIML approaches for Glaucoma prediction

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Abstract— Glaucoma is a leading cause of irreversible blindness, and artificial intelligence (AI) has emerged as a promising tool for its early detection and management. Recent studies span fundus- and OCT-based deep learning models, electronic health record-driven classifiers, and sensor-based systems incorporating ocular biomechanics and circadian signals. Meta-analyses confirm strong diagnostic performance of image-based AI, yet highlight persistent challenges in progression prediction, generalizability, and interpretability. EHR- and sensor-driven approaches provide complementary insights but remain limited by data quality and cohort size. This review synthesizes current advances, evaluates their limitations, and emphasizes the need for multimodal, explainable, and externally validated AI frameworks to achieve robust and clinically translatable glaucoma prediction

Keywords— Glaucoma prediction, Artificial intelligence, Deep learning, Fundus imaging, Optical coherence tomography (OCT), Electronic health records (EHR), Sensor-based diagnostics, Multimodal fusion, Disease progression, Explainable AI, Federated Learning, Disease progression, Clinical translation, Biomarker discovery.

I. INTRODUCTION

Glaucoma is rare in its occurrence but complex in its presentation. Being a mixture of slow progression and subtle clinical features complicates early diagnosis and timely intervention. It is a progressive optic neuropathy and one of the leading causes of irreversible blindness throughout the world [1]. The disease is characterized by the gradual degeneration of retinal ganglion cells and their axons, leading to structural damage to the optic nerve head and a corresponding loss of visual function. This damage typically manifests as characteristic retinal nerve fiber layer defects and progressive visual field loss. Often referred to as the "silent thief of vision," glaucoma is particularly insidious because it is largely asymptomatic in its early stages. This makes early notice and continuous surveillance very important [1]. Patients frequently remain

unaware of their condition until substantial and permanent optic nerve damage has occurred, at which point therapeutic interventions can only aim to slow further progression rather than restore lost sight. Conventional diagnostic methods, such as optic disc examination, retinal nerve fibre layer (RNFL) assessment using optical coherence tomography (OCT), and visual field testing, have been highly effective but time-intensive, and also demand specialist expertise, often missing subtle early changes [2]. This silent, progressive nature makes timely diagnosis and intervention exceptionally challenging, yet critically important for preserving vision.

According to the recent estimations, the number of individuals affected by glaucoma will rise to over 111 million by the year 2040, this would result in an escalating public health crisis [9]. This demographic trend is compounded by a significant bottleneck in diagnostic capacity. The scarcity of ophthalmologists, especially in underserved and remote regions, further worsens this issue, resulting in a diagnostic delay that can lead to permanent loss of vision [19]. The core challenge is of scalability; any solution being meaningful must be more automated, accessible, and efficient than the current standard to meet the growing global demand for screening and monitoring.

Artificial intelligence (AI) has emerged as a assuring tool to address these challenges. Deep learning systems that are trained on fundus photographs and OCT scans have gained diagnostic performance equivalent to ophthalmologists, with features like meta-analyses reporting pooled sensitivities and specificities above 0.90 [2]. Nevertheless, active models face limitations in predicting disease continuum, guaranteeing generalizability across imaging devices and populations, and providing clinically interpretable outputs [2,3]. There are many alternative models being explored. The models based on Electronic health record (EHR), cloud systemic and clinical data thereby identifying high-risk individuals and therefore offering scalable pre-screening solutions [4].

Whereas, Sensor-based systems that integrate continuous intraocular pressure monitoring and ocular biomechanics provide dynamic functional insights, nevertheless present studies remain constricted by small cohorts and device availability [5]. Reviewing the tabular data models further highlights challenges with heterogeneity and reproducibility [6].

Altogether, these findings highlight both the guarantee and the present restrictions of AI in glaucoma. A future research direction is to develop a multimodal, explainable, and externally validated frameworks that unify structural, functional, and systemic data in order to enable robust and clinically translatable glaucoma prediction [1–6]. Predominantly, the findings highlight both the guarantee and the present restrictions of using AI in diagnosis of glaucoma. A research direction for the future is to develop a multimodal, explainable, and externally validated frameworks that unify structural, functional, and systemic data which can enable robust and clinically translatable glaucoma prediction [2–7].

Irrespective of the rapid progress, most of the existing approaches remain separated, depending on a single data modality or a limited number of validation cohorts. Which results in models performing well in controlled research settings but struggle to reach the same real-world clinical environments where patient populations, imaging devices, and disease presentations are highly heterogeneous.

This paper provides a comprehensive review of recent advances in AI-based glaucoma prediction, with a focus on imaging, EHR, and sensor-driven methods. By comparing their methodologies, datasets, and reported performances, this review highlights both the strengths and the limitations of current approaches and identifies key directions for future research.

II.BACKGROUND AND RELATED WORK

A. Imaging-based approaches

The most widely studied applications of artificial intelligence in glaucoma are Imaging-based methods, particularly those using fundus photographs and optical coherence tomography (OCT) [1]. To classify glaucomatous and healthy eyes, as well as to segment optic disc and cup regions for cup-to-disc ratio analysis, the Convolutional neural networks (CNNs) have been extensively used[1]. Studies consistently report diagnostic performance with sensitivities and specificities exceeding 0.90 in controlled datasets [2]. However, the sensitivity of these models often face challenges in generalizing across diverse populations, imaging devices, and real-world settings[3].

Fig1. Architecture of the AI-based glaucoma screening (AI-GS) network[3]

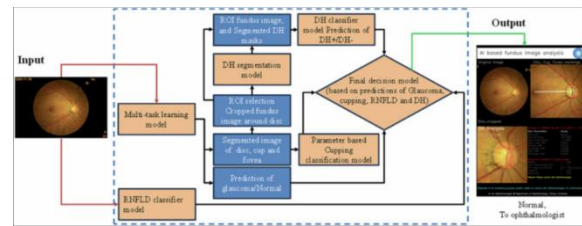


Table 1: CNN Variants for Glaucoma Detection

Model	Performance & Notes
DenseNet121	Accuracy: 0.90–0.97; fundus detection
Inception V3	Accuracy: 0.88–0.95; optic disc/cup analysis
VGG16 / VGG19	Accuracy: 0.85–0.93; fundus classification
3D CNN (OCT)	Accuracy: 0.86–0.94; depth-based OCT analysis
Hybrid CNN + LSTM	Accuracy: 0.91; progression modeling
Multimodal DL	Accuracy: 0.93–0.97; integrates fundus + OCT + clinical data

Strong accuracy is demonstrated by models that use OCT scans and fundus images for being trained, whose pooled sensitivities and specificities often exceed 0.90[2]. These approaches account from rich structural information but are sensitive to changes in imaging devices and patient populations[2]. In addition to this, despite being effective for cross-sectional diagnosis, they usually show a weaker performance in predicting the progression of disease.

Fig2. Screening using OCT images

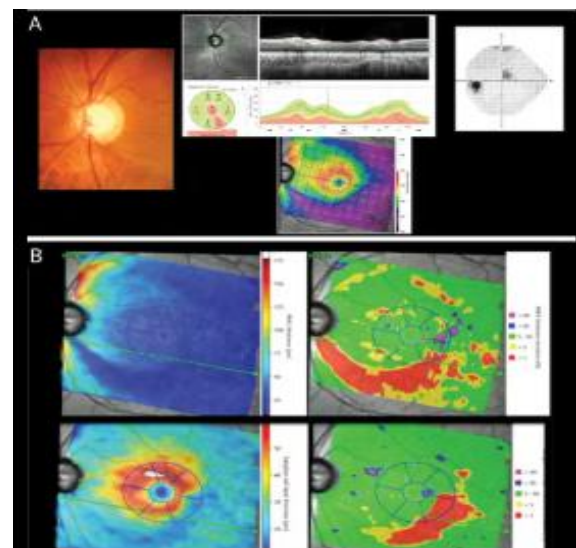


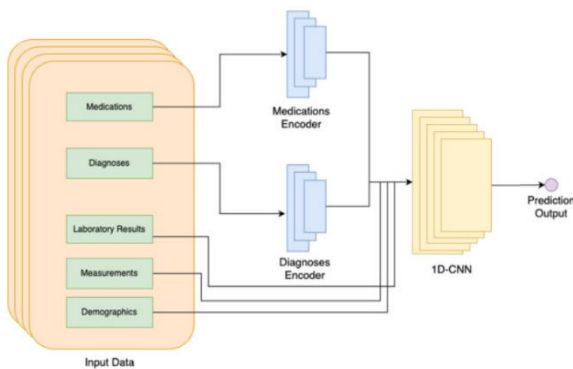
Table 2: Deep Learning on Fundus & OCT Images

Model	Performance & Use Case
ResNet50	Sensitivity: 0.84–0.95; fundus-based diagnosis
InceptionResNetV2	Sensitivity: 0.96–0.97; ultra-widefield fundus
AG-CNN	Sensitivity: 0.95; attention on optic disc/cup
DiagnoseNet	AUROC: 0.94 (diagnosis), 0.87–0.88 (progression)
3D DL (OCT)	AUROC: 0.80–0.91; volumetric retinal analysis
Multimodal DL + GAN	AUROC: 0.99; combines fundus + VF + clinical data

B. EHR- Based models

Electronic health records (EHRs), they provide a rich source of structured clinical and demographic information for a successful glaucoma prediction. On applying Machine Learning algorithms to EHR data have documented promising results, with large-scale cohorts achieving robust differentiation between patients with and without glaucoma [4]. These models are specifically valuable for population-level screening and for stratification of any risk, as they have the ability to identify individuals who may require further ophthalmic evaluation. However, their predictive power is limited due to the absence of structural imaging features, therefore making them less accurate for definitive diagnosis.[4]

Fig3. Schematic of prediction pipeline[4]



The application of machine learning to organized clinical data has demonstrated potential for extensive population screening. By integrating demographic, systemic, and long-term health data, these models can pinpoint individuals who are at a higher risk of developing glaucoma. Nonetheless, the absence of structural imaging information hampers diagnostic accuracy, confining their function primarily to prescreening or triage.[6]

Table 3: EHR-Based Glaucoma Prediction (All of Us Dataset)

Model	Performance & Highlights
Logistic Regression (L2)	Accuracy: 0.63; AUROC: 0.686
XGBoost	Accuracy: 0.889; AUROC: 0.828
FCN	Accuracy: 0.891; AUROC: 0.796
1D-CNN + Autoencoders	Accuracy: 0.905; AUROC: 0.863

C. Sensor-driven model

Using Sensor-based systems offers an alternative approach, as it captures continuous physiological data relevant to glaucoma. These models have been trained using wearable devices that monitor intraocular pressure (IOP) fluctuations, combined with cardiac and corneal biomechanical signals, thereby training predictive algorithms with promising accuracy levels [5]. Therefore, these approaches highlight the significance of functional and biomechanical information in disease monitoring. The small scale of existing studies and their high costs, along with the restricted availability of specialized sensors, limits their broader applicability. [5]

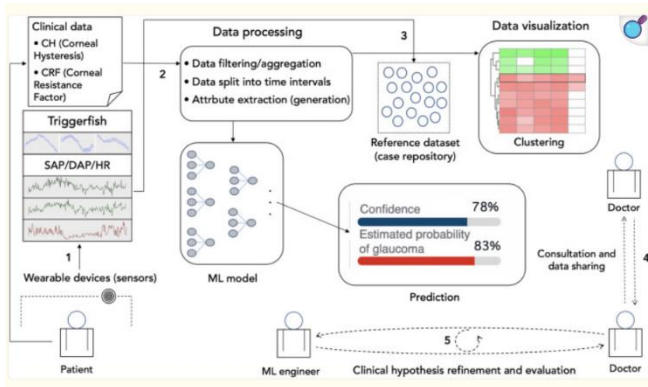
Devices that are wearable and implantable, capable of regular intraocular pressure monitoring on being combined with biomechanical and physiological dynamics. Predictive models on being trained on such data achieve competitive accuracy, but their widespread usage is deprived by small study sizes, high prices, and limited device accessibility.[5]

Table 4: Sensor + Biomechanics-Based Models

Model	Performance & Input
Baseline Logistic Regression	Accuracy: 0.59; IOP only
G0 Models	Accuracy: 0.70 (XGBoost); sensor data
G1 Models	Accuracy: 0.83 (LogReg); sensor + biomechanics

(GlaucomAI System)

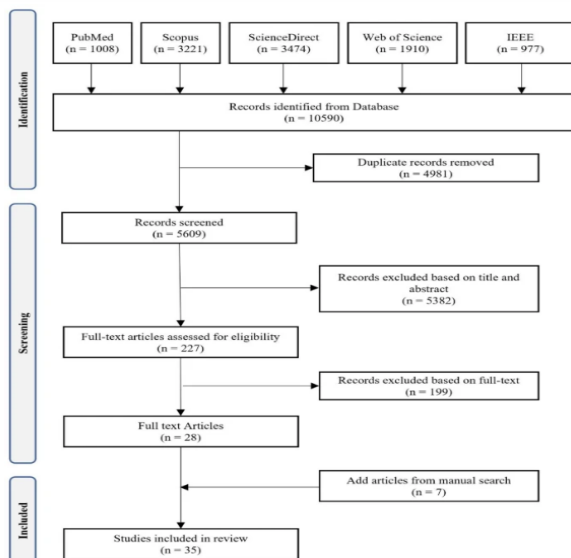
Fig4. Overview of data flow and interactions of users of the system. [5]



D. Structured Data Approaches

In addition to imaging techniques, the use of structured or tabular clinical data has been investigated for predicting glaucoma. These datasets generally encompass demographic details (like age, gender, and ethnicity), systemic health indicators (including diabetes, hypertension, and cardiovascular issues), family medical history, medication usage, and ocular examination findings [6]. Various machine learning algorithms, such as logistic regression, random forests, support vector machines, and gradient boosting, along with the more recent deep sequence models, have been utilized on extensive electronic health record (EHR) databases to assess glaucoma risk. The reported outcomes are encouraging, with certain studies achieving AUROC values between 0.80 and 0.86 in cohorts of over 60,000 patients, highlighting the potential for utilizing routinely gathered data for large-scale prescreening efforts.[6]

Fig5. Flowchart of the study selection process (PRISMA)[6]



One of the primary benefits of leveraging structured data is its scalability: it can identify high-risk individuals who might otherwise remain undetected and guide them toward further ophthalmological assessment. Nonetheless, these models do not incorporate detailed ocular biomarkers such as optic nerve head structure or retinal nerve fiber thickness, which constrains their diagnostic accuracy. Moreover, inconsistencies in data completeness, coding practices, and patient diversity across different health systems present obstacles for reproducibility and generalization. Despite these challenges, structured data methodologies offer a valuable supplementary approach to imaging and sensor-based techniques, especially for assessing population-level risk and implementing early detection strategies.[6]

Table 5: Structural Feature Models (THU Dataset)

Model	Performance & Notes
RNFLD Classifier	Accuracy: ~88%; detects nerve fibre layer defects
DH Segmentation	Accuracy: ~85%; localizes haemorrhage zones
Cupping Parameter (FFCN)	Accuracy: ~90%; uses metrics like CDR, rim area
Final Decision Model	Accuracy: ~94%; combines outputs from all models

Table 6: Tabular Data-Based ML Models Dataset

Model	Key Details
MTL_LWBNA-UNet	Segments optic disc, cup, fovea; binary classification
Dataset	AIROGS + THU
Accuracy	~97%
AUC	~0.99
Notes	Lightweight UNet with attention; ensemble logic used for final decision

E. Reviews and multimodal perspectives

The reviews of AI applications in glaucoma highlight both the progress accomplished and the differences that remain. The key challenges that remain are, reproducibility across datasets, fairness in diverse populations, and the interpretability of deep learning models [2], [7]. A recurring theme is the need for multimodal integration, which is a unified combination of structural imaging, functional testing, and systemic health data. Such advances more closely mirror real-world

clinical decision-making and hold the greatest promise for achieving clinically translatable AI solutions.[30]

Although many existing models depend on a single modality, integrating multiple modalities is recognized as an essential area for advancement [30]. The combination of imaging, clinical information, and physiological data mirrors how diagnosis is typically conducted in practice and could enhance reliability, predict progression, and increase interpretability. Nevertheless, multimodal research is still limited and necessitates more extensive and varied datasets for proper validation [30].

Table 7: Multi-Model AI for Fundus-Based Glaucoma Detection

Model	Performance & Notes
SVM	Accuracy: 76–94%; common baseline
Random Forest	Accuracy: 80–98%; interpretable ensemble
Deep Learning (ANN, MLP, ResNet18)	Accuracy: 90–98.3%; high-dimensional feature learning
Logistic Regression	Accuracy: 72–81%; baseline for structured data
XGBoost / GB	Accuracy: 83–98%; top performer in many studies
Ensemble Methods	Accuracy: 85–98%; improves robustness
K-Means Clustering	Internal Accuracy: ~94%; used for staging

III. COMPARATIVE ANALYSIS

Artificial Intelligence models developed for glaucoma prediction using diverse data modalities have their own strengths and drawbacks. Imaging-based methods being dominant over the field, offer high diagnostic accuracy but mostly struggling in generalization [1]. Whereas, Convolutional Neural Networks (CNNs) trained on fundus photographs and Optical Coherence Tomography (OCT) scans continuously achieve high performance on par with ophthalmologists, along with meta-analyses reporting pooled sensitivities and specificities above 0.90 [2]. Advanced architectures like hybrid multi-model systems can further refine this [3], but their performance degrades when applied to different devices or diverse patient populations [2]. On the other hand, EHR-based models provide scalable risk stratification by applying algorithms like XGBoost to large-scale tabular clinical data but lack

the ophthalmic detail for definitive diagnosis, confining their role to pre-screening [4], [6].

Sensor-driven approaches, such as the "GlaucomaAI" system, contribute dynamic physiological data by capturing 24-hour intraocular pressure (IOP) fluctuations and corneal biomechanics, but their broader application is obstructed by high costs and limited availability [5]. The result from reviews is that multimodal integration is the only logical step, which includes unifying structural, functional, and systemic data to mirror real-world clinical decision-making [30]. To overcome data privacy and diversity challenges in this endeavor, Federated Learning has emerged as a promising approach [7]. Ultimately, the future of using AI in glaucoma care lies in creating an equitable, fair, and transparent systems that clinicians can trust and thereby can benefit all patient populations [22].

IV. DISCUSSION

The advancement of Artificial Intelligence is rapid in prediction of glaucoma; still considerable important challenges continue to limit its clinical effect. Image-based models perform exceptionally well on internal datasets but they lack the ability to generalize to external populations [2]. There is a substantial reduction in sensitivity and specificity due to differences in imaging apparatus, data collection methods, and demographic variations, which raises issues regarding reliability in practical applications [2]. For instance, while a lightweight, attention-based UNet model can achieve an accuracy of ~97% and an AUC of ~0.99 on a combined dataset like AIROGS + THU, such performance is not always guaranteed in a real-world clinical setting [12]. Tackling this problem necessitates thorough cross-center validation and the development of more robust, diverse training datasets [18].

A major difficulty also exists in guessing the advancement of the disease. Existing methods primarily emphasize the binary distinction between glaucomatous and healthy eyes, failing to capture the progressive and longitudinal characteristics of glaucoma fully [9]. Accurate modeling of disease advancement is very essential for making decision on the treatment choices; however, few studies have successfully utilized longitudinal data. This remains a critical area for development, with hybrid models like CNN + LSTM showing initial promise in progression modeling [29].

The accountability of AI models continues to be a barrier to adoption. Many deep learning systems operate as “black boxes,” providing probability scores without transparent reasoning [13]. For healthcare professionals, confidence in these tools relies on the capacity to associate predictions with understandable biomarkers. Incorporating Explainable AI (XAI) methods, such as attention heatmaps and Shapley values, is crucial for overcoming this obstacle and building clinical trust [24].

Data limitations result in further additional challenges. There are concerns regarding bias, reproducibility, and equity because most of the studies rely on datasets which are small or not diverse enough [18]. The unequal distribution of disease prevalence and the underrepresentation of specific ethnic groups intensify these issues. To address these challenges, it is essential to develop larger and more varied datasets, preferably utilizing collaborative methods like Federated Learning to uphold patient privacy [7]. Furthermore, specific techniques like fair identity normalization are being developed to ensure equitable screening performance across all populations [22].

Ultimately, each method has its own advantages and disadvantages. Imaging-focused models excel at assessing structure but often miss functional elements [8]. EHR-driven systems facilitate large-scale prescreening but lack ophthalmic specificity [4]. Sensor-based approaches offer real-time physiological insights but face limitations due to device availability and cost [5]. This underscores the necessity for multimodal integration, where structural, functional, and systemic data are merged to better represent actual clinical practice [30]. Such approaches hold the greatest promise for enhancing diagnostic precision, predicting disease progression, and fostering the clinical acceptance of AI-driven glaucoma systems [30].

Table 8: Comparison of accuracy metrics

Model type	Reported Accuracy
Imaging-Based Models	0.90 – 0.99
EHR-Based Models	0.63 – 0.91
Sensor-Driven Models	0.70 – 0.83
Multimodal AI Models	0.93 – 0.99

V. CONCLUSION

This review highlights how the field of artificial intelligence in the research of glaucoma has developed

from single-modality image-based models to diverse computational approaches that involve structured clinical data and sensor-driven analytics ([1], [4], [5], [6]). Various models demonstrate strong capability in identifying clinically relevant patterns and supporting decision-making, reinforcing the value of machine learning in understanding disease signatures beyond human visual interpretation.

Across the various studies examined, a consistent trend is evident, AI is not only being used as a diagnostic aid but also as a tool to analyse patterns of disease characteristics, variability in clinical measurements, and associations across multimodal datasets. These advancements reflect a broader shift towards quantifying glaucoma in a more holistic, data-centred manner. ([6], [11], [28], [29])

Therefore, the findings of this review demonstrate that AI has already established a meaningful presence in glaucoma research, offering new ways to interpret ophthalmic data and understand disease behaviour. The collective evidence confirms that AI has become an important component in the ongoing evolution of glaucoma-related computational research. ([9], [18], [20], [27])

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