Review Article - Narrative Review

Taiwan J Ophthalmol 2024;14:340-351

Access this article online

Quick Response Code:

Website:
http://journals.lww.com/TJOP

DOI:
10.4103/tjo.TJO-D-24-00044

Application of artificial intelligence in glaucoma care: An updated review

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Abstract:

The application of artificial intelligence (AI) in ophthalmology has been increasingly explored in the past decade. Numerous studies have shown promising results supporting the utility of AI to improve the management of ophthalmic diseases, and glaucoma is of no exception. Glaucoma is an irreversible vision condition with insidious onset, complex pathophysiology, and chronic treatment. Since there remain various challenges in the clinical management of glaucoma, the potential role of AI in facilitating glaucoma care has garnered significant attention. In this study, we reviewed the relevant literature published in recent years that investigated the application of AI in glaucoma management. The main aspects of AI applications that will be discussed include glaucoma risk prediction, glaucoma detection and diagnosis, visual field estimation and pattern analysis, glaucoma progression detection, and other applications.

Keywords:

Artificial intelligence, automated image analysis, glaucoma, machine learning

Introduction

Artificial intelligence (AI) is the ability of machines to perform tasks through demonstrating human-like intelligence.[1] With a data-intensive nature,[2,3] ophthalmology is amongst the first medical disciplines that harnessed the power of AI. From automated retinal image analysis,[4,5] visual function prediction,[6,7] to clinic-free text extraction,[8] various AI-based methods have been shown to facilitate ophthalmic disease management. With improved quality and quantity of ophthalmic data, as well as the maturation of AI techniques such as machine learning (ML) and deep learning (DL),[9] ophthalmic AI has entered a pragmatic phase focusing on real-world clinical application.

The benefits of AI applications are particularly explored for vision conditions with high prevalence and possible blinding effects. These include glaucoma, a leading cause of blindness characterized by progressive loss of visual field (VF).[10] Despite decades of investigation, the exact pathophysiology of glaucoma remains unclear. Due to its often insidious onset and irreversible damage,[10] clinicians strive to optimize glaucoma care through methods that can more effectively and reliably detect disease, monitor progression, and predict patient outcomes.[11] With existing challenges in the current management approach, there is strong interest in whether the superhuman power of AI could help overcome these limitations.

To better understand the potential role of AI applications in present and future glaucoma care, this study reviewed relevant literature published in recent years that investigated AI applications in different aspects of glaucoma management.

Methods and Literature Search

This is a descriptive review. The primary literature search was performed using PubMed by crossing keywords related to

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Submission: 14-04-2024
Accepted: 05-06-2024
Published: 13-09-2024

How to cite this article: Wu JH, Lin S, Moghimi S. Application of artificial intelligence in glaucoma care: An updated review. Taiwan J Ophthalmol 2024;14:340-51.

glaucoma, aspects of glaucoma care (e.g., "glaucoma development," "onset prediction," "glaucoma diagnosis," "progression detection," etc.), and AI techniques (e.g., "artificial intelligence," "machine learning," "deep learning," etc.) to search for articles published from January 1, 2020, to March 8, 2024. No filter for language or article type was applied. We excluded editorials, letters, non-English articles, preprint articles, review articles, conference abstracts/articles, case reports, and case series. Google Scholar was used during the secondary literature search for the potential inclusion of missing studies.

Application of Artificial Intelligence in Glaucoma

The following discussion is organized into five sections based on the clinical aspects of AI application in glaucoma care, which include glaucoma risk prediction, glaucoma detection and diagnosis, VF estimation and pattern analysis, glaucoma progression detection, and other applications.

Glaucoma risk prediction

With characteristics such as chronicity, inheritability, heterogeneity, progressivity, and treatability, glaucoma is an ideal candidate for disease risk assessment and prediction.[3,12] Scientifically, risk prediction of glaucoma onset and progression may help to uncover previously unrecognized factors pertinent to disease mechanisms. Clinically, it may also help to differentiate individuals of varying risk profiles for whom different treatment plans should be administered to achieve optimal outcomes.

Prediction of glaucoma development

Standard clinical assessment of glaucoma includes color fundus photographs (CFPs), VF testing, and optical coherence tomography (OCT) imaging. Several recent studies have shown that they can successfully train AI to predict the future development of glaucoma using CFPs or OCT.[13-17] One study trained a DL model to predict glaucoma development using CFPs from the ocular hypertension treatment study (OHTS), and the model achieved an accuracy of 0.88 when predicting glaucoma development 1–3 years before disease onset.[13] Similarly, an area under the receiver operating characteristic curve (AUC) of 0.88–0.89 was achieved in external validation by a DL model that predicts subsequent glaucoma onset using baseline CFPs.[14] Interestingly, the DL algorithm by Lee *et al*. could estimate retinal nerve fiber layer thickness (RNFLT), an important structural parameter usually measured by OCT, based on CFPs.[15] The DL-estimated RNFLT helped to predict glaucoma onset among glaucoma suspects, and eyes estimated with lower baseline RNFLT and faster RNFLT thinning rate showed a significantly greater risk of subsequent glaucoma development.[15]

VF archetypal analysis (VF-AA), a form of unsupervised ML approach that identifies patterns of VF defects,[18] has also demonstrated the ability to predict glaucoma development.[19,20] The VF-AA by Thakur *et al*. achieved an AUC of 0.71 for predicting glaucoma approximately 4 years before disease development.[19] Singh *et al*. trained a VF archetype (AT)-based model to predict primary open-angle glaucoma (POAG) onset using baseline VF tests from the OHTS, which achieved a C-index of 0.75.[20] Furthermore, they found the presence of high-risk ATs at baseline to modify the relationship between POAG and VF pattern standard deviation (PSD), a risk factor for POAG previously reported in the OHTS.[20] Compared with traditional VF metrics, which show limited clinical interpretability due to significant measurement fluctuation,[21,22] VF-AA might provide more accurate and reliable risk stratification.

Demographic and clinical data from the electronic health records (EHR) can also aid in the prediction of glaucoma development.[23,24] Using a big multi-center EHR dataset, multiple ML models achieved an AUC ≥ 0.81 for predicting glaucoma development 1 year before disease onset.[23] With inputs from CFPs and demographic and clinical data, the DL models by Ha *et al*. achieved AUCs ranging from 0.98 to 0.99 for predicting normal-tension glaucoma (NTG) development among normotensive glaucoma suspects.[24] They reported diastolic blood pressure (BP), baseline intraocular pressure (IOP), and RNFLT to be the most important predictors for time-to-conversion.

Prediction of glaucoma progression

Glaucoma demonstrates significant clinical heterogeneity, and genetics is believed to play a major role in determining the disease course across individuals.[25,26] Notably, patients with prior fast or progressive damage tend to have an overall more aggressive disease course, putting them at greater risk of further and more severe functional loss. The prediction of glaucoma progression is thus important for disease forecasting and identifying high-risk individuals in need of more intensive intervention.[27,28]

Numerous recent efforts have trained AI to predict future rapid VF loss or progression using VF results.[20,29-38] These include the above-mentioned study by Singh *et al*., in which the authors identified specific baseline VF ATs that correlated with an increased risk of subsequent fast VF progression.[20] A similar baseline VF-AA was performed in another study to predict future central VF (CVF) progression.[39] Shuldiner *et al*. also trained various ML algorithms to predict the likelihood of future VF progression using the baseline VF, and the support vector machine model achieved the best AUC of 0.72.[31]

AI prediction of VF progression using baseline and/or longitudinal structural data has consistently shown high AUCs (>0.8) in multiple studies.[33-37,40] One of them found the ML model trained on OCT macular ganglion cell/inner plexiform layer thickness to outperform that trained on RNFLT, suggesting the varying structural-functional association of different retinal regions and layers.[33] In another study that used different subsets of OCT and OCT angiography (OCTA) data as ML inputs, the ML model showed the best prediction when fed with combined OCT-OCTA data, indicating the possibly complementary nature of OCTA to OCT in glaucoma evaluation.[40] Distinctive from other studies, Hussain *et al*. proposed a generative DL model to predict VF changes 12 months from baseline.[32] Their model could not only analyze past multi-modal inputs from clinical data, VF and OCT but also generate synthetic follow-up OCT images, achieving a best-performing AUC of 0.83 for predicting fast VF progression.[32]

Fast structural glaucomatous progression on OCT could also be predicted by AI.[41-43] Lee *et al*. developed a random forest model to predict fast RNFLT thinning based on baseline optic nerve head (ONH) features and clinical data.[41] In addition, they identified higher IOP, greater lamina cribrosa curvature, VF mean deviation (MD) converging toward-5 DB, and thinner peripapillary choroid as the most predictive baseline features of fast RNFLT progression. Yoon *et al*. trained ML to predict fast RNFLT thinning using initial systemic profiles in the EHR.[42] In addition to previously known ophthalmic risk factors, the model identified several novel systemic risk factors associated with rapid RNFL thinning, including higher lymphocyte ratio and platelet count.

Another analysis approach is to use treatment upgrades, such as the progression to surgical intervention, to indicate glaucoma progression, which highlights the value of AI in facilitating surgical decision-making.[44] This approach has been used in a few studies.[45-50] Wang *et al*. developed a DL model that used multi-modal baseline data (clinical data, VF, and OCT) to predict surgical intervention at different time points.[46] The best AUC (0.92) was achieved for 3-month prediction, while AUCs > 0.8 were observed for all models that predicted surgical intervention within 3 years.[46] Another study that utilized multi-modal data also reported AUCs ranging from 0.92 to 0.93 when predicting surgical intervention at 1–3 years.[49] The best-performing AI survival model by Tao *et al*., trained on 361 baseline features, achieved a mean AUC of 0.80.[48] Moreover, the transformer-based models by Hu and Wang, which were trained on clinic notes from the initial follow-up period, demonstrated AUCs ranging from 0.70 to 0.73.[47]

Summary

AI can help to capture potential preglaucoma individuals before the occurrence of clinical signs, as well as identify glaucoma patients with impending progression and/or a fast-progressing course. Such information would allow the clinicians to approach these at-risk individuals in a more proactive fashion (e.g., by providing regular monitoring to individuals at high risk of glaucoma development, and by referring glaucoma patients more prone to future progression early for surgical evaluation). With precision medicine being the end goal of glaucoma management, this prospect of AI application is invaluable and could help prevent glaucoma-related blindness.[51]

Glaucoma detection and diagnosis

Image-based ophthalmic disease diagnosis through AI has obtained huge success,[5,52-54] including in glaucoma.[55] Compared to human interpreters, AI demonstrates greater accuracy, reliability and efficiency in glaucoma detection and diagnosis.[55] The text in this section is organized based on the image/data modality used to perform this task.

Color fundus photographs-based detection

As summarized in a prior review,[55] AI already achieved an excellent performance on CFPs-based glaucoma detection in earlier works (mean AUC: 0.97), although there was a lack of prospective, external validation. Findings from recent studies have further added to the evidence supporting its clinical utility.[56-62]

The DL models by Hemelings *et al*. achieved an AUC of 0.995 for glaucoma detection using optic disc-centered CFPs.[58] In their subsequent work, the improved DL models were further proven capable of identifying glaucoma-induced damage outside the ONH,[57] and the results could be generalized to 13 external datasets (AUCs: 0.85–0.99).[59] Meantime, an AI-and telemedicine-based glaucoma screening tool was developed by Bhuiyan *et al*. to detect glaucoma suspects through CFPs, which achieved accuracies of 0.90 and 0.84 in internal and external validation, respectively.[56] High myopia or long axial lengths (ALs) often pose challenges for clinicians during glaucoma assessment.[63] However, ML models consistently achieved AUCs of > 0.9 for discriminating healthy from preperimetric glaucoma/glaucoma in an Asian cohort with long AL, indicating its possibly superior performance to clinicians in this challenging population.[62]

Vision transformers (ViTs), a rising ML approach that is considered the next state-of-the-art for ophthalmic image analysis,[64] have been applied to CFPs-based glaucoma diagnosis.[65-67] One study compared ViTs-based models to convolutional neural network (CNN) models for the detection of POAG among CFPs from the OHTS.[66] The former consistently outperformed the latter in external validation, with the AUC difference ranging from 0.08–0.20. Interestingly, the localized highlight of the neuroretinal rim was shown on the saliency map in the ViTs-based models. In contrast, the same maps in the CNN models showed a more diffuse distribution around the optic disc.[66] Another work comparing ViTs and CNN models for glaucoma detection from CFPs showed similar results of superior performance by ViTs.[67]

Since OCT data are not always accessible in clinical settings, AI could help with glaucoma discrimination by estimating OCT measurements through CFPs. For instance, Jammal *et al*. compared the diagnostic performance of clinicians to predictions by a DL algorithm trained to quantify RNFLT loss on CFPs.[68] The DL algorithm performed comparably, if not superior, to clinicians at discriminating eyes with repeatable glaucomatous VF loss.[68] Chen *et al*. trained a DL algorithm to extract thickness information from CFPs, and the DL-generated RNFLT thickness for glaucoma detection was similar to the OCT-generated original images.[69] Yang *et al*. also trained a DL model to predict RNFLT around optic disc regions in CFPs, and the model achieved the highest AUC of 0.91 for the detection of NTG/glaucoma suspects using DL-estimated regional RNFLT.[70]

Optical coherence tomography and optical coherence tomography angiography-based detection

OCT-based glaucoma diagnosis through AI developed slightly later than that of CFPs.[55] Nonetheless, compared to CFPs, OCT may provide more objective and defined information on retinal structures relevant to glaucoma pathophysiology.

Many recent studies have suggested an excellent performance of AI-assisted glaucoma detection through OCT (AUCs generally >0.90), with the ONH noted as a salient region for detection.[71-84] The DL models by Braeu *et al*. achieved AUCs >0.95 in diagnosing glaucoma from ONH OCT scans.[71] Furthermore, they identified the inferior and superior quadrants of the ONH neuroretinal rim to be critical to the diagnosis. Wu *et al*. compared five ML models for glaucoma detection using various OCT parameters.[73] They revealed that the ganglion cell layer measurements were most predictive of early glaucoma, while the RNFLT metrics were more important predictors in advanced cases. Constructed on data from an Asian cohort, the two ML models by Li *et al*. were trained for glaucoma detection using measured RNFLT data and compensated RNFLT data corrected for anatomical factors.[72] Intriguingly, when testing the models on Caucasians, the compensated data model showed better performance (AUC: 0.93 vs. 0.83), suggesting the importance of considering racial differences in ocular biometry when applying AI.[72]

OCTA is an emerging imaging technique in glaucoma diagnostics.[85,86] Since several commercial OCT devices perform simultaneous calculation of OCTA vessel densities (VDs) and OCT thickness measurements on the same scan slab, an increasing number of new studies have utilized OCTA or combined OCT-OCTA data for glaucoma detection.[87-93]

OCTA-based glaucoma detection through AI seems to perform noninferiorly to that based on OCT. One study reported various ML algorithms that achieved AUCs >0.85 based on OCTA VDs, similar to the diagnostic performance achieved with RNFLT as the input, and revealed the infero-temporal vascular sector to be the most discriminative OCTA region.[88] In addition, they suggested the added value of OCTA when a VD-based model achieved an AUC of 0.76 in glaucoma severity classification (vs. RNFLT-based model: 0.67).[88] In another study, en-face VD images (AUC: 0.97) improved ML performances based on standard OCT measurements (AUC: 0.93) and standard OCTA measurements (AUC: 0.91).[89] Even for glaucomatous eyes with high myopia, a DL model based on macular superficial OCTA images achieved an AUC of 0.95, which was comparable to the results by models trained with macular OCT metrics (AUCs: 0.98–0.99).[92]

Among studies that utilized combined OCT and OCTA data for glaucoma diagnosis, Bowd *et al*. compared ML models trained with OCT, OCTA, and combined OCT-OCTA measurements.[93] Although the combined model showed the highest AUC (0.93), other single-modal models achieved comparable results (AUCs: 0.90–0.91). Rabiolo *et al*. also did not find the combined approach to be superior, and they reported better diagnostic ability of OCT indices than the OCTA ones for DL-based glaucoma detection.[90]

Of note, the inferotemporal region has been consistently suggested as a key region for glaucoma diagnosis across various AI-based OCT/OCTA studies,[83,90,91] showcasing the ability of AI to provide insights into important structural-functional relationships in glaucoma.

Other multi-modal models

Several recent investigations have attempted a multi-modal approach in ML model development, and most of them achieved outstanding results comparable or superior to that derived from single-modal models reported in the current literature.[94-101] Xiong *et al*. compared the glaucoma diagnostic performance of ML models using VF, OCT, and paired OCT-VF data.[95] The multi-modal model achieved an AUC of 0.95 in the primary validation test (vs. VF-based results: 0.87; OCT-based result: 0.81; glaucoma specialists: 0.88) and consistently outperformed other models and glaucoma specialists in the external validation.[95] Song *et al*. also reported that the deep transformer-based model trained with combined OCT-VF data outperformed existing single-modal OCT or VF models by a large margin.[96]

The input of demographics, clinical data, and ocular measurements from the EHR has led to the discovery of novel predictors of glaucoma.[98-101] For instance, a multi-modal model (trained on OCT, CFPs, and EHR data) that achieved an AUC of 0.97 highlighted some previously unknown clinical features, such as pulmonary function parameters and retinal outer layers, for glaucoma diagnosis.[99] In another study, systolic BP was among the top predictors for discriminating glaucoma.[100] Using various data (VF, OCT, and IOP) and ML feature extraction, one study even proposed an integrated glaucoma risk index that was able to classify glaucomatous eyes from nonglaucomatous ones with a low misclassification rate of 0.07%.[98]

Summary

Compared with clinicians, AI could achieve a similar, even superior, glaucoma diagnostic performance.[55] Moreover, the process taken for AI to be trained and perform this task is more cost- and time-efficient, with much less concern over grading subjectivity and variability. In addition, this technique can be used in conjunction with telemedicine, providing a means to break down barriers in eyecare delivery.[102]

However, it should be noted that the academic settings where prior studies were conducted may not represent clinical settings, and there remains a lack of independent, external validation to support the generalizability of the results. Moreover, some potential real-world challenges that AI-based glaucoma diagnosis may encounter include racial or individual differences in ONH structure,[103] heterogeneity in clinical presentations, and low-quality ocular images.[104] Currently, AI-based glaucoma diagnosis may be more suitable as an assistive tool. More pragmatic evidence is needed to fully leverage the benefits of this technique.

Visual field estimation and pattern analysis

VF testing can demonstrate a very important aspect of the functional changes experienced by the patients. However, since the test is time-consuming and dependent on the attention/performance of the subject, the results are often variable.[21,22] Furthermore, the interpretation of the output can be subjective, and thus, efforts have been made to train AI to estimate and analyze VF changes.[105] This section focuses on AI estimation of VF results from other imaging/data modalities and VF loss pattern analysis.

Visual field results estimation

OCT-based estimation of global or point-wise VF indices through AI has been performed in multiple studies.[84,106-109] For 24-2 VF MD and PSD, the mean absolute error (MAE) generally ranged between 1.5–3.0 dB and 1.5–2.0 dB, respectively.[84,106] One study even showed the DL-estimated VF to discriminate eyes with glaucomatous VF defect with an AUC of 0.88.[84] Nevertheless, the error of VF estimation appeared to increase as glaucoma progresses,[109] suggesting a varying functional association of OCT measurements along the disease severity spectrum.

In the meantime, some studies have attempted to estimate CVF, especially the central 10° of VF, through AI.[110-118] The CNN model by Kamalipour *et al*. based on OCT achieved an average point-wise mean MAE of 4.0 dB over the 10-2 map, and a mean MAE of 2.9 dB for 10-2 MD.[110] Using OCTA as input, Mahmoudinezhad *et al*. reported a mean MAE of 2.5 dB and 1.8 dB for 10-2 point-wise and MD prediction, respectively.[111] While Kihara *et al*. compared the performance of DL models based on OCT, infrared reflectance (IR) optic disc images, and combined OCT-IR data.[118] The combined data model achieved the smallest point-wise MAE of 3.1 dB (vs. OCT model: 3.2 dB; IR model: 3.6 dB), implying the potential benefits of a multi-modal approach in AI VF estimation.[118]

Given the multifactorial pathophysiology of glaucoma, some patients might show discrepant extent of structural and functional damage. Therefore, information from multiple independent examinations is generally required to make clinical decisions. With OCT being the sole information source during OCT-based VF estimation, to ensure accurate estimation and unbiased interpretation, quality assessment and clinician evaluation of the OCT data should be performed prior to the AI estimation.

Visual field loss patterns analysis

As aforementioned, AI-based analysis of VF loss patterns, such as the VF-AA, has garnered attention in the past decade. According to the study by Yousefi *et al*., the patterns of 24-2 VF loss identified by ML differ slightly from that identified by experts in the OHTS.[119] The most prevalent VF loss patterns were temporal wedge, partial arcuate, nasal step, and paracentral VF defects per ML models versus partial arcuate, paracentral, and nasal step defects per the experts. Furthermore, one of the ML-identified VF patterns could predict future rapid VF progression after adjustment for age, sex, and baseline VF MD.[119] VF-AA has also been performed for CVF, and the CVF patterns identified were found to improve the prediction of longitudinal 10-2 VF MD worsening slope.[39] Notably, eyes demonstrating more nasal CVF loss patterns at baseline were more likely to show long-term worsening of MD.

VF loss patterns in advanced glaucoma are of specific interest due to the often subtle change that can be difficult for clinicians to observe. The lack of proper characterization of end-stage VF loss has also hindered the investigation of structure-function associations and vision-related quality of life in this patient group. To address this, Wang *et al*. performed VF-AA on the CVF in end-stage glaucoma.[120] In addition to the identification of 14 CVF patterns, they also delineated the "more vulnerable superonasal zone" of the CVF, where new defects are more likely to occur during the follow-up. Moreover, they found most initial CVF loss to demonstrate nasal loss patterns, one of which is most likely to develop into a total loss.[120]

Some factors have been found to affect the patterns of VF loss.[121] One VF-AA study revealed the presence of racial/ethnic differences in the VF loss patterns of POAG.[121] Compared to non-Hispanic Whites, Blacks showed a higher risk of developing VF ATs representing early VF loss and advanced VF loss patterns. In another study, even different testing algorithms of VF showed differing patterns of VF loss in VF-AA.[122] Compared with consecutive Swedish Interactive Threshold Algorithm (SITA) Standard examinations, switching from SITA Standard to SITA Faster (the most recent and fastest testing algorithm) was associated with less preservation of VF loss and greater likelihood of preserving normal VF patterns, which should be considered during progression assessment.[122]

Summary

Considering the time and space needed to conduct VF testing, AI-based VF estimation can serve as an alternative when a VF device is not available or when immediate VF results are not accessible.[106] This application would also allow a more individualized VF testing strategy that optimizes the cost-effectiveness of eyecare allocation (e.g., in patients with a lower risk of CVF defects, 10-2 VF tests can be administered less frequently if AI-estimated results are available).[110] Meanwhile, compared to human interpretation, AI-based VF loss patterns analysis can provide more objective, quantitative, and clinically interpretable information. With the VF test being an indispensable part of glaucoma evaluation, these applications of AI may assist clinicians in patient assessment and decision-making.

Glaucoma progression detection

As described earlier, effective monitoring of glaucoma progression informs the clinician about disease trajectory and how to optimize visual outcomes. With prompt detection of progressive changes, clinicians can intervene in a timely manner, which may help to delay or prevent further vision loss from occurring. To facilitate glaucoma progression detection, many studies have thus explored the performance of AI-assisted methods in detecting functional and/or structural glaucomatous progression.

Visual field progression detection

Functional glaucoma progression is conventionally assessed using global and/or point-wise indices of the VF using standard automated perimetry. However, the former is insensitive to localized disease progression, while the latter generally possess higher measurement variability.[123] Several studies have thus compared AI to these conventional methods in VF progression detection.[38,124-127] Shon *et al*. used various CNN models and two traditional models (linear regression on global indices and point-wise linear regression [PLR]) to detect VF progression in POAG.[126] The CNN models achieved AUCs ranging from 0.78 to 0.87, while the global linear analysis and PLR demonstrated an AUCs of 0.40 and 0.62, respectively. Similarly, the ML-based index developed by Yousefi *et al*. outperformed conventional methods in detecting VF progression.[123] Furthermore, the time to detect progression in 25% of eyes was 6.6, 5.7, 5.6, and 5.1 years using global VF MD, region-wise, point-wise, and ML-based methods, respectively, supporting the use of ML to facilitate early VF progression detection.

An additional advantage of AI-based methods, compared with traditional methods, is the opportunity to incorporate other data to improve classification.[125,128] For instance, a recent study showed that, when using both VF and clinical data, the VF progression detection accuracy of ML models improved (AUC: 0.89–0.93; vs. VF-only: 0.79–0.82).[125] Nevertheless, similar to clinicians and conventional methods, AI seems to perform worse in progression detection as glaucoma worsens,[127] which is a limitation to its clinical application.

Optical coherence tomography progression detection

Structural glaucoma progression is most commonly assessed using OCT parameters. In comparison to VF testing, the strengths of OCT progression assessment include smaller measurement variability,[21,129] higher sensitivity in the early disease stage,[130] and the possibility to capture progression earlier than the VF does in some cases.[131]

A few studies have used AI to assist in the detection of OCT progression.[43,132,133] Using RNFLT from the baseline and a follow-up visit, the CNN model by Mariottoni *et al*. achieved an AUC of 0.94 and outperformed conventional trend-based analysis in detecting glaucoma progression determined by glaucoma specialists using longitudinal RNFLT data.[43] The DL auto-encoders by Bowd *et al*. facilitate the detection of progressive RNFLT changes by generating individualized OCT region of interest (ROI) maps.[132] Compared to trend-based analysis using RNFLT, the analysis using RNFLT from DL-generated ROI achieved higher sensitivity (0.90 vs. 0.63) at a fixed specificity. In another study, longitudinal RNFLT predicted by DL based on CFPs showed robust performance in detecting trend-based fast structural progressors, achieving an AUC of 0.96 and a sensitivity of 0.85 for 0.90 specificity.[133]

Summary
For VF progression detection, AI could help to overcome common limitations of global/local VF indices and perform comparably or superior to traditional methods. With regard to OCT progression detection, in addition to its computational advantage, AI could be utilized to pinpoint the OCT ROI or improve the quality of OCT data (e.g., by providing measurement prediction or image quality enhancement).[134,135] Along with the advents in glaucoma progression prediction (discussed in Prediction of glaucoma progression), AI may facilitate a more robust and personalized monitoring of glaucoma.

Other applications
Anterior chamber structural assessment
AI has been demonstrated to be useful in the assessment of anterior chamber structure through gonioscopy and anterior segment-OCT (AS-OCT).[136-142] For instance, Lin *et al*. showed CNN models can accurately identify the trabecular meshwork in gonioscopy videos in real time, which may have implications for surgical training or intraoperative guidance.[136] ML models have also shown high accuracy in the grading of the anterior chamber angle and the detection of angle closure using AS-OCT,[137-139,141,143,144] providing a reliable method for image-based angle closure screening.

Surgical outcome prediction
Surgical outcome prediction helps to guide postoperative care. Several ML models have been proposed to predict the outcome of filtration surgery, particularly trabeculectomy.[145-148] One of them achieved an AUC of 0.74 in predicting trabeculectomy success using preoperative systemic, demographic, and ocular data in the EHR.[147] A DL model incorporated intra-operative surgical notes in addition to EHR data, which further improved the prediction (AUC: 0.75 vs. EHR data only: 0.71).[148]

AI could also provide insight into new surgical options that have not been well validated. Kurysheva *et al*. compared the anatomic and functional efficacy of early lens extraction (LE), an emerging treatment for primary angle closure glaucoma (PACG), to that of laser peripheral iridotomy (LPI), an established surgical treatment.[149] Considering the correlation among various anterior chamber measurements, an ML classification method was applied to evaluate the overall class similarity of the postoperative eyes to the controls. The authors reported a better efficacy of LE than LPI due to the stronger class similarity to the controls, lower postoperative IOP, and better anterior chamber topography, supporting its use in treating PACG.[149]

Large language models
Large language models (LLMs) represent a rising DL technique featuring the ability to perform various natural language processing tasks.[150] Their possible utility as diagnostic tools and patient resources has been examined within the field of glaucoma. Delsoz *et al*. compared the capabilities of ChatGPT, an online LLM chatbot, and senior ophthalmology trainees to diagnose glaucoma based on clinical case reports.[151] Intriguingly, ChatGPT demonstrated similar or superior accuracy as compared with the trainees, suggesting its potential to assist in triaging or diagnosing individuals with glaucoma. In another study, GPT-4 was compared to glaucoma specialists for diagnosing glaucoma and responding to commonly asked ophthalmic questions.[152] Again, GPT-4 outperformed glaucoma specialists in diagnostic accuracy. Furthermore, response completeness by GPT-4 to ophthalmic questions was rated more favorably than that by the specialists, showing its potential to serve as an alternative patient resource.[152]

Conclusion

From disease diagnosis to outcome prediction, recent studies have shown exciting results of AI application in various key aspects of glaucoma care. Nonetheless, there remain some limitations and concerns toward its clinical implementation.

First, more external validation under prospective, clinical settings and the identification of the best-performing models are required to clarify the performance of AI in the real world. Second, given the race-dependent performance of most clinical instruments,[153-155] exploration of possible racial differences in AI-based glaucoma diagnostics is essential. Third, while AI-generated VF/OCT data seem convenient and accurate, how we can best leverage from them through integration with relevant clinical data awaits further investigation. Last, as the machine element of AI matures, it is equally important that the human element, especially the regulations on its ethical responsibility, medical liability, and role in relation to glaucoma specialists, continues to evolve.[156,157]

Building on the current milestones and limitations, possible next steps include the validation of present findings in pragmatic, real-world studies, optimization of AI performance through refinement of training/input data and algorithm details, integration of generative data with known risk factors for prognostication, and exploration of the societal impacts and corresponding policies regarding its real-world implementation.[102,158,159]

In conclusion, AI application shows the potential to improve glaucoma care. With the assistance of AI, clinicians may be one step closer to the practice of precision medicine in glaucoma.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Financial support and sponsorship

This work is supported by the National Institutes of Health/National Eye Institute Grants (R01EY034148), University of California Tobacco Related Disease Research Program (T31IP1511), and an unrestricted grant from Research to Prevent Blindness (New York, NY). The sponsor or funding organization had no role in the design or conduct of this research.

Conflicts of interest

Sasan Moghimi reported grants from the National Eye Institute. Dr. Shan Lin, an editorial board member at Taiwan Journal of Ophthalmology, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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