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# ARTIFICIAL INTELLIGENCE IN AGE-RELATED MACULAR DEGENERATION: POTENTIAL CLINICAL IMPLICATION

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**ABSTRACT**

**Introduction:** Age-related macular degeneration (AMD) constitutes a significant health concern. AMD is associated with vision impairment. A timely diagnosis and personalized therapeutic strategies are key determinants of a favorable disease course. Diagnosis and monitoring of disease progression are mainly based on imaging modalities. Currently, the interpretation of imaging results is performed by clinicians, which is time-consuming, expensive and often limited due to disparities in access to healthcare. The application of artificial intelligence (AI) for image analysis seems to be an innovative approach. This approach will facilitate the clinical management of patients with AMD, who require frequent follow-up visits to monitor disease progression, evaluate therapeutic efficacy, and determine the necessity of therapeutic escalation.

**Materials and Methods:** This study is a literature review based on recent literature including clinical trials, meta-analyses and randomized controlled trials. The methodology involved a literature search from 2020-2025 across electronic databases, including PubMed, Scopus and Google Scholar. The keywords search terms like “Artificial intelligence and age-related macular degeneration”, “Artificial intelligence and optical coherence tomography”.

**Results:** AI models present high diagnostic accuracy in AMD, achieving sensitivity and specificity above 90%. AI model results are often comparable or better than clinical assessment. AI effectively detects disease and predicts progression, supporting treatment planning, including anti-VEGF scheduling. Performance may decline across devices and heterogeneous cohorts. Recent innovation, specially multimodal systems including various imaging tests, indicate high diagnostic maturity and clear clinical usefulness.

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**KEYWORDS**

Artificial Intelligence, Age-Related Macular Degeneration, Optical Coherence Tomography, Retinal Image Analysis, Teleophthalmology

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**Introduction and background**

Retinal diseases that include age-related macular degeneration (AMD), substitute a leading global health problem. AMD is a spreading retinal condition, contributing significantly to visual impairment and blindness worldwide, particularly in the elderly. In 2020, AMD ranked second among the causes of blindness worldwide [1]. Correspondent to the Preto et Al., analysis AMD caused blindness cases at 1.85 mln of people worldwide, remaining the important cause of vision loss among working-age adults [2].

AMD is a disease that involves changes in the deep layers of the retina, the macula and the blood vessels surrounding it, which causes loss of central vision. There are two main types of AMD - neovascular and non-neovascular AMD, which can be classified based on features visible in fundus examination and OCT. Non-neovascular AMD is more common, accounting for about 80-85% of all AMD cases, and is associated with promising prognosis. Neovascular AMD has a less favorable prognosis, accounting for most cases of severe vision loss among AMD patients [2]. The incidence of AMD is expected to rise due to an aging population and the increasing incidence of risk factors, which include hypertension, cardiovascular disease and diabetes [3]. That emphasizes the need for diagnosis and timely intervention. Early diagnosis is crucial to prevent vision loss [4]. Methods for assessing the retina include fundus photographs and optical coherence tomography (OCT) images, fluorescein angiography, autofluorescence, and ocular ultrasound. OCT is the most accurate method for creating cross-sectional images of the retina without the use of radiation [5].

OCT is a modern diagnostic tool whose popularity and application possibilities have been increasing in recent years. OCT is a non-invasive test, using light waves to visualize each retinal layer and choroid, allowing for precise visualization of the part of the retina affected by AMD. Imaging results allow for the detection of AMD and also for differentiation into subgroups - neovascular or non-neovascular AMD. OCT is also a useful tool for assessing treatment response and guiding further treatment plans. [6].

AI can be used not only to interpret imaging tests but also to improve their quality. In the study presented by Lazaridis et al., deep learning models were used to enhance the OCT signal, improving the signal-to-noise ratio. Improving these parameters significantly improved the agreement between the studied parameters [7].

Advances in retinal imaging technologies have improved retinal visualization, allowing physicians to detect initial pathological changes that correspond to early stages of disease. Regardless, each of them requires personal analysis and evaluation by a clinician which is time-consuming, subjective, and limited due to differences in access to healthcare across geographic regions [8,9,54]. The sheer volume and complexity of image data often exceeds the capabilities of manual interpretation. In this context, artificial intelligence (AI), particularly machine learning and deep learning techniques, has become an innovating tool in ophthalmology. Recently, AI is becoming a significant part of medicine. Highly advanced AI applications can be used to pre-screen, diagnose, and predict the prognosis of various eye diseases [10,11].

Originally, AI relies on rule-based systems focused on automatic feature extraction, but the development of convolutional neural networks (CNNs) and other deep learning architectures has enabled more accurate detection of retinal pathologies [12]. These models have demonstrated the ability to detect reference corneal retention from fundus examination results with diagnostic performance similar to that of ophthalmologists, representing a breakthrough in the use of AI in medicine. Recent innovations have expanded the use of artificial intelligence (AI) in retinal diseases. Deep learning has been successfully applied to the detection and classification of AMD, allowing for the rapid identification of drusen and early changes in the retinal pigment epithelium, often imperceptible to the human eye [13,14].

Additionally, systems integrating OCT and fundus images – multimodal, sometimes combined with clinical data – have shown greater effectiveness in predicting disease progression and response to treatment [15]. The first FDA-cleared standalone AI system for diabetic retinopathy screening was introduced in 2018, demonstrating its clinical value and highlighting the potential of AI for clinical interpretation [16,18].

Despite numerous advances, certain limitations prevent widespread implementation of artificial intelligence (AI) in everyday medical practice. Generalizability of algorithms remains a significant issue, as systems used in specific populations or on specific imaging devices may not perform well across diverse clinical groups [17].

Furthermore, the "black box" nature of deep learning models raises questions about data confidentiality, which is essential for clinician trust and general acceptance. Ethical considerations, including data privacy, bias in training datasets, and equitable access to AI-assisted care, complicate the implementation of AI in everyday practice [19]. Standardizing training protocols and creating high-quality databases seem essential to ensure reproducibility and high-quality results. The use of AI in teleophthalmology offers the potential to improve patient care, particularly in underserved regions. Screening systems using AI can detect high-risk patients, thereby minimizing treatment delays, enabling early intervention, and improving the quality of care and patient outcomes. Cutting-edge AI models are trained to analyze multimodal data, potentially enabling the simultaneous diagnosis of multiple retinal pathologies [20]. The results seem exciting, but the literature still focuses on the use of AI for treating single diseases or single imaging modalities. A comprehensive understanding of the current status, limitations, and future prospects for AI in ophthalmology is lacking. Bridging this gap is crucial to improving retinal care, especially for patients with limited access to medical care. [14,21].

### **Materials and methods**

This study presents a literature review from the last five years, combining the latest reports on the employment of artificial intelligence in the diagnosis and treatment of AMD. The literature review included randomized controlled trials, clinical trials, and meta-analyses to ensure a reliable and comprehensive assessment of current advances in the field of artificial intelligence.

Publications from 2020–2025 were reviewed, and articles were identified in electronic databases such as PubMed, Scopus, and Google Scholar. The search strategy was based on keywords including "artificial intelligence and age-related macular degeneration" and "artificial intelligence and optical coherence tomography." This approach identified studies addressing AI's diagnostic effectiveness, the competence to monitor disease progression, and the prediction of required treatment based on the analysis of diagnostic images using AI models. Duplicate and irrelevant articles were excluded. The comprehensive nature of the database search and selection of articles identified enabled the selection of appropriate high-quality evidence, enabling a comprehensive review of recent innovations and technological advances regarding the use of AI in the retinal disease AMD.

## Findings

Possibilities of using AI in diagnostics of retinal diseases have increased in recent years. Recent technological advancements allow the use of AI for diagnostics with high accuracy [22]. Throughout the latest scientific reports - deep learning systems (DL), convolutional neural networks (CNNs) and transformer-based or multimodal architectures are characterized by great diagnostic possibilities. That in many cases it is comparable to the expert assessment of clinicians [14,23].

The diagnostic efficacy of AMD is high, but slightly variable. This may be due to the greater number of AMD phenotypes—wet and dry. OCT is more valuable for diagnosing AMD and detecting neovascular changes. In some reviews, the AUC and accuracy for AMD detection range between 90-95% ( $\approx 0.92$  to  $0.96$ ) and sensitivity is 90-94%. It is worth noting that models using OCT imaging often outperform those using only fundus assessment [44].

Multimodal imaging, combining OCT, fundus photography, and sometimes angiography, yields improved diagnostic results compared to single-modality imaging. Recent studies suggest that multimodal imaging increases diagnostic accuracy by 5–7% and AUC by 0.95–0.97 for combined examinations (DR, DME, and wet AMD), suggesting greater sensitivity in detecting subtle retinal abnormalities and more accurate referral and treatment planning. These benefits are particularly important for complex conditions such as diabetic macular edema (DME) and wet AMD. In these complex conditions, changes on OCT provide more information than those on fundus examination [23].

The study of Yu et al., demonstrated that the use of multimodal analysis of OCT examinations and retinal fluid volume measurement by the AI system allows for the effective identification of patients suffering from AMD who require referral with a sensitivity and specificity of  $>90\%$ , and furthermore, it was proven that screening is preferred by patients [26].

Referring to the article by Chen et al., [25] AI models showed higher accuracy and sensitivity in predicting AMD progression - accuracy (mean difference: 0.07, 95% CI: 0.07, 0.07;  $p < 0.00001$ ) and sensitivity (mean difference: 0.08, 95% CI: 0.08, 0.08;  $p < 0.00001$ ) compared to retinal specialists, and specificity was also slightly higher (mean difference: 0.01, 95% CI: 0.01, 0.01;  $p < 0.00001$ ).

In another analysis by Kang et al. [24] the sensitivity and specificity of wet AMD diagnosis based on AI algorithms are similar to diagnoses made by physicians; “the summary sensitivity and specificity were 0.94 (95% confidence interval (CI) 0.90 to 0.97) and 0.99 (95% CI 0.76 to 1.00)”.

Based on the findings of Cheung et al., [30] machine learning achieves very high diagnostic accuracy, sensitivity of 0.918 [95% CI: 0.678, 0.98] and specificity of 0.888 [95% CI: 0.578, 0.98] for AMD screening.

AI is utilized additionally to detect and quantify volume of fluid in the retina. The amount of fluid is one of the most reliable indicators for determining long-term outcome. Application of machine learning to examine total retinal fluid volume using OCT may be beneficial in tailoring interventions and predicting outcomes in patients with neovascular AMD [31,32]. Detection performed by AI has achieved improved accuracy compared to human retinal specialists. This may facilitate detection of fluid in the retina, which is significant for diagnosis, treatment, and prognosis [33].

The diagnostic efficacy of AMD is high, but slightly more variable than in Diabetic Retinopathy. This may be due to the greater number of AMD phenotypes—wet and dry. OCT is more valuable for diagnosing AMD and detecting neovascular changes. In some reviews, the AUC and accuracy for AMD detection range between 90-95% ( $\approx 0.92$  to  $0.96$ ) and sensitivity is 90-94%. It is worth noting that models using OCT imaging often outperform those using only fundus assessment [44].

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AI may also prove beneficial in analysis of retinal imaging. Machine learning models were used to detect visual acuity in patients treated by anti-VEGF injection in 2 years observation. The results turned out to be

promising “R2 of 0.24 to 0.29 (MAE = 9.1–9.8 letters) for predicting VA change and 0.37 to 0.41 (MAE = 9.3–10.2 letters) for predicting actual VA at 2 years”, which can be helpful in decision-making about treatment protocols [34].

Determining the most favorable timing of anti-VEGF injections reduces time requirements and resources that would otherwise be spent on additional, unnecessary interventions. Characterizing an appropriate schedule for each patient, tailored individually to their disease activity and rate of progression, will enable for optimal utilization of human and financial resources in healthcare. In research by Chandra et al., AI was used to assess the need for injections of anti-VEGF over a two-year period in patients with neovascular AMD. Predicting the appropriate timing for injections using an AI model, using readily available clinical data and patient imaging results, can help optimize treatment protocols and outcomes. [38].

Comparable conclusions were shown in the research by Gutfleisch et al. Machine learning (ML) was used to assess the individual -specific time intervals between anti-VEGF injections on patients with neovascular AMD. ML was developed via transfer learning and logistic regression, assessing treatment response based on OCT analysis, and the results proved very promising. Overall accuracy in this research was 78%, which is a notable result, comparable to the assessment by a specialist [35].

A deep learning algorithm was utilized to evaluate the efficacy of the drug and treatment regimen. The study drugs were the anti-VEGF inhibitors brodalumab and aflibercept, and treatment outcomes were evaluated based on intraretinal fluid volume, subretinal fluid volume, and pigment epithelial detachment. Deep learning methods are efficacious in assessing the above-mentioned values, which are essential markers of disease activity and significant for the final visual outcomes. [40].

One of the adverse events resulting from non-neovascular AMD is the occurrence of geographic atrophy, which results in irreversible loss of vision in the central part of the eye. Early indicators of geographic atrophy (GA) include thinning of the photoreceptor and outer nuclear layer. During advanced stages of the disease, subsidence of the outer plexiform layer occurs. Methods of detection that subclinical features are AI models, based on regular (one in 6 months) OCT imaging. Moreover, AI-based tools aid guidance for the treatment of GA in clinical practice [36,41,42].

AI capabilities in OCT imaging analysis were also used to assess the effectiveness of pharmacological treatment for geographic atrophy. Accurate OCT image analysis based on deep learning allows for highly sensitive assessment of local progression rate by estimation of retinal pigment epithelium loss, photoreceptor integrity, and hyperreflective foci, which correlates well with advancement of the disease. [36,37].

Based on the research by Mai et al., it appears that OCT analysis performed by AI is suitable for surveillance disease progression in patients with geographic atrophy secondary to AMD treated with complement inhibitors. [39].

Convolutional neural network (CNN), type of deep learning network that learns from filter or kernel optimization [27]. CNN processes various data types like images, text and audio. CNN is a common algorithm used in AMD detection, specially ResNets are efficient in identifying AMD, with elevated diagnostic efficacy. To create CNN models more reliable, new data would be employed to train the model, such as new diagnostic methods: FFA, ICGA and ultra-widefield retinal images [28].

Neural networks typically are trained by supervision, using human generated labels, which requires substantial time and entails extra expenses. What the Yellapragada et al., study showed neural networks may exert significant influence even as a self-supervised model. In the described research self-supervised neural networks showed equivalent effectiveness as supervised ones or ophthalmologists in categorizing advanced AMD [29].

An innovative study by Abdelmotaal et al., considers the use of a generative adversarial network (GAN), specifically a pix2pix GAN architecture, to synthesize difficult-to-obtain medical images. Generating synthetic images can be helpful in many clinical situations. This is particularly useful when an imaging modality is unavailable or a given examination cannot be performed due to a patient's health conditions. The results suggest that the pix2pix GAN network can generate clinically useful images, comparable in quality to real-world images. However, despite its promising capabilities, this technology is not yet advanced enough to be implemented in everyday medical practice, and rather, it offers interesting prospects for future development. [43].

The implementation of AI in teleophthalmology yielded results comparable to traditional ophthalmological examinations. A large study demonstrated a sensitivity of 92–96% in terms of reference drug retention when combining AI with remote screening methods. This may suggest significant assistance through the use of AI, which will improve screening, especially those performed via teleradiology, without compromising diagnosis. The specification of algorithms should be taken into account; the quality of

diagnostic images seems crucial, as well as appropriate adaptation of the protocol to the clinical situation (nonmydriatic or mydriatic imaging). It is important that standardized protocols for the evaluation of diagnostic tests are developed in the future [23,45,46].

Despite numerous unexpected yet promising findings, limitations still remain. High-performance models were biased toward the specific device used in a given analysis, and the dataset was also relatively homogeneous. When testing these models on external populations or across different imaging devices, performance often decreased. The disparity between study groups—low representation of rare disease phenotypes (inherited retinal diseases or some AMD subtypes)—and varying image quality across clinical centers also reduce sensitivity, especially for less common conditions [47]. These findings may justify the need for domain adaptation, federated learning, and differential database selection to improve results across centers [48].

Recent developments aim to overcome these limitations. Significant developments have occurred in hybrid and transformer architectures designed to provide better access to long-range information and multimodal imaging. These architectures protect the confidentiality of the data used to train these systems. These training systems improve external validity without sharing raw data; and allow for the creation of models capable of simultaneously classifying retinal and optic nerve disorders. Previous multimorbidity classification and disease-independent screening models have demonstrated high accuracy (AUC and accuracies often exceed 93%). Consequently, there is a shift from models capable of classifying single diseases to comprehensive retinal screening tools. [49]. In summary, the research data demonstrate that AI used to assess ophthalmological conditions related to retinal diseases has reached good diagnostic maturity for several tasks: AMD detection, especially when OCT is included and improvement of teleophthalmology. Persistent shortcomings include the diversity of databases and the difficulty of resolving uncertainties in real-world conditions; improving the above-mentioned shortcomings will be crucial for the clinical implementation of AI models [14,17].

## Discussion

The dynamic technological progress in recent years, including advances in artificial intelligence (AI) and deep learning (DL), suggest promising potential about the prospects of integrating these technologies in routine clinical practice. Ophthalmology, a medical field, is particularly conducive due to the considerable number of imaging tests employed in ophthalmic diagnostics. Retinal diseases, particularly AMD, are showing an increasing prevalence. AMD is one of the principal causes of visual impairment. A progressively aging population and the high prevalence of lifestyle diseases indicate that the incidence of AMD will rise substantially, and the patient population is expected to expand [1,2]. This raises the need to develop appropriate diagnostic methods that can be used for screening tests. Methods to shorten waiting periods for first appointment, enable appropriate follow-up of patients currently impacted by AMD, and methods that individualize treatment regimens are also crucial [3,4]

Diagnostic modalities commonly employed for the diagnosis and management of AMD include fundus examination, OCT, FAF, AF, among others. All of these tests can be conducted by optometrists, but their interpretation currently remains the domain of a specialist. Compounding the problem is that retinal specialists are encumbered by the analysis of substantial volumes of data, constraining their accessibility to patients. The application of AI models to evaluate imaging studies appears transformative in this context. This would streamline clinical workflows, facilitate more consistent patient monitoring, and enhance accessibility to healthcare services in areas with constrained access with limited access to specialized medical care [8,9,13]

Recent research demonstrates that AI can achieve diagnostic accuracy in OCT interpretation comparable to, and sometimes exceeding, that achieved by retinal specialists. However, despite their positive results, the research results themselves do not address the clinical challenges associated with the hypothetical implications of AI for everyday use [7,10,11].

One of the main issues to be addressed is the security of personal data, the confidentiality of which should not be compromised. AI has enormous potential, but limitations that must be addressed before the technology can move from the estimation phase to routine use. Explainability is the primary determinant for the restricted acceptance of AI in everyday clinical practice. Most AI models function as "black boxes". Black box is a term describing how AI operates when it delivers accurate, highly reliable results in a manner non-interpretable to the end-user, but the sequence of actions required for the AI to deliver such a result is inaccessible to the user [14,19,21,50].

A widely documented constraint is the dataset bias used to train AI. Most AI models were evaluated based on results obtained from a highly homogeneous cohort or using a single imaging device. Such

homogeneity can lead to limitations in the obtained results, limiting their generalizability to the entire population and across different imaging devices [14]. The integration of AI into teleophthalmology is one of the most promising applications of this technology, with the use of AI for screening tests seeming particularly promising [50]. Such an innovation seems highly advantageous not only from an economic perspective, but more importantly, it would enable more patients to have access to specialist healthcare services, thus mitigating geographic and socioeconomic disparities in access to medical care. AI's capabilities include remotely acquiring diagnostic imaging, storing them, evaluating the results, and generating patient-directed feedback, thus referring patients for further tests if necessary. Recently, the use of AI to evaluate multimodal models has become popular. This approach appears particularly advantageous because when several tests, such as an OCT and fundus examination, the specificity and sensitivity in diagnosing or assessing AMD progression is higher. Traditional methods based on the examination of the fundus of the eye are being superseded by systems integrating many imaging methods such as OCT, fundus autofluorescence or fluorescein angiography. [23,26,51] Cross-device and cross-population validation remains a persistent obstacle. Promising methodological innovations may be federated learning, where models are trained across sites, increasing data diversity. The ethical implications of implementing AI in medicine is also increasingly being considered. The objective of AI's application in ophthalmology is not to supplant clinicians, but to support them in diagnosis. Hybrid models where AI guides patient selection and clinicians interpret results can significantly reduce clinicians workload without compromising quality [48]. Based on the analysis of the cited studies, it can be concluded that AI has evolved from a conceptual framework into a diagnostic tool supporting clinical decision-making. Fully harnessing its clinical potential requires addressing key limitations that currently limit AI implementation in everyday practice. Improving validation, eliminating bias and clarifying ethical issues would enable full use of AI's capabilities.

#### **Future directions**

Although recent advances have demonstrated that AI can meet or exceed the experts-level performance in interpreting imaging tests in AMD patients, the forthcoming decade will define whether these technologies develop into transparent, safe, and widespread diagnostic tools. Future research should prioritize clarifying the transparency and interpretability of the models to enhance clinician confidence and enable clinical acceptance. [14]. In the future, AI could analyze multimodal data, support longitudinal patient management and disease monitoring, before clinical symptoms appear. [52,53]

#### **Authors Contributions**

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