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Potential performance of artificial intelligence in diagnosis of hypertensive retinopathy: A systematic review and meta analysis from current evidence

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Systematic Review

ABSTRACT

Hypertensive retinopathy (HR) is a retinal condition caused by chronic hypertension that often progresses silently and usually detected incidentally, making early diagnosis essential to prevent further progression. While current evaluations rely on ophthalmologists or retinal specialists, artificial intelligence (AI) offers a promising, time-efficient, and resource-effective alternative for HR diagnosis. This study aims to provide a robust and reliable evaluation of the diagnostic potential of AI for hypertensive retinopathy through a comprehensive systematic review and network meta-analysis, which has not been previously reported. An extensive literature search was conducted across six databases, including PubMed, ScienceDirect, SpringerLink, Taylor & Francis Online, ProQuest, and Sage Journals. The inclusion criteria were diagnostic studies published within the past decade that involved both healthy populations and patients with hypertensive retinopathy, in which the diagnosis of hypertensive retinopathy was performed by artificial intelligence and compared with that of ophthalmologists. The primary outcomes of interest included the sensitivity, specificity, and accuracy of AI in diagnosing HR from fundus image photography. Quality assessment was performed using the quality assessment of diagnostic accuracy studies (QUADAS) tool, and meta-analysis was conducted using STATA. From 1,530 articles screened, 10 studies were included in this analysis, comprising a total of 38,761 fundus images. A total of 38,761 fundus images from 10 studies were included in this analysis. The results indicated that AI demonstrated high sensitivity [90% (95% CI: 86% – 93%)] and specificity [95% (95% CI: 92% – 97%)] with p-value of 0.001. Based on these findings, AI shows promise as a future diagnostic option for HR due to its high sensitivity and specificity.

INTRODUCTION

Hypertension currently represents a significant epidemiological issue, resulting in approximately 10 million fatalities annually. The HR represents a form of retinal angiopathy induced by hypertension. In the initial phases, individuals with hypertension may exhibit no pathological alterations. Increased systemic arterial pressure in patients with hypertension may result in fundus changes, including a reduced retinal arteriovenous diameter ratio, arteriosclerosis retina, and haemorrhage.[1] In comparison to the more severe fundus lesions observed in patients with HR, timely diagnosis and treatment of early fundus changes may allow for reversibility of these alterations. Early screening and diagnosis can effectively prevent its progression.[2]

Professional skills and experience are necessary for the driven manual diagnosis of HR. Furthermore, screening presents significant challenges, particularly in developing countries and rural regions, due to insufficient healthcare facilities and low public awareness. Conversely, systems based on AI are anticipated to address the aforementioned challenges efficiently. Artificial intelligence is a science that investigates ideas, methods, and technologies to simulate and expand human intelligence.[3] The AI has demonstrated limitless promise since its 1956 proposal and has been instrumental in picture recognition, data mining, and language processing. The AI technology has advanced quickly in recent years and is now widely used in many different sectors. Among these, AI image analysis technology has advanced significantly, especially in the field of ophthalmology. Recently, the main research on AI in ophthalmology is to analyze fundus images for assisting the diagnosis of eye diseases, including hypertensive retinopathy.[4]

It is efficient in terms of time, requires fewer human resources, and enhances diagnostic accuracy. Consequently, the automatic diagnosis of hypertensive retinopathy proves advantageous.[5,6] To date, there have been no published studies in the form of meta-analysis that present the latest developments on the use of AI in the diagnosis of hypertensive retinopathy. It is anticipated that this analysis will contribute to the advancement of scientific understanding in this field, along with the identification of potential areas for future research and more effective clinical applications of AI for the diagnosis and treatment of hypertensive retinopathy. This systematic review and meta analysis aims to provide a comprehensive and up-to-date perspective on the state of research in the use of AI in hypertensive retinopathy analysis in ocular images.

METHODS

Eligibility criteria

Before conducting the literature review, inclusion and exclusion criteria were established to enhance the specificity of the review. Diagnostic studies published within the past decade were included in the criteria. The PICOs framework serves as a basis for defining inclusion criteria that comprise: 1) Population: the normal population (without hypertensive retinopathy) and patients with hypertensive retinopathy; 2) Intervention: interpretation of fundus image and diagnosed hypertensive retinopathy by artificial intelligence; 3) Comparison: interpretation and diagnosed by (ophthalmologist or retinal specialist); 4) Outcome: sensitivity and specificity in hypertensive retinopathy diagnosed; 5) Study design: diagnostic study. Exclusion criteria were adopted: 1) non-human trials and studies; 2) diagnostic studies that did not specify retinopathy abnormalities; 3) non-English studies; 4) gray literature. There is no predefined duration for the studies included in this review. However, the majority of the studies have a follow-up period ranging between 3 and 12 months.

Information sources and search strategy

The literature review was conducted by two independent researchers (EDP and NAD). Several databases were used, including PubMed, ScienceDirect, SpringerLink, Taylor & Francis, ProQuest, and Sage Journal. The keywords used ("hypertensive retinopathy" OR "HR") AND ("artificial intelligence" OR "AI" OR "machine learning" OR "deep learning") AND "diagnostic study".

Selection process

Subsequently, two independent researchers (EDP and NAD) independently extracted and processed the selected studies into a google sheet. Subsequently, all authors evaluated the accuracy and eligibility of the information. Subsequently, EDP and the supervising authors conducted an analysis and reported the findings. Disagreements arising during the writing process were resolved through discussions, and when necessary, an external independent member (not listed as an author) was consulted to facilitate consensus.

Data items

In recent years, researchers have been interested in the capabilities of AI in various fields, including the medical domain, particularly in diagnostics and therapy. The rapid and advanced capabilities of AI offer significant advantages, especially when applied to medical diagnostics. So, the primary objective of this paper is to diagnose hypertensive retinopathy in patients quickly and accurately using AI, thereby assisting clinicians. ophthalmologist, and retinal specialist. This includes AI to interpret fundus image photography and classify it into HR or non HR compared to clinicians, ophthalmologists, or retinal specialist’ssinterpretation. A review was carried out to ascertain their sensitivity and specificity.

The comprised articles were limited to publications from the past 10 years that applied artificial intelligence in the form of both machine learning and deep learning. This review was based on the reported values of true positives, false positives, true negatives, and false negatives in each study. This study’s primary outcome of interest is sensitivity and specificity, which determines the diagnostic accuracy, of diagnostic patients with hypertensive retinopathy. Whereas the secondary outcome of interest is the cut-off value and consistency within the diagnostic based on the value of theta and beta results.

Study risk of bias assessment

A risk of bias in the selected studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) 2 tool for diagnostic studied by EDP. The other authors supervised the process. The tool considers four domains: patient selection, index test, reference standard, and flow-timing.

Effect measures and synthesis methods

The meta-analysis was conducted using STATA 17.0, with the primary effect measure of this review being the pooled sensitivity and specificity that evaluated based on the values of true positive, false positive, false negative, and true negative, with a 95% confidence interval (CI). Heterogeneity analysis was done using STATA 17.0, where an I2 score of above or equal to 50%. In contrast, the p-value below 0.05 indicates a significance result. Besides that, the author explored the Receiver Operating Characteristic (ROC) curve analysis or Hierarchical summary receiver operating characteristic curve (HSROC) model as the secondary effect measure They are theta and beta values to identify cut-off values and consistency.

RESULTS

Study selection

After conducting a literature search, 1,530 articles published in the past ten years across six databases were identified. Several articles (n=1,164) were automatically excluded by the databases due to not meeting the study design criteria. Additionally, 254 articles were excluded because they did not meet the eligibility criteria, such as review articles, books, and paid articles. Furthermore, 102 articles were excluded for not meeting the inclusion criteria. Figure 1 shows the PRISMA flow diagram. Ultimately, 10 articles were included in this study.

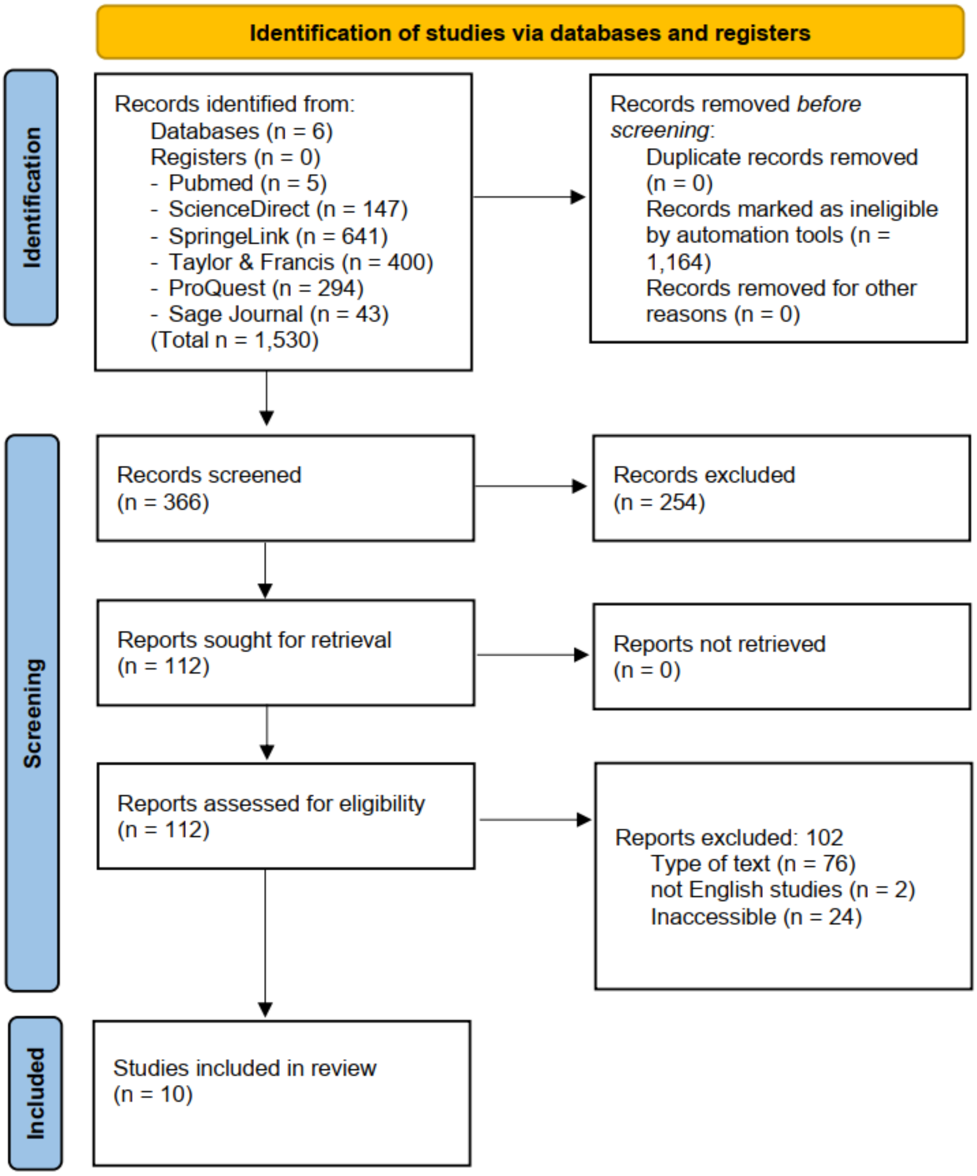

Figure 1. PRISMA flowchart of study selection

Risk of bias in studies

All studies demonstrated strong performance in patient selection, index text, and provided information about reference standard, as assessed for risk of bias. The studies incorporated in this meta-analysis exhibited inadequate performance in evaluating the flow and timing of patient selection. All studies demonstrated a low risk regarding clinical applicability concerns when assessing patient selection, the index test, and the reference standard. This demonstrates the substantial credibility of the meta-analysis. The remaining studies are assessed as having a low risk of bias (Figure 2).

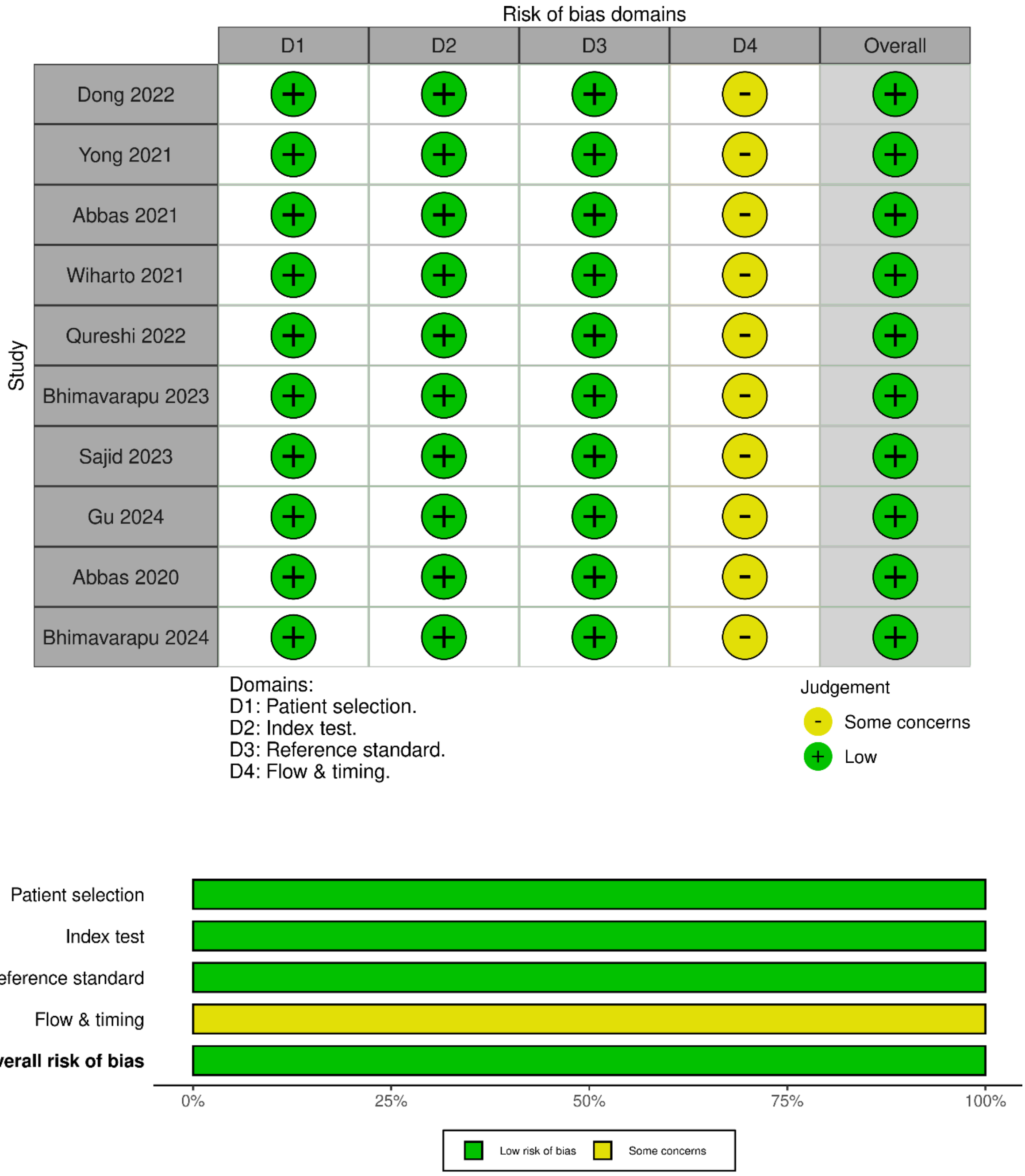

Figure 2. QUADAS 2 tool: Traffic light plot and summary plot

Summaries of included studies

Ten studies were included in this review, which focused on deep machine learning as the artificial intelligence while interpreting the fundus image photography compared to clinicians, ophthalmologists, and retinal specialists's interpretation. Table 1 shows the included studies involved in this meta-analysis.

Table 1. Included studies

No	Author, year	Country	Pixels (Image)	Sample (Image)	True positive (tp)	False positive (fp)	False negative (fn)	True negative (tn)
1	Dong 2022 [7]	China	NA	8,198	1,379	1,699	261	4,859

No	Author, year	Country	Pixels (Image)	Sample (Image)	True positive (tp)	False positive (fp)	False negative (fn)	True negative (tn)
2	Yong 2021 [8]	China	800 x 660	51.481	8,370	7,104	1,926	34,081
3	Abbas 2021 [9]	West Asia	700 x 660	1,400	253	95	27	1,025
4	Wiharto 2021 [10]	Indonesia	NA	25	4	2	1	18
5	Qureshi 2022 [11]	West Asia	700 x 600	9,500	1,786	304	114	7,296
6	Bhimavarapu 2023 [12]	West Asia	525 x 525	152	29	5	1	118
7	Sajid 2023 [13]	West Asia	700 x 600	9,170	1,816	73	18	7,263
8	Gu 2024 [14]	China	NA	4,795	719	38	240	3,798
9	Abbas 2020 [15]	West Asia	700 x 600	4,270	794	171	60	3,245
10	Bhimavarapu 2024 [16]	West Asia	NA	1,200	237	15	3	945

Sensitivity and specificity of AI for the diagnosis of HR

Out of the ten studies from 38,761 fundus image photography total, sensitivity and specificity were the outcomes of interest while using the values of true positive, false positive, false negative, and true negative. The secondary objective of interest pertains to the threshold value and the consistency within the diagnostic, based on the theta and beta results.

The first analysis is the primary outcome related to sensitivity and specificity. Data analysis indicates high sensitivity, specifically 90% (95% CI: 86%–93%). Similarly, specificity was also high, at 95% (95% CI: 92%–97%). The analysis results were statistically significant, with a p-value of 0.001 (Figure 3). The second analysis is the secondary outcome related to the cut-off value and consistency. In this review, cut-off and consistency are mentioned by HSROC (Hierarchical summary receiver operating characteristic curve). A theta value as the cut-off shows a great value of -0.182 which indicates thateven with a low cut-off value in AI application, a high accuracy is achieved through elevated sensitivity and specificity. However, the consistency (beta value=0.03) is relatively low (Figure. 4).

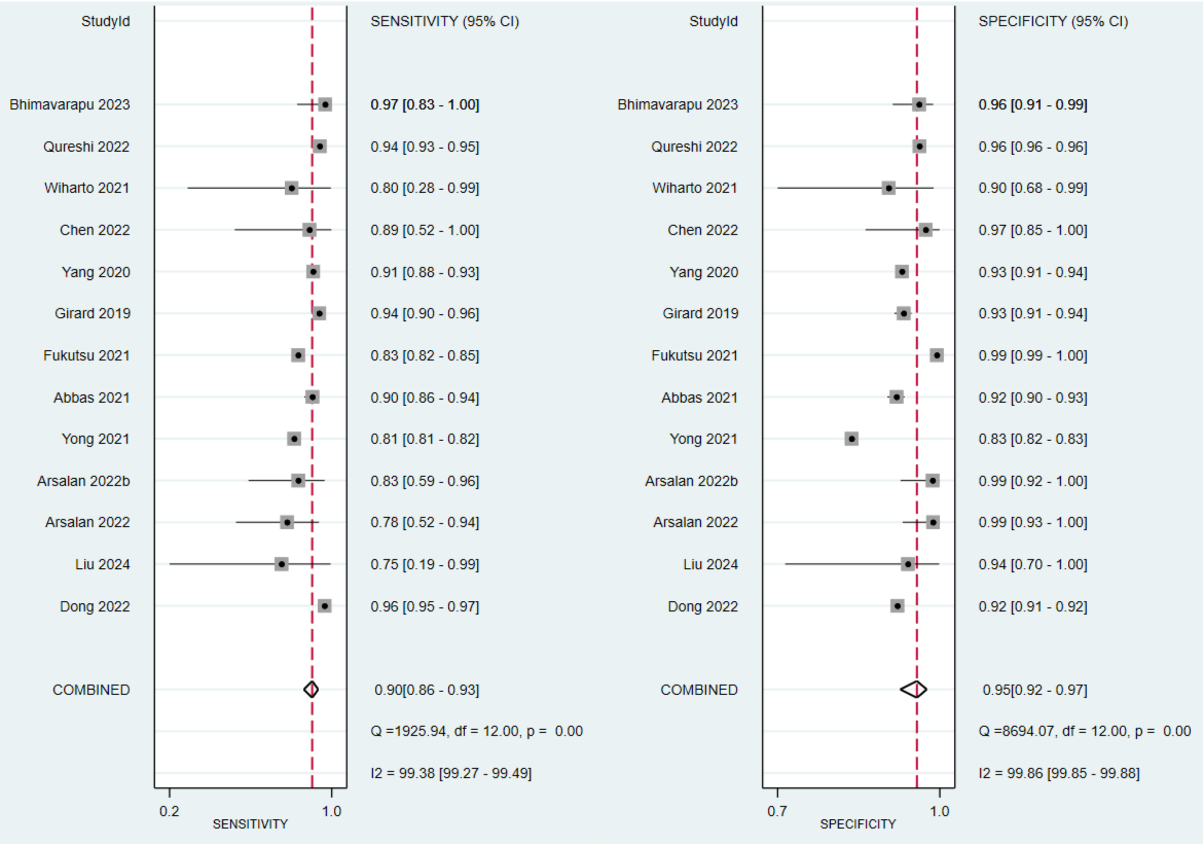

Figure 3. Forrest plot diagram of AI performance in the diagnosis of hypertensive retinopathy.

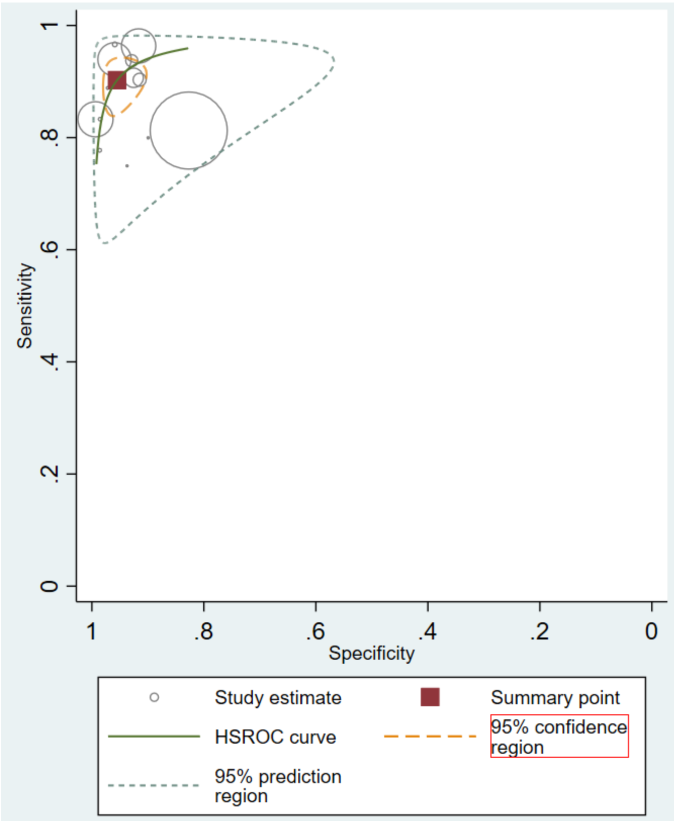

Figure 4. HSROC model.

DISCUSSION

This meta-analysis demonstrates that artificial intelligence (AI) exhibits promising diagnostic efficacy in detecting hypertensive retinopathy (HR), based on evidence from ten prospective studies involving a total of 38,761 eyeballs. The results indicate that AI shows superior diagnostic efficacy for HR, with a sensitivity of 90% and specificity of 95% across all studies analysed. The study reveals a false negative rate (FNR) of 10% and a false positive rate (FPR) of 5%, indicating notable concerns. In this review, AI can achieve high diagnostic accuracy even when operating at relatively low cut-off thresholds. However, the analysis also reveals a relatively low level of consistency across studies, indicating variability in model performance. Such inconsistency may stem from differences in data quality, image acquisition techniques, or algorithmic parameters used in each study. In this review, systematically selecting and evaluating studies conducted in real-world clinical settings, this analysis ensures methodological rigor and minimizes the biases often encountered in retrospective designs. Collectively, these methodological strengths enhance the reliability and clinical applicability of the findings, contributing to a more balanced understanding of AI's diagnostic potential in hypertensive retinopathy.

AI has emerged as a transformative tool in ophthalmology, particularly in the detection and classification of retinal diseases such as HR. Numerous studies have highlighted the potential of AI to enhance diagnostic precision, reduce human error, and facilitate early disease detection. However, inconsistencies in diagnostic performance across previous investigations have been observed, which may stem from variations in fundus image quality, algorithmic design, and camera performance.[7–16] These discrepancies underscore the need for a more systematic and comprehensive evaluation of AI diagnostic capabilities in HR.[17] Employing AI to assess hypertensive retinopathy in ocular images reflects a progressive step forward in the evolution of ophthalmology and diagnostic technologies.[18]

Our analysis demonstrated that the included studies were conducted in diverse clinical environments, including hospitals, outpatient clinics, and medical research centers. The variability in diagnostic performance across these settings may be attributed to differences in patient characteristics, data collection protocols, and clinical expertise.[7–16] Studies conducted in research institutions often employ more standardized imaging procedures and involve expert ophthalmologists in diagnosis, resulting in greater precision and lower error rates compared to routine clinical settings.[19] Such discrepancies can influence the training and validation processes of AI models, as image quality, labeling accuracy, and population representativeness are critical determinants of algorithmic performance and generalizability.[20–22] Despite the inclusion of consistency metrics and defined diagnostic thresholds, a considerable degree of heterogeneity was observed among the studies. Sensitivity and specificity remained the primary measures for assessing the diagnostic correlation between AI-derived outcomes and hypertensive retinopathy. This variation likely results from differences in algorithm architecture, fundus camera resolution, and labeling protocols, all of which may affect diagnostic thresholds and performance outcomes.[23]

This meta-analysis demonstrated that AI achieved high diagnostic accuracy for hypertensive retinopathy, with pooled sensitivity and specificity values of 90% and 95%, respectively, across all included studies. These findings reinforce the growing body of evidence supporting AI as a powerful diagnostic tool in ophthalmology. Recent advancements in AI-based image analysis have revolutionized medical research and clinical applications, enabling automated and precise interpretation of ocular images. In ophthalmology, AI systems particularly those utilizing deep learning, can detect, classify, and monitor retinal diseases such as diabetic and hypertensive retinopathy with performance comparable to that of trained specialists.[24] Beyond diagnostic accuracy, the global shift toward digital health during the COVID-19 pandemic has further emphasized the importance of AI-assisted diagnostics. The ability of AI to process large datasets and provide remote image interpretation has facilitated continuity of care when in-person consultations were limited. As retinal disease diagnosis often depends on the availability of subspecialty expertise, AI offers an opportunity to expand screening coverage, especially in resource-limited or rural settings where ophthalmologists are scarce. Furthermore, with the rapid increase in the global aging population, the integration of AI into clinical workflows could accelerate early detection and intervention for sight-threatening conditions, ultimately reducing preventable blindness and improving population eye health outcomes.[25]

There are several terms and classifications in AI that need to be known to make it easier to understand the application of AI for retinal disease. The AI represents a phenomenon wherein non-living entities replicate aspects of human intelligence. Machine learning (ML) is a subfield of artificial intelligence where a program performs tasks by processing large datasets and progressively identifying patterns, categorizing data into distinct classes. Deep learning (DL) is a subset of machine learning, characterised by the utilisation of multiple layers of artificial neural networks (ANN). The DNN refers to multi-layered deep learning algorithms, frequently comprising more than 100 hidden layers. Convolutional neural networks (CNNs) are a specific category of deep neural networks (DNNs) that are particularly effective for the analysis of images and videos.[26,27] These algorithms segment files into pixels, convert them into numerical or symbolic representations, and analyse it into a dense neural network to generate an output layer.[28]

All research in this review used image resolutions of about 700 × 660 pixels. Improved image quality has been associated with enhanced diagnostic outcomes in previous studies.[29] Evidence suggests that extended algorithm training, the use of larger datasets, and enhanced data quality contribute to improved diagnostic accuracy of AI models. Studies have consistently shown that diagnostic efficacy increases with the volume and diversity of training data. For instance, Gulshan (2016) trained a deep-learning model using 103,698 retinal fundus images, achieving high sensitivity (97.5%) and specificity (93.4%) for detecting retinopathy in an independent validation set.[30] Similarly, Ting (2019) analyzed 208,758 retinal images from 110,784 participants, demonstrating improved diagnostic accuracy across multiple retinal diseases, including hypertensive and diabetic retinopathy.23 A more recent meta-analysis incorporating over 1.3 million retinal images further confirmed that models trained on larger and more diverse datasets exhibit greater robustness, reduced overfitting, and higher generalizability in real-world clinical applications.[31] These findings suggest that the inclusion of high quality research, characterized by extensive AI model training and robustly designed clinical trials, likely contributes to the greater consistency and reliability observed in diagnostic performance.[32]

The study revealed a false negative rate (FNR) of 10% and a false positive rate (FPR) of 5%, indicating notable concerns. Although AI holds potential as an innovative diagnostic instrument, it continues to encounter significant challenges. To address these issues, further investigation of imaging features, augmentation of training and test set sample sizes, and enhancement of algorithm performance are all feasible strategies.[33] Ophthalmologists will be essential in evaluating the clinical efficacy of AI technologies and in synthesising complementary imaging data with clinical information to enhance diagnostic insights.[5] While AI is capable of independently diagnosing HR issues, the responsibility for issuing reports and assuming legal risks will rest with ophthalmologists. Legislation is necessary to clarify the responsibilities of physicians and AI service providers, thereby promoting the wider implementation of AI diagnostic services.[34,35] Both doctors and patients currently maintain a favourable perspective on the diagnostic efficacy of AI, potentially facilitating future collaboration.[36]

Our meta-analysis revealed that AI demonstrates high diagnostic accuracy for hypertensive retinopathy, achieving a pooled sensitivity of 90% and specificity of 95%. Despite these promising results, several challenges persist in the practical implementation of AI-based diagnostic systems. A significant challenge in employing AI is the "black box phenomenon", which refers to AI systems characterised by opaque internal mechanisms, rendering their internal workings challenging or impossible to comprehend. Users receive inputs-outputs; however, the reasoning process underlying outputs is not disclosed. The accessibility and affordability of these systems present challenges for the developing world, despite primary concerns related to image quality, incomplete datasets, and the occurrence of false positive and false negative results.[33] The development, validation, testing, and implementation of these AI models necessitate significant financial resources, which may serve as a considerable constraint. Evaluating the financial implications of AI in the diagnosis of retinal diseases is complex due to its restricted application in routine practice. Preliminary evidence indicates that AI has the potential to lower costs.[37]

In addition to the "black box phenomenon," where the internal mechanisms of AI systems are unclear, there are concerns regarding image quality and misclassifications that considerably affect the accuracy.[38] Misidentifying vessels or confusing arteries with veins can result in incorrect conclusions.[39] Furthermore, although AI systems provide significant insights, the ultimate responsibility for decision-making remains with doctors, underscoring the necessity for accountability and transparency in their application. In the future, there is a growing desire to explore new AI techniques, like federated learning and transfer learning, to make AI models work better and be more useful in a wider range of clinical situations and populations.[33] AI technologies and turning them into useful tools for doctors and patients around the world. This review aims to encourage more progress and new ideas in the field of AI-driven retinal disease diagnosis by looking at these future views and research paths.[40,41]

This systematic review has several limitations that should be acknowledged. Variability in fundus camera manufacturers, image quality, and clarity across the included studies may have influenced diagnostic accuracy and contributed to heterogeneity in the findings. In addition, although the QUADAS-2 tool was applied to minimize bias, some methodological differences between studies, such as patient selection and reference standards could not be fully standardized. Nonetheless, a strength of this review is its comprehensive search strategy across multiple databases and the use of a validated tool to assess study quality, which enhances the robustness of the evidence synthesis. Future studies are recommended to employ standardized imaging protocols, ensure high-quality image acquisition, and conduct multicenter trials to improve the generalizability and reliability of artificial intelligence applications in diagnosing hypertensive retinopathy.

CONCLUSION

Artificial Intelegence demonstrates high diagnostic accuracy in detecting hypertensive retinopathy HR, offering substantial potential to support clinical decision making, treatment planning, and patient follow-up. To further enhance diagnostic performance, future research should prioritize the use of larger, multicenter datasets; improved patient data quality; advanced feature extraction; optimized algorithm design; and high resolution imaging. Integrating AI with ophthalmologists' clinical expertise will be crucial for strengthening early HR screening, diagnosis, and management while improving efficiency and healthcare resource utilization.

CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REGISTRATION AND PROTOCOL

This review has been reviewed and registered with PROSPERO-NIHR (International prospective register of systematic reviews – National Institute for health research) under registration number CRD42025644580.

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DATA AVAILABILITY STATEMENT

The data will be made available upon reasonable request.

SUPPLEMENTARY MATERIALS

All methods, analyses, figures, and tables essential to the study are fully presented in the main manuscript; no supplementary material is provided.

AUTHOR CONTRIBUTIONS

EDP and NAD have the equal contribution: Conceptualitation, formal analysis, writing draft preparation, and validation. All authors have read and agreed to the published version of the manuscript.

DECLARATION OF USING AI IN THE WRITING PROCESS

We affirm that the preparation of this article did not involve the use of any artificial intelligence tools.

LIST OF ABBREVIATIONS

AI: Artificial intelligence; ANN: Artificial neural network; CNNs: convolutional neural networks; DL: Deep learning; DNN: Deep neural networks; FN: false negative; FNR: false negative rate; FP: false positive; FPR: false positive rate; HR: hypertensive retinopathy; HSROC: Hierarchical summary receiver operating characteristic curve; ML: Machine learning; PICOs: Population, Intervention, Comparison, Outcome, Study design; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO-NIHR: International Prospective Register of Systematic Reviews – National Institute for Health Research); QUADAS: Quality assessment was performed using the Quality Assessment of Diagnostic Accuracy Studies; ROC: Receiver Operating Characteristic; TN: true negative; TP: true positive.

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