Beyond Vision: Potential Role of AI-enabled Ocular Scans in the Prediction of Aging and Systemic Disorders

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ABSTRACT

In all medical subfields, including ophthalmology, the development of artificial intelligence (AI), particularly cutting-edge deep learning frameworks, has sparked a quiet revolution. The eyes and the rest of the body are anatomically related because of the unique microvascular and neuronal structures they possess. Therefore, ocular image-based AI technology may be a helpful substitute or extra screening method for systemic disorders, particularly in areas with limited resources. This paper provides an overview of existing AI applications for the prediction of systemic diseases from multimodal ocular pictures, including retinal diseases, neurological diseases, anemia, chronic kidney disease, autoimmune diseases, sleep disorders, cardiovascular diseases, and various others. It also covers the process of aging and its predictive biomarkers obtained from AI-based retinal scans. Finally, we also go through these applications existing problems and potential future paths.

Keywords: AI-Driven ocular scans, Area under the curve (AUC); deep learning; retinal age (RA); fundus autofluorescence; ROPtool; Convolutional Neural Network (CNN); Color Fundus Photography (CFP); Machine Learning (ML) (Siriraj Med J 2024; 76: 106-115)

INTRODUCTION

In the realm of artificial intelligence (AI) within computer science, algorithms are trained to perform human-like tasks, spanning areas like robotics, natural language processing, and machine learning.[1] AI's rapid response, decision-making, and learning capabilities have led to its widespread use in recommendation algorithms, search engines, and autonomous vehicles. The eye's unique translucent refractive interstitium allows for the non-invasive assessment of blood vessels and nerves, making it a valuable diagnostic tool for systemic conditions such as diabetes and hypertension.[2] With advancements in AI techniques, ocular images have become crucial in diagnosing diseases like diabetic retinopathy, age-related macular degeneration (AMD), and glaucoma.[3-5] AI enables the identification of previously unseen associations between ocular features and systemic illnesses, expanding diagnostic possibilities. Recent studies have linked ocular characteristics to diseases like diabetes, cardiovascular issues, Alzheimer's, and kidney disease. This review aims to summarize the latest developments in ocular image-based AI's applications in diagnosing various systemic diseases.

Search strategy and article selection

A search strategy was implemented to identify and review the literature pertaining to the application of AI in ophthalmology and its relation to various other disorders

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via searching through engines like PubMed, MEDLINE, Scopus, and Google Scholar using the keywords "AI-enabled retinal scans," "aging biomarkers", "artificial intelligence," "machine learning," "deep learning," "artificial neural networks," "Retinal age," and "natural language processing".

Inclusion criteria

Articles related to artificial intelligence in ophthalmology; Original articles of full-text length covering the diagnostic capabilities and AI in ophthalmology and its relation to various other disorders.

Exclusion criteria

Abstracts, editorial comments, and chapters from books; Animal, laboratory, or cadaveric studies. Non-ophthalmic studies.

Artificial intelligence

Artificial intelligence (AI) involves computer-based simulations of intelligent behavior with limited human intervention. The inception of robots marked the beginning of AI, with the term "robot" originating from the Czech word "robota", denoting bio-engineered devices for forced labor.[6] AI in medicine encompasses virtual and physical domains. The former encompasses deep learning, information management, and decision support systems, while the latter involves robots assisting patients and physicians in an innovative engineering field addressing complex problems. Speed, capacity, and software advancements could eventually enable computers to match human intelligence. Modern cybernetics has significantly contributed to AI progress.[6] Medical AI tackles the challenge of assimilating and applying vast clinical knowledge. AI systems aid clinicians in diagnosing, treatment decisions, and outcome predictions. Techniques like deep learning, and non-neural networks are used. Deep learning (DL) has transformative potential in healthcare, mapping inputs to outputs across interconnected neuron layers. DL excels in clustering, regression, classification, and prediction tasks. However, it is more resource-intensive than traditional machine learning methods, particularly in imaging. Supervised and unsupervised learning, along with semi-supervised learning are also some of the training strategies that can be acquired through this mechanism. Area under the curve (AUC) is one of the metrics utilized by the AI, the receiver operating characteristic (ROC) area under the curve (AUC) quantifies the model's overall ability to distinguish between positive and negative instances. Plotted on the ROC curve are the true positive and false positive rates at different categorization criteria. AUC 1 indicates an error-free model, while AUC 0.5 indicates a random estimating model. Because AUC is a crucial metric for assessing an AI algorithm's efficacy, a higher AUC suggests improved prediction accuracy and offers pertinent details regarding how well an AI model can differentiate between multiple classes. However, it does not fully capture the utility of a model in a clinical setting as different tasks, such as screening, may require separate sensitivity metrics.[6,7]

As healthcare data is so vital, data mining has emerged as a significant and challenging field in the healthcare industry. Recent developments in data mining techniques have established a solid basis for a multitude of uses, such as disease diagnosis, pattern recognition, enabling patient-friendly and affordable medical treatments, and intrusion detection. Artificial intelligence supports this process by functioning as a machine learning subfield to improve predictive capabilities. Three well-known supervised learning classifiers are used in the field of classification and prediction: Random Forests, Support Vector Machines (SVM), and Naive Bayes. Based on Bayes' theorem, Naive Bayes is a probabilistic classifier that is independent of features. SVM is an effective classification method that finds the best hyperplane to divide classes. SVM and Naive Bayes both improve the precision of medical predictions. Robust ensemble learning techniques like the Random Forest algorithm make a substantial contribution to classification tasks by preventing overfitting, optimizing model performance, and utilizing insights from multiple decision trees. Furthermore, a variety of statistical and machine-learning methods are used by artificial intelligence to model complex data relationships. One of the most important metrics for evaluating regression models is the R-squared value, sometimes referred to as the coefficient of determination, which shows how well the model accounts for the variance in the dependent variable. Greater consistency between predictions and observed results and a more accurate depiction of the data are indicated by higher R-squared values. Medical AI has potential, but its acceptance among clinicians requires evidence through randomized controlled experiments. Medical AI is poised to enhance 21st-century healthcare, augmenting future clinicians' medical intelligence.[6,7] A graphical overview of the process that AI goes through to achieve a diagnosis of systemic illness is illustrated in Fig 1.

Use of AI-based retinal scans as biomarkers for the aging process

In recent estimations, the global elderly population aged 65 years and above reached approximately 750

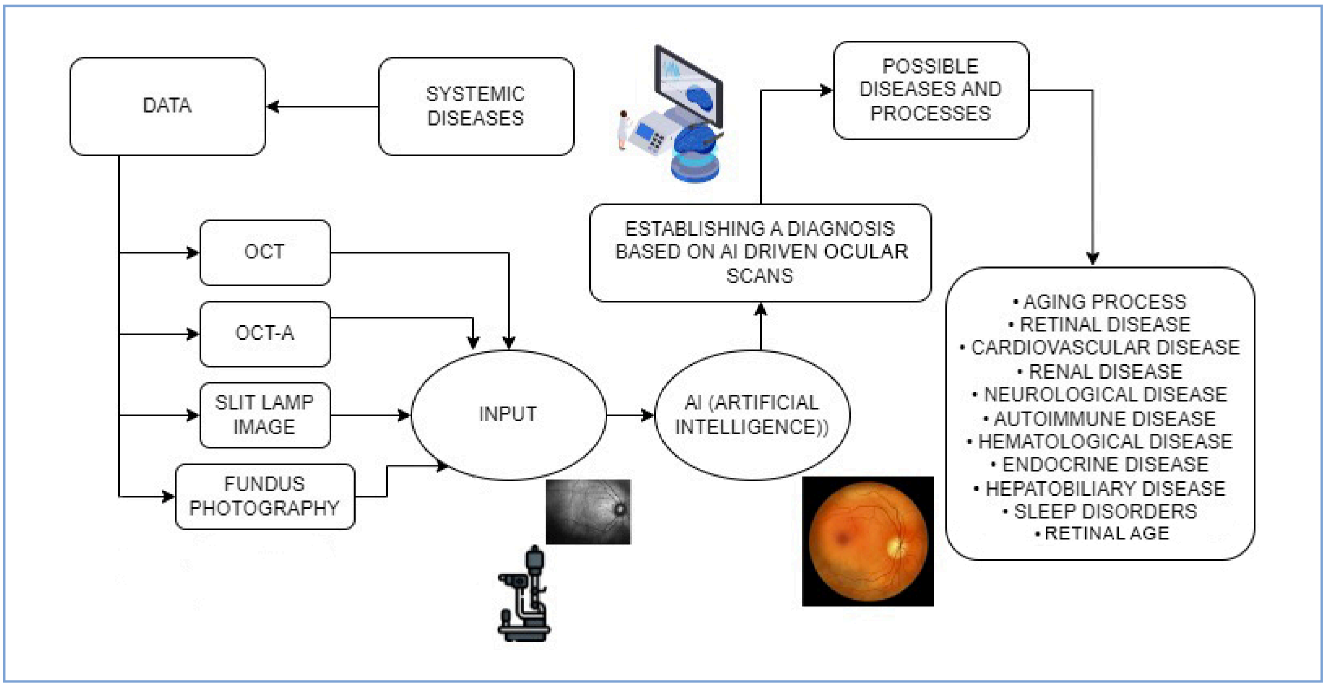

Fig 1. A graphical overview of the process that Artificial Intelligence goes through in achieving diagnosis for various systemic illnesses by utilizing Ocular scans.

million and is projected to double in the future.[8] Aging significantly influences the pathophysiology of various diseases, making it a crucial risk factor.[9] This exploration focuses on the use of retinal scans and deep machine learning (DL) as an innovative method to predict aging and biomarkers, utilizing retinal age (RA) to calculate morbidity and mortality risk, as well as studying aging genetics.

Chronological age (CA) has long been associated with age-related morbidity and mortality; however, individual variations suggest that the rate of aging differs among people.[10] Biological age (BA) accounts for gradual cellular and physicochemical changes, offering a more accurate indicator of health status.[11] Current BA assessment methods, such as blood profiles and DNA methylation, are costly, invasive, and ethically concerning.[12-15] Retinal assessment provides a non-invasive, cost-effective, and user-friendly alternative, given the retina's physiological similarities with other organs and its responsiveness to aging-related changes.[16]

Research has demonstrated retinal microvascular variations linked to circulatory pathophysiological changes, as well as molecular alterations associated with neural retinal layers and neurodegenerative disorders.[17] DL models have been employed to predict RA, showing remarkable accuracy in determining retinal age compared to chronological age. Model performance was evaluated using samples of retinal images from two separate sets from biobank databases. Upon completion of training, the DL model exhibited the ability to predict RA and CA ($p<0.001$) with a mean absolute error of 3.55 years. The difference between predicted RA and CA, termed the age gap, serves as a potential biomarker. Positive age gaps indicate older retinas, while negative gaps suggest younger retinas. Studies have revealed that an increase in the retinal age gap correlates with a significant rise in mortality, highlighting its potential as an independent predictor of age-related mortality.[18]

In a study conducted with participants from the Korean Health Screening, a DL algorithm called RetiAGE predicted BA accurately, demonstrating excellent performance (95% confidence interval [CI]: 0.965–0.970) and accurate predictions of mortality, especially in cancer and cardiovascular disease events.[19] Genetics significantly influence the aging process, with ALKAL2 identified as a key gene associated with age-related changes. This discovery sheds light on the molecular mechanisms governing aging, offering opportunities for therapeutic interventions and targeted research initiatives. Furthermore, predicting age using retinal images operates independently of existing methods, providing a unique perspective on aging. Integrating retinal imaging with other markers enhances understanding of an individual's BA. Unlike invasive blood tests, non-invasive retinal imaging facilitates actionable biological and behavioural interventions.[20]

In summary, the integration of retinal scans and DL techniques offers a ground-breaking approach to predicting aging and associated biomarkers. The non-invasive nature of retinal assessment, coupled with its accuracy and potential for genetic insights, positions it as a promising tool for understanding age-related conditions and developing targeted interventions in the future.

Use of AI-based ocular scans in diabetic retinopathy

Since diabetic retinopathy (DR) is a major contributor to visual impairment in developed nations, innovative approaches to patient screening, complication avoidance, and care optimization are required. An emphasis on AI-based models, especially those that enable large-scale screening, has resulted from the increasing prevalence of DR. Starting with fundus pictures, these models are essential for identifying DR-related changes such as haemorrhages, exudates, cotton wool patches, and neovascularization. They determine whether DR is present or absent and provide a grade based on accepted DR grading schemes.[21]

Numerous artificial intelligence systems have been developed to achieve these goals. When the IDx-DR system was tested on a number of populations, including the 3,640 participants in the Kenyan Nakuru Eye Study[22], it demonstrated a sensitivity of 87% and a specificity of 70%. Additionally, it demonstrated strong performance in tests utilizing the Messidor-2 dataset, yielding a 97% sensitivity and 59% specificity.[23] These encouraging results led to IDx-DR's approval by the US Food and Drug Administration in 2018.[24] The RetmarkerDR software showed a sensitivity of 73% for any DR, 85% for referable DR, and 98% for proliferative DR.[25] EyeArt performed well on the Messidor-2 dataset, achieving a sensitivity of 94% and a specificity of 72%.[26] Using a sensitivity of 96% for any DR, 99% for referable DR, and 99% for DR that posed a risk to vision, it was employed in the smartphone-based DR screening of 296 patients.[27,28] Additionally, EyeArt was applied to a dataset with over 30,000 images, achieving a sensitivity of 96% for referable DR.[29] In addition, other systems that have proven to be as reliable in DR screening are the Google Inc.-sponsored system, RetinaLyze, EyeWisdom®, and the Bosch DR Algorithm.[21]

AI models are not only good at screening, but they also assist in grading and staging direct response content. Gulshan et al. demonstrated high sensitivity and specificity in identifying the presence of diabetic macular edema and the severity of DR.[30] Ting et al. supported these findings by looking at nearly 500,000 images.[31] Moreover, the high reliability of AI-based screening was validated by a recent study that tested a deep learning algorithm using over 200,000 fundus images from 16 clinical settings.[32] Ultimately, promising strategies for combating DR are offered by AI-based models. Because of their remarkable sensitivity and specificity, these systems enhance patient care, facilitate early intervention, and greatly aid in the widespread prevention of DR-related complications and visual impairment.

Use of AI-based ocular scans in macular degeneration

In developed nations, age-related macular degeneration (AMD) is a major cause of visual impairment, which calls for the use of AI-based techniques for precise analysis. The main source of data is optical coherence tomography (OCT) images, which need to be precisely segmented in order to identify retinal structures. During follow-up, AI-based segmentation algorithms, utilizing unsupervised learning techniques, have demonstrated remarkable success in identifying retinal features and measuring retinal fluids.[33,34] These algorithms operate autonomously, eliminating the need for human interpretation of the images. They excel in fluid localization and quantification, as well as in evaluating retinal integrity. Advances in predicting visual outcomes and evaluating treatment responses have been made possible by AI in AMD research. The prevalence of AMD-related lesions and the progression of the disease varied between AMD eyes treated initially and twice, according to AI models.[35] AI also measured the number of drusen, evaluated their distribution, and examined hyper-reflective foci on OCT scans to forecast the likelihood of disease progression and the beginning of complications.[36]

Schmidt-Erfurth et al. made a substantial contribution by estimating the risks of AMD progression, highlighting the prognostic significance of intra-retinal cystoid fluid, and creating automated techniques for fluid volume calculation.[37] By examining fluid changes following injections, AI forecasted visual results for a treat-and-extend regimen. AI also measured leakage on angiography and segmented macular neovascularizations.[38,39] AI proved helpful in conjunction with new treatments like pegcetacoplan, as it accurately identified atrophic margins and tracked their expansion in the context of geographic atrophy.[40] Self-monitoring AI systems, like the Notal Vision Home OCT and ForeseeHome, have proven accurate and feasible.[41] Patients who used these systems for daily self-imaging demonstrated good agreement with expert-based grading, and over a 3-year period, ForeseeHome successfully identified changes in visual acuity and indicated the likelihood that a disease would progress in 2,123 patients.[41,42] These uses highlight

AI's critical contribution to improving patient care and AMD research.

Use of AI-based ocular scans in glaucoma

Artificial intelligence has been applied in glaucoma diagnosis using various imaging techniques, such as fundus photographs, optical coherence tomography (OCT), and visual field (VF) tests. Deep convolutional neural network models have shown high accuracy in distinguishing normal and glaucomatous VF, as well as diagnosing glaucoma based on Retinal Nerve Fiber Layer (RNFL) thickness and Optic Nerve Head (ONH) parameters. AI can effectively learn complex glaucoma features from fundus photographs and holds promise in OCT-based glaucoma assessment using RNFL or Ganglion Cell-Inner Plexiform Layer (GCIPL) thickness parameters.[5]

Use of AI-based ocular scans in cardiovascular diseases

Given that cardiovascular illnesses are one of the leading causes of death worldwide, early detection is vital to patient health.[43] Because fundus vessels are directly visible in hypertensive retinopathy, it is a useful biomarker for hypertension in ophthalmology. Researchers have studied cardiovascular and ocular diseases in greater detail thanks to AI. By taking advantage of the rare opportunity to observe fundus vessel parameters directly through the eye, researchers studying cardiovascular disease have investigated parameters such as diameter, density, and tortuosity.[44] Based on retinal images, artificial intelligence (AI) has made it possible to identify key cardiovascular risk factors like age, gender, blood pressure, and smoking status.[45] In contrast to conventional methods, risk factors can be directly acquired through AI analysis; however, there is a tendency to overuse AI in the prediction of these factors. This over-reliance has affected the information's accuracy and could hinder the advancement of AI-based retinal image screening.[46]

Furthermore, using fundus images to detect the coronary artery calcification fraction has been made possible by AI. Son et al. compared the predictive power of fundus images and clinical data by classifying subjects according to age interval and coronary artery calcification fraction. The values of the Area Under the Curve (AUC) for age, bilateral images, and unilateral images were 0.828, 0.832, and 0.823, respectively. Interestingly, the AI model concentrated on the blood vessels in the retina, highlighting atherosclerosis and hypertension as important indicators of cardiovascular disorders.[47] order to predict hypertension, Kim et al. created an AI system with an astounding AUC of up to 0.961, highlighting the significance of determining the risk of cardiovascular events based on vascular status as reflected in the eyes.[48] Additionally, using clinical data and retinal images, artificial intelligence has been used to predict the frequency of cardiovascular events. Researchers developed prediction models using the atherosclerosis score and coronary artery calcification fraction identified by AI as predictors in long-term studies. Subject grouping and the prediction of cardiovascular events in different groups were made possible by the prediction of coronary artery calcification or atherosclerosis scores using fundus images.[49,50] These findings highlight the possibility of using fundus images to identify pertinent biomarkers for cardiovascular disease and to forecast the course of the condition in the future.

Use of AI-based ocular scans in diabetes

Early and effective screening techniques are required due to the significant health burden posed by the increasing prevalence of diabetes worldwide. Even though they are accurate, traditional oral glucose tolerance tests are intrusive and have limited applicability. Because chronic hyperglycemia affects the retinal microvasculature, there is a well-established correlation between diabetes and ocular changes, including retinopathy.[2] Researchers have investigated AI-based screening with retinal images by taking advantage of this relationship. In 2020, an artificial intelligence (AI) system examined 1222 retinal fundus photos from rural Chinese citizens, detecting hyperglycemia with 78.7% accuracy and an area under the curve (AUC) of 0.880.[51] Expanding on this, Zhang et al. combined fundus images with patient metadata in 2021 to predict the incidence of type 2 diabetes within five years, using over 100,000 images. The method was inventive, but the non-standardized risk score casts doubt on its applicability in a wider context. AUCs for diabetes detection in external datasets were higher than 0.80, and the prediction model's AUC was 0.824. The AI system was incorporated into smartphones for cloud-based retinal image analysis to improve accessibility, increase screening options, and lowering healthcare inequities.[51] The fact that diabetic complications go beyond eye problems highlights the need for all-encompassing AI-based strategies.

Use of external eye images in the prediction of laboratory results

Another study which was done on diabetic patients proved to be useful in detecting systemic parameters through the use of external eye images. This study developed and evaluated a deep learning system (DLS) using external eye photographs to predict systemic parameters related to liver, kidney, bone, thyroid, and blood. Trained on 123,130 images from 38,398 diabetic patients, the DLS outperformed baseline models in predicting abnormalities such as elevated AST, low calcium, decreased eGFR, low hemoglobin, low platelets, elevated ACR, and low WBC in validation sets. The DLS demonstrated superior performance by achieving absolute AUC improvements of 5.3–19.9%. Notably, the study suggests that external eye photographs could serve as a non-invasive screening tool for systemic diseases, showcasing potential applications for accessible and widespread disease detection. The results indicate promising performance, even with low-resolution images, opening possibilities for the use of consumer-friendly devices like smartphones. The study emphasizes the importance of further research to explore the generalizability and practical implications of this approach in diverse populations and clinical settings.[52]

Use of AI-based scans in neurological diseases

Alzheimer's disease

It is imperative to conduct early screening for Alzheimer's disease (AD), particularly in light of the rapidly aging population. By using fundus images from AD patients and healthy individuals from 11 different studies conducted in different countries, researchers such as Cheung et al. have made significant progress. They produced impressive results when building and validating a model for AD diagnosis, with AUCs in external validation sets ranging from 0.73 to 0.91. Their AI model performed better in patients with ocular diseases and was able to distinguish between patients who tested positive and those who tested negative for beta-amyloid.[53]

Furthermore, retinal thickness is a useful parameter for AI-based detection as it indicates the progression of AD.[54] Retinal thickness images from optical coherence tomography (OCT) have been successfully used in AD detection algorithms with an AUC of 0.795.[55] AI systems perform even better when multiple imaging modalities and clinical data are combined. To create sophisticated AI models for AD detection, multimodal retinal images—including OCT, OCT-Angiography, and Ultra-widefield scanning laser ophthalmoscopy were combined with patient specific data. With parameters such as the OCT-derived ganglion cell-inner plexiform layer thickness map, these combined models produced remarkable outcomes with AUCs greater than 0.8.[56] These developments highlight AI's potential for early AD screening.

Use of AI-based scans in renal diseases

Chronic kidney disease

Innovative methods for identifying chronic kidney disease (CKD) through ocular manifestations have been made possible by the complex relationship between the kidney and the eye, which share similarities in structure, development, physiology, and pathogenic pathways.[57] It has been discovered by researchers that renal disease can be linked to ocular abnormalities like those seen in tubulointerstitial nephritis uveitis syndrome (TINUS) and that retinal microvascular parameters can predict the onset of chronic kidney disease (CKD).[58] Interstitial nephritis, a disorder that frequently precedes or coexists with ocular symptoms, is diagnosed in conjunction with symptoms of TINUS in children, which include fever, pain, photophobia, and acute bilateral non-granulomatous anterior uveitis.[59] According to a study on the relationship between CKD and age-related macular degeneration (AMD), patients with moderate CKD had three times the frequency of early AMD without geographic atrophy and choroidal neovascularization than patients with mild or no CKD.[60] Kidney function tests, urine analysis, and kidney puncture biopsy have historically been used in the diagnosis of kidney disease. Although these techniques work well, they can be laborious and could use more succinct screening methods. Artificial intelligence (AI) advances in the last few years have completely changed early detection techniques, especially when it comes to retinal imaging.

A deep learning model that uses retinal images to predict early renal functional impairment is a ground-breaking development. With an astounding AUC of more than 0.81, the model performed better in patients with higher HbA1c levels, the researchers found.[61] Furthermore, compared to the images-only model, the combination of retinal images and clinical data greatly improved the detection of CKD. The combined model had an AUC of about 0.8 in the entire population.[61] Notably, the AUC exceeded 0.9 in patients with hypertension or diabetes. This demonstrates the AI's capacity to classify CKD patients according to their estimated glomerular filtration rate (eGFR) and to differentiate between healthy people and CKD patients.

AI models based on retinal images were used to predict the course of CKD in cohort studies.[62] To predict the likelihood of developing CKD and advanced CKD in healthy subjects, researchers built predictive models using metadata, fundus images, or a combination of both. Cox proportional hazards analysis was used to evaluate these models, and the combined model produced impressive results: it had a C-index of 0.719 and an impressive prediction accuracy of up to 0.844 on the internal validation set. These studies do have certain limitations, though. Researchers used a high-sensitivity but low-specificity AI model to improve screening performance, which may increase the number of CKD misdiagnoses. Furthermore, there may be limitations to the model's applicability in different research contexts due to the lack of universal acceptance of the risk stratification criteria used in these studies.[62] Additionally, there is room for improvement because the emphasis is on predicting the risk of progression in healthy subjects rather than patients with early-stage CKD. These studies highlight the promise of AI-driven retinal imaging in revolutionizing early CKD detection, despite these drawbacks.

Use of AI-based ocular scans in hematological diseases
Anemia

Deep learning algorithms utilizing ocular imaging have emerged as a promising approach to forecasting anemia, the most prevalent hematological disorder. Researchers have explored subtle retinal changes and conjunctival symptoms as potential markers of anemia.[63] A notable study by Chen et al. presented a novel framework that combined semantic segmentation and a convolutional neural network to predict eyelid hemoglobin levels, achieving a promising R2 value of 0.512.[64] However, conjunctival imaging-based models encounter challenges concerning acquisition criteria, image extraction, and algorithm selection. To overcome these limitations, Mitani et al. developed a deep learning system based on Color Fundus Photography (CFP) for anemia screening, which showed significant promise. Utilizing data from the UK Biobank, the integrated AI system effectively determined hemoglobin levels and anemia, and it also performed well for diabetes patients (AUC = 0.89).[65]

Zhao et al. extended the focus to retinal features and employed Ultra-Widefield (UWF) retinal images as input, achieving an impressive AUC of 0.93 for accurate anemia prediction.[66] Recent research has investigated the relationship between anemia and alterations in capillary plexus density and retinal microvascular perfusion observed in optical coherence tomography angiography (OCTA). A lightweight network utilizing OCTA images achieved an excellent AUC of 0.99, demonstrating respectable performance. However, validation on a larger and more diverse dataset is essential to establish its reliability.[67]

In a different approach, Wu et al. devised a method to detect anemia in pregnant individuals by combining metadata and quantitative OCTA measurements, achieving an AUC of 0.874.[68] In conclusion, deep learning systems based on ocular imaging hold enormous potential for predicting anemia. Despite encouraging results, further validation and improvement are required to address issues related to data size and external validation. If these challenges are overcome, these techniques have the potential to revolutionize anemia screening and management by offering non-invasive, effective, and reliable diagnostic tools for this common hematological illness.

Use of AI-based ocular scans in autoimmune conditions
Multiple sclerosis

A number of autoimmune diseases, such as multiple sclerosis, inflammatory bowel disease, and Sjögren syndrome, are examples of the complex relationship between the immune system and the eyes. These conditions can cause symptoms that affect the eyes, such as uveitis, optic neuritis, and dry eyes. Retinal thickness may be a useful biomarker for the advancement of multiple sclerosis, according to studies examining the connection between the disease and the eyes.[69] In this context, optical coherence tomography (OCT) images have become a popular source for artificial intelligence (AI) diagnosis. Researchers that have gathered OCT images from multiple sclerosis patients and controls include Cavaliere et al. They examined various retinal and choroid regions in detail using the OCT ETDRS and TNSIT scan modes. Through the application of a support vector machine algorithm, they developed a diagnostic model by identifying variables with the highest area under the curve (AUC) of 0.97. This novel method showcased the ability of AI to detect multiple sclerosis in its early stages and the effectiveness of OCT-based diagnostic systems in disease detection and tracking.[69,70]

Martin et al. similarly examined OCT pictures from 48 patients with early-stage multiple sclerosis and 48 healthy people. They established an efficient classifier by precisely measuring the thickness of the retinal and choroidal layers, which allowed them to identify regions with significant discriminant capacity. The top-performing classifier demonstrated remarkable 0.98 measurements for both specificity and sensitivity. Their research clarified the various layers of the eye and suggested that the papillomacular bundle may be the first region to be affected in the early phases of multiple sclerosis. The significance of accurate layer analysis in early disease detection is highlighted by this discovery, however It's crucial to acknowledge the limitations, considering the high AUC scores, and to be cautious about potential overfitting, emphasizing the need for further validation on new data.[70] All of these studies highlight how OCT images can revolutionize AI-driven multiple sclerosis diagnosis. AI systems can provide invaluable insights into disease progression by utilizing the detailed information provided by OCT scans, which can help clinicians diagnose and intervene early in patients' lives.

Use of AI-based ocular scans in Hepatobiliary conditions

A ground-breaking study has unveiled a strong correlation between major hepatic diseases and ocular features, paving the way for automated screening and identification of these conditions through fundus or slit-lamp images. The study's models demonstrated impressive performance in detecting liver cirrhosis and cancer, even in cases where these conditions manifested subtly, such as through yellowing of the sclera and conjunctiva due to elevated bilirubin accumulation.[71] Surprisingly, the fundus models performed as effectively as the slit-lamp models, revealing minute retinal alterations imperceptible to the human eye. Researchers speculated that these modifications were linked to advanced liver disease characteristics, including hyperammonaemia, hypoalbuminemia, imbalanced estrogen, and pathological changes like splenomegaly and portal hypertension.[72]

Hyperammonaemia, a common liver disease condition, damages retinal Müller cells, leading to hepatic retinopathy, while hypoalbuminemia causes fluid leakage into retinal tissues, forming retinal exudates.[73] Imbalanced estrogen can induce retinopathy[74], and complications of decompensated cirrhosis result in thinning retinal arteries and tortuous vessels.[75] Splenomegaly leads to observable blood cell sequestration in fundus images, aiding hepatobiliary disease diagnosis, even in mild cases. These ocular changes offer valuable diagnostic insights, enhancing disease identification and understanding, even for milder hepatobiliary diseases like chronic viral hepatitis and non-alcoholic fatty liver disease.[72]

The study employed deep neural networks (ResNet-101) to develop screening models for hepatobiliary diseases using OCT and fundus images.[72] Notably, the iris, an unexplored area in hepatobiliary diseases, emerged as a significant diagnostic contributor. The models enable early detection and extensive, non-invasive screening, outperforming traditional approaches based on serum markers or systemic risk factors. These models can be integrated into existing fundus camera or slit-lamp systems, offering practical and effective opportunistic screening tools as quick and extensive screening is necessary because major hepatobiliary diseases are thought to be the cause of about two million deaths globally each year.[76] While the study acknowledges limitations such as sample size and potential biases, the authors emphasize the need for larger, diverse datasets to enhance accuracy and generalizability.[72]

CONCLUSION

The utility of AI in medical diagnosis is growing as more links between ocular and systemic disorders are discovered. Ocular pictures are being employed in the identification of endocrine, cardiovascular, neurological, renal, hematological, and many other disorders thanks to the development of AI, ML, DL, and medical big data. Although there is still much to learn about the fundamental connections between the eyes and other diseases, doing so will require continuing advancements in AI algorithms and our understanding of physiological and pathological mechanisms. Only then will we be able to fully comprehend the relationships between ocular and systemic health. AI is expected to revolutionize illness identification and patient treatment in the medical industry in the future.

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