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ROLE OF ARTIFICIAL INTELLIGENCE IN DIABETES MELLITUS AND DIABETES RETINOPATHY

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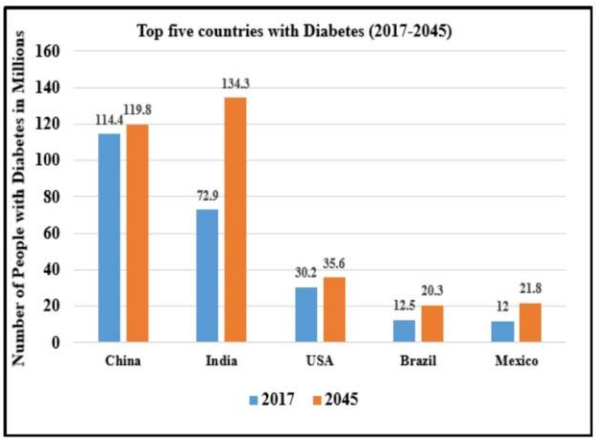
ABSTRACT

The use of artificial intelligence as proven to be valuable and transformative in the treatment of diabetes. AI can draw significant conclusions that improve the accuracy of diagnostic and prognostic decision making. machine learning and deep learning are the most commonly used technologies in the field, as they have make remarkable advancements due to enhanced computer speed and more resources for computation. Millions of people around the globe are suffering from diabetes. most of the patients are not familiar with their health issues and the risk factor they face before the diagnosis of diabetes. The paper reviews substantial work related to diabetes mellitus and retinopathy based on different classification techniques. In this paper, a generic smart frame work for realistic health management of diabetes mellitus is presented and implemented. The paper review includes applications of AI in early diagnosis of type 2 diabetes, AI in prediction and prevention of diabetes, applications of AI in screening and classification of diabetes, limitations in AI in diabetes research and care, diabetes retinopathy screening, grading of diabetes retinopathy severity, diabetic retinopathy treatment, AI techniques used in retinal images analysis, challenges of AI in diabetes care, potential enhancement and future directions of AI in diabetes retinopathy management, advancements in diagnosing diabetic retinopathy.

KEYWORDS: diabetic mellitus; artificial intelligence; machine learning; deep learning; diabetic retinopathy; diabetes care; techniques.

INTRODUCTION

Diabetes mellitus refers to a collection of long term metabolic conditions marked by consistently high blood glucose levels.[1] Hyperglycemia, a defining characteristic of diabetes mellitus, can result in serious complications including retinopathy, cardiovascular diseases, kidney failure and mucormycosis infections.[2] Diabetes is a metabolic condition characterized by bodies inability to produce sufficient insulin or by the development of insulin resistance, which impairs the effectiveness of the insulin that is produced. The primary function of insulin is to regulate blood sugar levels through a variety of mechanisms.[3] Diabetes mellitus primarily characterized into three types; type 1 diabetes [T1DM], type 2 diabetes [T2DM], and gestational diabetes [GDM].[4] Type 2 diabetes, which is the most common variant, is marked by gradual increase in insulin resistance and a reduction in the ability to secrete insulin. Gestational diabetes is a transient condition that occurs during pregnancy and typically resolves following delivery.[1,5] Successful management of diabetes across all types relies on prompt diagnosis.[6]



Artificial intelligence is a swiftly advancing domain with a growing range of applications in prediction, risk evaluation, and the early detection of diabetes. Machine learning algorithms processes significant potential to transform clinical practices through the auto machine of diagnostic processes.[7] the field of diabetic care is leading the way in the adoption and integration of machine learning technology, presenting considerable oppurtunities for enhancing patient outcome.[7,8] diabetic retinopathy, a prevalent microvascular complication associated with diabetes mellitus ,ranks among the primary cause of preventable blindness, especially within the working age demographic .the incidence of diabetic retinopathy is anticipated to continue increasing, posing a significant challenge to health care systems globally.[9]

The global incidence of diabetes mellitus and diabetic retinopathy is anticipated to rise significantly. concurrently, the worldwide prevalence of vision threatening diabetic retinopathy [VTDR], which encompasses diabetic macular edema [DME], severe non proliferative diabetic retinopathy [NPDR], and proliferative diabetic retinopathy [PDR], is also expected to increase. It is projected that the number of individuals affected by vision threatening diabetic retinopathy will grow by 57.0 percent, from approximately 28.5 million in 2020 to around 48.8 million by 2045.[10] Implementing screening measures to identify early sight threatening lesions associated with DR is crucial approach to mitigate the impact of vision loss and blindness resulting from this condition.[11,12]

Machine learning techniques facilitate the creation of AI applications that uncover previously unnoticed patterns within data, eliminating the necessity to define specific deficient rules for each task or to consider intricate interactions among input features. consequently, machine learning has emerged as the preferred framework for developing AI tools.[13] In light of this context we examine the latest programs in the application of AI within diabetes management in clinical settings, followed by a discussion on the opportunities and challenges associated with these AI applications. Additionally, we investigate the potential for integrating and enhancing existing digital health technologies to establish an AI assisted digital health care ecosystem, which encompasses both the prevention and management of diabetes, representing a promising vision for the future of diabetes care.

METHODS

The article review was conducted using the google scholar and PubMed. This reliable tools were chosen due to their extensive health care related content. The review focused on English language documents published between 2020 to 2024.

Artificial Intelligence in the Early Diagnosis of Type 2 Diabetes

Type 2 diabetes mellitus, which does not require insulin for management, represents the most prevalent form of diabetes, comprising approximately 90 to 95 percent of all diabetes cases. It is projected that the number of individuals affected will reach 439 million by the year 2030 (Wu et al., 2014). Recent advancements in artificial intelligence models have demonstrated potential in forecasting the development of type 2 diabetes among high-risk patients. These models leverage intricate relationships between distinct individual metrics and binary classification algorithms, which have been developed from the ground up to effectively predict the onset of diabetes. A collection of binary classification algorithms, structured fundamentally and enhanced through the Adam optimization method, attained a commendable accuracy rate of approximately 86%. This technique, grounded in artificial neural networks, holds significant promise for providing accurate data tailored for individualized treatment, thereby serving as a crucial resource for decision-making processes.

APPLICATION OF AI IN DIABETES PREDICTION AND PREVENTION

Forecasting Diabetes Onset

The forecasting of diabetes onset is an integral component of preemptive healthcare, focusing on the precise identification of individuals at a high risk of developing diabetes before the onset of the disease. This technological advancement has the potential to significantly reduce the prevalence of diabetes by facilitating early medical interventions for at-risk individuals. The ability to predict diabetes onset predates the introduction of machine learning technology. Abbasi et al. highlighted the effectiveness of various statistical models, including logistic regression, the Cox proportional hazards model, and Weibull distribution analysis, in forecasting diabetes onset among non-diabetic individuals over a span of 5 to 10 years, achieving a concordance index (C index) between 0.74 and 0.94.[14]

Machine learning (ML) represents a promising approach that has the potential to enhance predictive accuracy in comparison to traditional statistical models. Choi et al. found that the area under the curve (AUC) for predicting new-onset diabetes within a five-year period among hospitalized patients was 0.78, based on an ML-driven logistic regression model.[15] Ravaut et al. recently demonstrated that an ML model utilizing administrative health data achieved an AUC of 0.80 for predicting diabetes onset within the same timeframe.[16] In a similar vein, Nomura et al. created an ML-based prediction model aimed at identifying diabetes indicators prior to the disease's onset, employing the gradient-boosting decision tree technique, which yielded an AUC of 0.71 and an overall accuracy of 94.9%.[17]

Recently, a DL system developed Common algorithms employed in supervised learning encompass[18] (1) artificial neural networks, including Boltzmann machines, restricted Boltzmann machines, multi-layer perceptrons, radial basis function networks, recurrent neural networks, Hopfield networks, convolutional neural networks, and spiking neural networks; (2) Bayesian learning techniques, such as naive Bayes, Gaussian naive Bayes, multiple naive Bayes, average one-dependence estimators, Bayesian belief networks, and Bayesian networks; (3) decision trees, which include classification and regression trees, Iterative Dichotomiser 3, the C4.5 algorithm, the C5.0 algorithm, chi-squared automatic interaction detection, decision stumps, and supervised learning in quest; (4) ensemble methods, such as random forests, bagging, boosting, AdaBoost, and XGBoost; and (5) linear models, which consist of linear regression, logistic regression, generalized linear models, Fisher linear discriminant analysis, quadratic discriminant analysis, least absolute shrinkage and selection operator regression, multi-modal logistic regression, naive Bayes classifiers, perceptrons, and linear support vector machines. In the realm of unsupervised learning, prevalent algorithms include[19][20] [(1) transformation equivariant representations, such as group equivariant convolutions and autoencoding transformations; (2) generative models, including flow-based generative models, generative adversarial networks, autoencoders, and disentangled representations; and (3) self-supervised methods, such as autoregressive models and self-attention models.

Artificial Intelligence in the Prediction of Diabetic Retinopathy

Diabetic retinopathy is the most common complication associated with diabetes. The management of diabetes and its related retinopathy is often fragmented, disorganized, and delivered in phases, frequently requiring substantial financial and resource investments for treatment. To address these gaps in healthcare delivery, innovative strategies that incorporate digital technologies are essential (Gunasekeran et al., 2020). Artificial intelligence systems have demonstrated remarkable accuracy in diagnosing diabetic retinopathy. By analyzing patient datasets, AI algorithms can identify the earliest indicators of severe retinopathy with a level of precision comparable to that of endocrinologists. A range of automated deep-learning-based screening algorithms for diabetic retinopathy has been developed, achieving notable specificity and sensitivity rates exceeding 90%. Nevertheless, the performance of these deep-learning algorithms in clinical settings is hindered by the limitations of available open-access datasets (T. Li et al., 2019).

APPLICATION OF AI IN THE SCREENINGAND CLASSIFICATION OF DIABETES

Screening for Diabetes

Current diagnostic protocols for diabetes [21] are primarily based on invasive assessments conducted in clinical settings, which may be affected by behavioral and ethnic variables. Given that the initial phases of Type 2 Diabetes (T2D) frequently present without symptoms, individuals may remain undiagnosed for extended periods.[22] Unfortunately, a diagnosis at a later stage can result in significant health issues and a reduced life expectancy. To mitigate this trend, researchers have focused on enhancing the diagnosis of T2D by striving to create precise diagnostic techniques utilizing easily accessible data and non-invasive, cost-effective testing methods.[23]

The constraints associated with traditional methods have spurred the adoption of AI-driven diagnostic tools that exhibit high classification accuracy and utilize extensive datasets, including information from wearable and continuous monitoring devices that are often challenging to interpret. These AI models are characterized by their non-invasive nature and enhanced accessibility, which may significantly increase the general population's willingness to undergo screening and facilitate the development of personalized screening strategies for individuals at high risk.

AI-driven screening for diabetes primarily emphasizes two key areas. Firstly, the application of AI in screening has proven effective in identifying predictors that do not exhibit clear correlations with diabetes. Tapak et al. employed various methodologies, including artificial neural networks, support vector machines, fuzzy c-means, random forests, logistic regression, and linear discriminant analysis, on a dataset comprising 6,500 individuals in Iran.[24] Ten risk factors were selected as predictors, excluding blood glucose-related data. The findings indicated that the support vector machine outperformed both logistic regression and linear discriminant analysis in terms of area under the curve (AUC). In a similar vein, Maniruzzaman et al. evaluated Gaussian process-based techniques utilizing different kernels (linear polynomial and radial basis) against linear discriminant analysis, quadratic discriminant analysis, and naive Bayes.[25] with the Gaussian process method featuring a radial kernel achieving the highest accuracy. Secondly, advancements in diverse sensing technologies and the creation of innovative datasets are expanding the possibilities for AI-based diabetes screening. Shu et al. conducted a comprehensive analysis of the impact of texture features derived from specific facial regions on diabetes detection, utilizing eight different texture extractors.[26] The most effective texture feature extractor for diagnosing diabetes mellitus attained an accuracy of 99.02%, a sensitivity of 99.64%, and a specificity of 98.26% when implemented with a support vector machine. Li et al. developed a non-invasive model for predicting diabetes risk based on the fusion of tongue features, successfully forecasting the likelihood of pre-diabetes and diabetes through machine learning techniques.[27] Their model achieved an average accuracy of 0.821 and an average area under the receiver operating characteristic curve (AUROC) of 0.924. Furthermore, Zhang et al. illustrated that deep learning models could effectively identify type 2 diabetes (T2D) using only fundus images or in conjunction with clinical metadata, yielding AUROCs ranging from 0.85 to 0.93.[28]

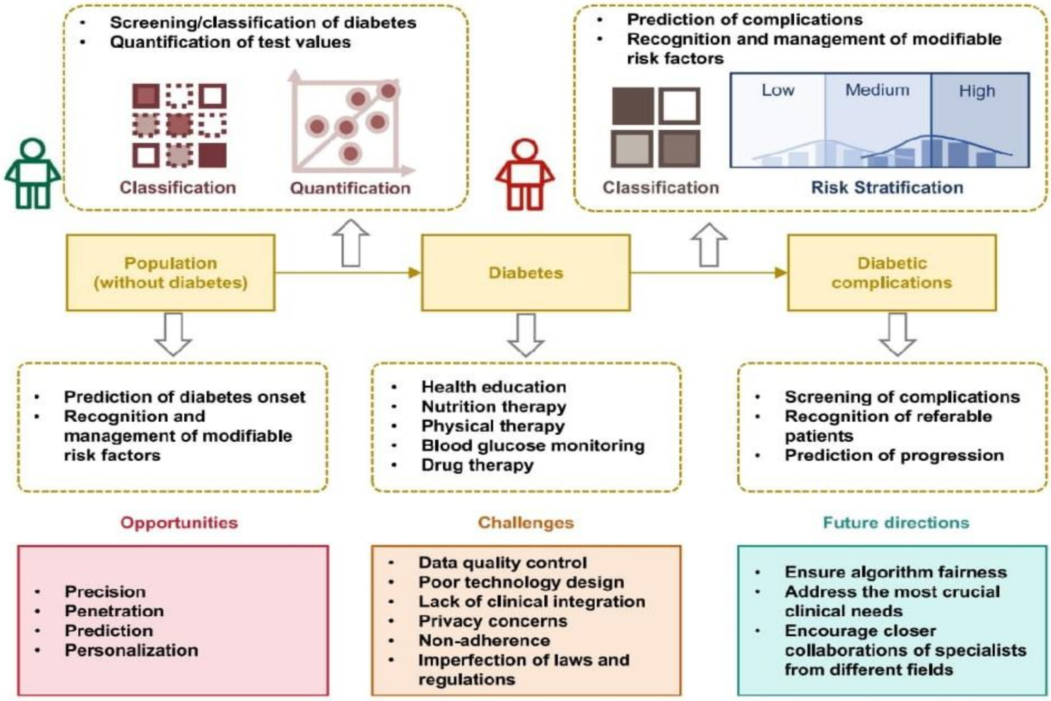
LIMITATIONS IN AI IN DIABETES RESEARCH AND CARE

Artificial intelligence (AI) undoubtedly stands as one of the most contentious subjects within the medical community today. Numerous experts believe that AI possesses significant potential for enhancing diabetes management. Devices powered by artificial intelligence, including continuous glucose monitors (CGMs) and insulin pumps, contribute to effective diabetes control and the mitigation of high blood sugar levels. Furthermore, AI could be utilized to predict which patients are at a higher risk of experiencing complications such as diabetic ketoacidosis. Additionally, AI has the capacity to assist in diabetes management by reminding patients to regularly check their blood sugar levels, take their prescribed medications, engage in physical exercise, plan their meals, consume healthy foods, and implement other necessary lifestyle changes. Although these applications are still in the early stages of development, they hold promise for enabling patients to achieve better diabetes control and avert severe complications. If individuals lack the knowledge to address a particular problem, machine learning cannot spontaneously generate the expertise required for humans to find a solution. We are acquainted with autonomous vehicles because humans comprehend the principles of driving. Similarly, robots excel in chess because humans have a deep understanding of the game. Industrial robots are utilized by humans who know how to operate them (Ben Dickson, 2013). There are several reasons why machine learning and artificial intelligence will not be able to completely resolve the diabetes epidemic. Firstly, artificial intelligence depends on vast quantities of data to learn and evolve. In the context of diabetes, experts currently do not possess enough information. We need data regarding individuals' daily habits, genetic factors, and other health conditions such as coronary artery disease and kidney disease, among others, to develop a machine-learning algorithm capable of predicting which individuals are at risk of developing diabetes. Even if all this information were available, organizing it in a format that artificial intelligence could interpret would be exceedingly challenging.

Machine learning algorithms derive their effectiveness from the quality of the data they receive, and the data available in healthcare databases is often suboptimal. There are frequently gaps and inaccuracies in the collected data, which can result in erroneous conclusions drawn by artificial intelligence systems. Consequently, human oversight is essential for reviewing and assessing the results produced. If this holds true, artificial intelligence will not be able to replace healthcare professionals. A significant number of diabetic patients continue to utilize traditional methods, such as finger pricking, to monitor their blood glucose levels with a glucometer, rather than adopting these advanced devices (Olansky & Kennedy, 2010). The high cost and limited availability of devices can lead to considerable expenses, including issues related to accessibility and the ongoing monitoring of one's health status. Wearable technologies may also influence clothing choices, compromise personal intimacy, and draw unwanted attention in professional settings. Such concerns can subtly impact how others perceive an individual's ability to manage their health or fulfill their job responsibilities (Williams, 2022).

DIABETIC RETINOPATHY SCREENING

In the pivotal research conducted by Abramoff et al., an artificial intelligence system utilizing supervised machine learning (ML) through logistic regression achieved a sensitivity of 96.8% and a specificity of 59.4% in identifying referable diabetic retinopathy (DR). Although the specificity is relatively low, it is anticipated that this system could significantly reduce the workload associated with manual screening performed by specialists.[29] A new deep learning (DL) model was developed by the same team, utilizing convolutional neural network (CNN) architectures influenced by AlexNet and VGGNet. This model exhibited an enhanced specificity of 87% for the detection of referable diabetic retinopathy (DR), while maintaining sensitivity.[30] EyeArt and Retmarker, two artificial intelligence systems demonstrating sensitivities of 93.8% and 85% for referable diabetic retinopathy (DR), respectively, have been linked to a reduction in the costs associated with DR screening.[31] Additional economic modeling research has indicated that both semi-automated and fully automated screening techniques conducted by human specialists are more cost-effective compared to conventional manual screening methods.[32,32] Furthermore, IDx-DR, recognized as the first medical device utilizing AI to identify cases of diabetic retinopathy beyond mild severity, received FDA approval in 2018.[33]



In low-income nations where healthcare resources are scarce, the absence of established diabetes mellitus (DM) screening and blood glucose management programs leads to an increased prevalence of diabetes-related complications. A study conducted in sub-Saharan Africa revealed that the rate of progression from no diabetic retinopathy (DR) to sight-threatening DR was five times greater than that observed in Europe.[34,35] Despite this alarming statistic, achieving universal annual DR screening for all DM patients remains a challenging objective.[35] Technological advancements may offer a potential solution. The application of artificial intelligence (AI) to analyze digital fundal photographs could significantly reduce the costs associated with nationwide screening programs while providing diagnostic performance that is comparable to or even exceeds current standards.[36,37] A pertinent concern is whether models developed and validated in countries with different ethnic compositions can be effectively applied to local populations. Research by Bellemo et al.[38] demonstrated that an ensemble model, which included adapted VGGNet and ResNet architectures trained on a database of color retinal images from Singapore, exhibited acceptable diagnostic performance in a real-world DM population in Zambia, achieving a receiver operating characteristic area-under-curve (AUC) of 0.973 for referable DR, with sensitivities of 99.42% for sight-threatening DR and 97.19% for diabetic macular edema (DME). Additionally, a prospective interventional cohort study in Thailand found that a deep learning-based system for detecting sight-threatening DR had an accuracy of 94.7%, surpassing the 93.5% accuracy of human experts.[39] Among innovative cost-effective strategies, retinal images can be captured using smartphone-based retinal cameras. A study utilizing EyeArt, an ensemble of deep artificial neural networks, demonstrated the feasibility of this method. The AI software achieved a sensitivity of 99.1% and a specificity of 80.4% in detecting sight-threatening diabetic retinopathy (DR) through the analysis of smartphone retinal images, processed online and compared against evaluations by human experts.[40]

GRADING DIABETIC RETINOPATHY SEVERITY

The classification of color fundus photographs into distinct grades of diabetic retinopathy (DR) severity, as illustrated, is based on alterations in retinal vasculature. These grades include no retinopathy, mild non-proliferative DR, moderate non-proliferative DR, severe non-proliferative DR, and proliferative DR.[41] This classification can provide valuable insights into the progression and prognosis of the disease.[42] Traditionally, this assessment has been performed through manual fundus examinations conducted by specialists, which are often limited in availability and accessibility.[43] However, emerging artificial intelligence-based tools have the potential to effectively categorize DR grades, thereby alleviating healthcare costs and reducing the associated burdens.[44,45]

Gulshan et al. developed a convolutional neural network (CNN) model utilizing the Inception-v3 architecture along with transfer learning, which produces five distinct binary classifiers for the grading of diabetic retinopathy (DR).[46] This model demonstrated commendable performance in DR grading, achieving a sensitivity of 84.0% (95% CI, 75.3%-90.6%) and a specificity of 98.8% (95% CI, 98.5%-99.0%) for identifying severe or worse cases of DR. Additionally, it recorded a sensitivity of 90.8% (95% CI, 86.1%-94.3%) and a specificity of

98.7% (95% CI, 98.4%-99.0%) for detecting diabetic macular edema (DME). In a separate study, Takahashi et al.[47] employed the GoogLeNet CNN to assess DR using four different 45-degree color fundus photographs (CFP) taken from each eye. This network achieved a mean accuracy of 81% and a prevalence-adjusted bias-adjusted kappa of 0.74, indicating that it provided the correct diagnosis with the highest probability in 402 out of 496 CFP images, thereby surpassing the performance of traditional manual grading by experts based on a single CFP image. Other studies have also reported elevated sensitivity and specificity rates for DR grading through the application of various models.[48,49,50]

Sandhu et al. integrated OCT and OCT angiographic images with primary clinical and demographic information gathered from 111 patients to develop an AI model aimed at screening and staging diabetic retinopathy (DR).[51] They introduced an innovative computer-aided design system to classify non-proliferative DR into mild and moderate categories. Their findings indicated an accuracy of 98.7%, with 100% sensitivity, 97.8% specificity, 99% differential scanning calorimetry (DSC), and an area under the curve (AUC) of 0.981. Notably, progressive enhancements in nearly all metrics were noted as OCT angiography, clinical, and demographic data were progressively incorporated into the model. In a separate study, Wang et al.[52] utilized ultra-widefield fluorescein angiographic images from 399 patients to train an AI model capable of distinguishing between normal, non-proliferative DR, and proliferative DR, achieving an accuracy of 88.50%.

DIABETIC RETINOPATHY TREATMENT

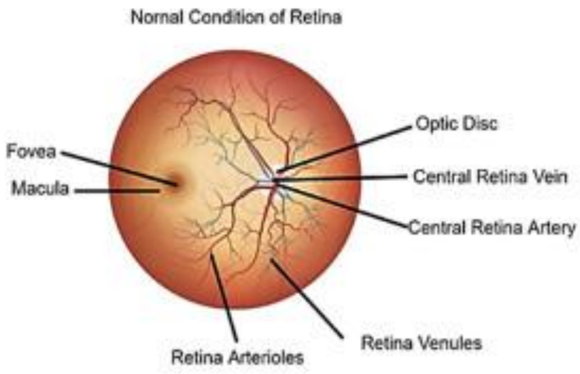
Intravitreal administration of anti-vascular endothelial growth factor (VEGF) agents, such as ranibizumab, bevacizumab, and aflibercept, is recommended for managing sight-threatening diabetic retinopathy (DR), particularly diabetic macular edema (DME).[53,54,55,56] Optical coherence tomography (OCT) is frequently employed to assess the therapeutic response. By analyzing OCT images, artificial intelligence (AI) models can forecast individual patient reactions to anti-VEGF treatment, potentially enabling tailored therapeutic strategies for DME.[57] +. Advanced AI algorithms have been created to evaluate various OCT parameters—including central macular fluid volume, ellipsoid zone integrity, intraretinal fluid, subretinal fluid, hyperreflective foci, and external limiting membrane—to predict visual acuity outcomes in DME, thus offering clinicians objective metrics for diagnosis and monitoring. Liu et al.[58,59] integrated deep learning (DL) with classical machine learning (CML) techniques, training models such as AlexNet, VGG16, and ResNet18 on a dataset comprising 304 pre-treatment OCT images from DME patients. The DL ensemble model generated fifteen OCT features, which were subsequently utilized to train traditional machine learning algorithms—Lasso, support vector machine, decision tree, and random forest—to forecast post-treatment central foveal thickness and best-corrected visual acuity one month following three months of anti-VEGF injections.[59] However, the model's inability to accurately predict post-treatment values indicated that OCT images alone were inadequate as the sole inputs for the model. Gallardo et a.[60] established a machine learning system to evaluate the burden of anti-VEGF treatment, categorized as low, moderate, or high based on injection intervals, within a treat-and-extend framework for DME and retinal vein occlusion, utilizing demographic data and OCT images collected from patients during two consecutive clinic visits.[61]

The suggested supervised machine learning model, utilizing a random forest approach, aims to forecast the treatment needs over a one-year period, achieving a satisfactory area under the curve (AUC) that enhances the interpretability of the decision-making process. Notably, all features associated with intra-retinal fluid were significant in distinguishing between low and high treatment demands.

Artificial intelligence (AI) not only aids in predicting treatment responses but can also be utilized to enhance the planning of therapeutic procedures. One such procedure is focal or grid laser photocoagulation, which involves delivering a series of controlled photocoagulations to retinal areas affected by pathology. This method is particularly relevant for treating diabetic macular edema (DME) and proliferative diabetic retinopathy (DR).[62,63] By normalizing oxygen partial pressures in peripheral avascular regions of the retina, this treatment promotes the regression of newly formed blood vessels, thereby reducing the incidence of aberrant vessel formation, vitreous hemorrhage, and membrane development. The effectiveness of the treatment is significantly influenced by the precise location and dosage of the photocoagulates administered.[64]

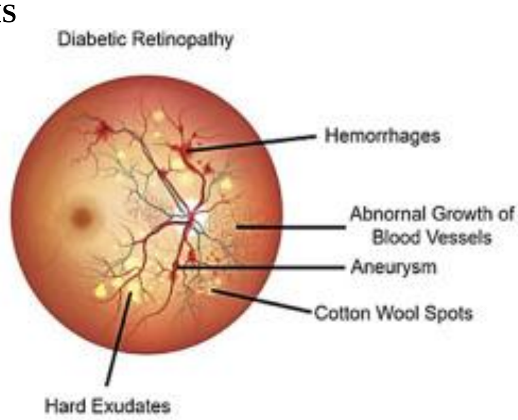
Standardized photocoagulation patterns often fail to accommodate the individual variations in the morphology of macular edema and the anatomical differences in retinal vasculature.[62,65] Additionally, the manual mapping of coagulation patterns necessitates a high level of surgical skill and is time-consuming.[65] AI can be employed to automate the segmentation of the retina, ensuring that only the designated areas are subjected to coagulation. This approach enhances the accuracy of laser photocoagulation while minimizing adverse effects. By integrating patient-specific data into advanced AI software, personalized and high-quality coagulation maps can be created. This results in significantly improved precision in targeting the exact burn locations and controlling the power delivered, leading to a nine-fold reduction in the likelihood of laser burns extending beyond the edges of the edema, as well as decreased preparation time for procedures and fewer postoperative complications.[65]

AI TECHNIQUES USED IN RETINAL IMAGES ANALYSIS



(a)

[a]Normal Condition of Retina



(b)

[b]Diabetic Retinopathy

Researchers in artificial intelligence have implemented a variety of models for the analysis of retinal images, with the most prevalent being the CNN-based architectures ResNet[66,67,68] and VGGNet.[69,70] The architecture of a CNN specifically tailored for image analysis is depicted in Figure 5. In practice, deep networks often encounter challenges related to optimization, primarily due to the vanishing gradient problem. ResNet addresses this challenge through the concept of residual learning, which incorporates skip or shortcut connections that allow the network to bypass one or more layers during both forward and backward propagation.[66,71] This mechanism ensures that the deeper layers do not yield higher training errors than their shallower counterparts, thereby facilitating the network's ability to learn identity functions. Additionally, ResNet's modular design allows for the scaling of the model by modifying the number of residual blocks, making it a versatile option for developers who can customize the architecture according to specific requirements and computational limitations. Despite its depth, ResNet is relatively efficient in terms of computational resource consumption.

VGGNet, on the other hand, is a series of deep CNNs recognized for its straightforward architecture, capacity to capture intricate image features, and outstanding performance in image classification tasks. VGG16, a prominent variant consisting of 16 layers[69,70], initiates with layers that include 64 channels, utilizing a 3x3 filter size with consistent padding, followed by a max-pooling layer with a stride of (2, 2), and subsequent convolutional layers that progressively increase the number of channels, reaching up to 128, while maintaining the uniform 3x3 filter size. VGGNet is primarily designed for image classification across large datasets, particularly the ImageNet database, which contains over 14 million images organized according to the WordNet hierarchy. In addition to image classification, efforts have been made to enhance VGG architectures to support a variety of computer vision applications and improve their classification capabilities.[71,72,73]

Inception-v3, DenseNet, AlexNet, ResNet, and U-Net represent various neural network architectures, each characterized by unique structural differences, that have been utilized in the analysis of retinal images.[74,75] Inception-v3, part of the GoogLeNet family, was specifically engineered for the extraction of multi-level features, making it suitable for large-scale image recognition tasks. It employs techniques such as factorization and batch normalization to reduce the number of parameters while enhancing performance.[76,77] DenseNet excels in image classification and segmentation, thanks to its dense inter-layer connections that facilitate improved gradient flow and promote the reuse of features.[78] AlexNet, one of the pioneering convolutional neural networks, is proficient in image classification due to its deep architecture and the application of the rectified linear unit (RELU) activation function; however, it may be less efficient compared to more recent models.[79] ResNet builds upon the concept of residual learning and incorporates split-attention mechanisms, enabling the model to concentrate on the most pertinent features for image classification.[80] In contrast to Inception-v3 and AlexNet, which serve more general purposes, U-Net was specifically designed for the segmentation of biological images.[81] Its distinctive "U-shaped" architecture enhances localization accuracy, a critical aspect in diagnostic imaging.[82]

CHALLENGES OF AI IN DIABETES CARE

Only two countries in Asia have diabetic retinopathy (DR) screening programs that meet the standards set by the International Council of Ophthalmology.[83] There exists a pressing need to standardize national protocols to address the discrepancies in screening and referral timelines.[84], as well as to develop comprehensive guidelines for the implementation of AI in DR screening to ensure consistent and effective practices.[85] While AI-driven DR screening has the potential to alleviate economic burdens and improve access to healthcare services[86], numerous challenges still need to be addressed.[87] Tackling these issues will necessitate collaboration across multiple disciplines, standardization of data, sharing of resources, real-world validation, and commercialization of solutions.[88] Specifically, deep learning algorithms require extensive datasets comprising thousands or even millions of images for effective training, which can be expensive to label and curate. AI developers frequently depend on available but limited training datasets, which may not be representative of real-world conditions, where image quality can be compromised due to inadequacies in clinical environments and may not consistently meet high standards.[89] Poor image quality and a low incidence of target pathology can lead to increased rates of false positives.[90]

Current methodologies for AI model development are largely disconnected from the intricate healthcare environments for which they are designed. Consequently, the pace of AI model development has significantly surpassed their integration into established clinical workflows.[91] This disconnect results in models that often lack well-defined use cases and are neither adequately tested nor implemented in clinical settings. Employing a mixed-methods strategy that combines design thinking with quality improvement techniques—focused on understanding variations in healthcare processes and incorporating user-centered design to ensure practical model functionality[92] has the potential to bridge this gap, facilitating smoother AI integration within the healthcare sector and promoting broader clinical adoption.[93]

AI screening systems have shown promising results in detecting DR from CFP and OCT images. However, there is still a need for validation, regulation, safe implementation, and demonstration of clinical impact before widespread adoption. Test-bedding new AI models in clinical settings is essential for identifying and remedying system bugs before full-scale deployment 152, 153.[94] Further, the AI tools may need to be validated and calibrated against local populations and clinical contexts: published results from one context may not always be generalizable or achievable in a different setting 154.[95] Finally, in complex AI models of DR diagnosis or treatment decision-making, interpretability is essential for gaining the trust of clinicians and patients alike. There is a need for transparent and interpretable AI in the reasoning processes behind the generated model outputs. Explainable AI is an active area of research and remains a challenge 155.[96]

Challenge	Description	Mitigating strategies
Data quality control	data quality may have the following problems: (1) poor quality of the data themselves, (2) poor quality of the data labels, and (3) insufficient data.	ensure the quality of data used in the training process
	AI may amplify implicit bias and discrimination if trained on data reflecting the health-care disparities	train AI algorithms on fair datasets that include and accurately represent social, environmental, and economic factors that influence health
Poor technology design	the initial versions of most AI systems are always challenging to navigate	understand the needs of the end user (for example, patients and providers)
	many EHR vendors did not follow basic usability principles	develop software and applications with input from end users
	patients reported lack of confidence with technology, as well as frustration with design features and navigation of commercially available mobile applications	utilize iterative design process
Lack of clinical integration	application of AI systems in the real world may lead to many unintended outcomes	develop AI algorithms that could be integrated into current clinical and digital workflows
	experts may struggle to develop trust with AI systems	demonstrate explainability analysis of AI systems
	AI systems could also be perceived as encroaching on clinicians' professional role	support the clinical decision-making of clinicians instead of making solely a competing diagnosis
Privacy concerns	implementing data privacy and security assurances is an overriding issue for the future of AI in medicine, since there are pervasive problems of hacking worldwide	• develop AI algorithms using federated learning or swarm learning • protect closed-loop automated insulin-delivery systems from hacking • ensure an individual's identity could not be determined by facial recognition or genomic sequences from massive databases
Non-adherence	user adherence is crucial to the effectiveness of AI applications in the real world, which can be affected by convenience, user experience, and true benefits brought by this technology	• use smart design, visible electronic health records • integrate electronic patient-reported outcomes in clinics • explore voice enablement in AI software and applications
Imperfection of laws and regulations	AI in medicine results in legal and regulatory challenges regarding medical negligence attributed to complex decision-support systems	• provide clear guidance on which entity holds liability when malpractice cases involving medical AI applications arise • update the credentials needed for diagnostic, therapeutic, supportive, and paramedical tasks with the deployment of automated AI for specific clinical tasks

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