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Diagnosis of Diabetic Retinopathy Using Artificial Intelligence

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Abstract

Purpose
The aim of this study was to explore the evolution of automated diagnosis of diabetic retinopathy from visualization and automatic segmentation of the ocular fundus imaging to the diagnosis of stages of diabetic retinopathy by deep learning algorithms in artificial intelligence programs.

Methods
Search published works in PubMed, Science Direct and similar search engines, from 2006 to 2023, using a combination of keywords in the medical field (ophthalmology, diabetic retinopathy, screening) and machine learning (artificial intelligence, deep learning, neural connection) has allowed us to identify the 160 publications we've analyzed. The article is formed by the consistent analysis of various computer programs as their complexity.

Results
Artificial intelligence programs, rapidly developing in recent years, are successfully used to diagnose vision-threatening diabetic retinopathy. Artificial intelligence programs have demonstrated sensitivity ranging from 82-99.1% and specificity ranging from 63-90% in detecting vision-threatening diabetic retinopathy.

Conclusion
Artificial intelligence programs will undoubtedly help doctors timely diagnose vision-threatening diabetic retinopathy. AI-enabled screening programs will help reach hard-to-reach, densely populated, low-income areas. The authors hope that similar programs that use artificial intelligence to diagnose diabetic retinopathy will become widely available throughout the world.

Keywords: NDiabetic Retinopathy, Artificial Intelligence Programs, Screening Programs, Vision-Threatening Stages and Deep Learning Algorithms

Summary Statement
- Diabetes mellitus is often complicated by vascular complications such as diabetic retinopathy.
- Diabetic retinopathy can lead to irreversible loss of vision,
- Artificial intelligence programs have been successfully used to diagnose vision-threatening diabetic retinopathy for timely treatment.
- Artificial intelligence - screening programs will help reach hard-to-reach, densely populated, low-income areas.

Introduction
Diabetic retinopathy (DR) is a complication of diabetes mellitus (DM). DR can result in vision loss due to complications such as hemophthalmus and retinal detachment, if diagnosis is delayed and treatment is inadequate. Therefore, it is crucial to regularly monitor patients with diabetes and screen them for timely DR diagnosis. Often there is not enough

specialists and time for this [1-3]. As is known, a high-quality examination of the fundus requires high specialization and experience, as well as time. On average, it takes 30 minutes to examine the ocular fundus using an ophthalmoscope or bio-microscope with lenses per patient. The average number of patients per day is 40-50. It is clear that in such a regime to qualitatively examine patients is very difficult, since the diagnosis of small changes on the eye fundus is very complex and requires a lot of strength and experience of the doctor. As a result, the probability of medical errors increases.

Recently, computer diagnostic systems have become widely implemented across the globe to enhance human productivity. The computer-aided diagnosis system involves detecting, segmenting, and classifying lesions present in ocular fundus images. Numerous conventional machine learning (ML) methods relied on manually-produced functions. The recent emergence of deep learning (DL) and its decisive victory over traditional ML methods for various applications has encouraged researchers to use it for DR diagnosis. The aim of this study was to explore the evolution of automated diagnosis of diabetic retinopathy from visualization and automatic segmentation of the ocular fundus imaging to the diagnosis of stages of diabetic retinopathy by deep learning algorithms in artificial intelligence programs [4-6]. Both current limitations and promising areas for further improvement in this field will also be presented.

Material and Methods

We conducted a search on PubMed, Science Direct, and similar search engines for studies published from 2006 to 2023 using a combination of keywords in the medical field (ophthalmology, diabetic retinopathy, screening) and in the field of machine learning (artificial intelligence, deep learning, neural connectivity). The primary criterion for article inclusion in the study was the use of artificial intelligence in the diagnosis of diabetic retinopathy. Several articles on related topics (diagnosis of arteriovenous disorders, optic edema) were also included. The majority of articles were written in English.

We identified 160 articles and incorporated them into the analysis. The paper is organized as follows: we sequentially analyzed different computer programs as they became more complex. This paper relies on previously conducted investigations and does not include novel studies involving human or animal participants.

Results and Discussion

Computer Programs for Automatic Segmentation of Pathological Areas of the Fundus

Fundus cameras capable of obtaining high-quality images of the ocular fundus without the need for pupil dilation (non-mydriatic cameras) are necessary to increase screening coverage for the population. Maximilian, Wintergerst and other co-scholars proposed ocular fundus imaging utilizing a Smartphone-based imaging (SBFI) adapter to facilitate affordable and mobile ocular imaging in low- and middle-income countries, as well as remote areas that are difficult to access [7, 8]. The images obtained can be analyzed by ophthalmologists or automatic algorithms.

Jaemin Son et al from Seoul National University have developed an ocular fundus examination algorithm that can detect haemorrhages, hard exudates, membranes, macular holes, myelinated nerve fibres and glaucomatous disc changes. The program produces dependable and easily comprehensible results that enable the possibility of clinical application as an automated ocular fundus image screening system. Akbar, Hassan et al. suggested an ocular fundus dataset that outperformed other datasets, providing researchers with the ability to diagnose various retinal pathologies automatically [9]. This includes changes in arterial and venous calibre ratios, optic disc edema and the emergence of hard and soft cotton-wool exudates [10,11].

Triwijoyo and Pradipto have developed a system aimed at detecting hypertensive retinopathy in its early stages. Their method involves the use of DeepNeuralNetworks (DNNs) and BoltzmannMachines to determine the arterial-venous diameter ratio (AVR) and the position of the optic disc (OD) on retinal images [12]. Kahaiatal proposed a Decision Support System (DSS) aimed at automatically screening early signs of DR. The system's classification scheme reaches a conclusion about the presence or absence of DR based on the manifestation of microaneurysms. The system's sensitivity is 100%, and its specificity is 67% [13].

Bouhaimed et al from Kuwait University conducted a study to assess the operational effectiveness of the Retinalyze System software in Horsholm, Denmark, during the automatic prescreening of ocular fundus images for diabetic retinopathy. The study found that the software had an 82% sensitivity and a 75% specificity in detecting red retinal lesions such as microaneurysms and haemorrhages. The predictive value of a positive result was 41%, while the predictive value of a negative result was 95%. In conclusion, the authors assert that this software produces minimal false-negative outcomes and has the potential to decrease the workload of DR screening [14].

Deep Learning Algorithms in Artificial Intelligence Programs

Over the past decade, a plethora of evidence has emerged on the use of deep learning (DL) in the diagnosis of DR. DL is a novel form of artificial intelligence that falls within the realm of machine learning [15]. This fourth industrial revolution methodology involves learning features from data, analyzing a large volume of information, and extracting relevant patterns from it.In deep neural learning, convolutional neural networks (CNNs) acquire their task-specific abilities through repetition and self-correction. The CNN algorithm analyses a labeled training set of images evaluated by experts and generates a diagnostic result. If the network's diagnosis is erroneous, the algorithm modifies its parameters to decrease the error. The network repeats the process for each image until the system's output matches that of human experts.

After optimisation, the algorithm can handle unknown images. Deep neural networks can detect subtle changes, patterns or anomalies that could be overlooked by human experts.One of the initial investigations into the automated identification of DR from colour images of the ocular fundus was performed by Abramoff et al in 2008 [16]. This involved a retrospective assessment of non-mydriatic images from the EyeCheck DR screening initiative. The authors achieved a sensitivity of 84% and a specificity of 64% in detecting DR. In 2013, Abramoff et al presented the sensitivity and specificity outcomes for the Iowa Detection Programme (IDP) for DR, revealing a sensitivity of 96.8% and a specificity of 59.4% [17].

Xu et al from the Shanghai Eye Disease Prevention and Treatment Centre have created Smart Eye, a system for processing and analyzing images used in DR screening. The performance and accuracy of the Smart Eye system in diagnosing DR and its stages were assessed using 19,904 ocular fundus images examined during the 2016-2017 screening program. The diagnostic sensitivity rates for no DR, mild NPDR, moderate NPDR, severe NPDR, and PDR are 86%, 83%, 89%, 89%, and 85%, respectively. The corresponding specificity rates are 63%, 71%, 64%, 70%, and 75%.The SmartEye system demonstrates a high degree of diagnostic accuracy in a screening programme for DR while using a non-mydriatic fundus camera. The SmartEye quantitative assay offers a novel and encouraging approach to the diagnosis and assessment of DR [18].

The Centre for Visual Information Technology (CVIT), in collaboration with the International Institute of Information Technology Hyderabad (IIIT-H), developed a new web-based tele-screening solution (called DrishtiCare) in 2011, which integrates various additional components for eye image analysis. The web-based platform is delivered on a Software as a Service (SaaS) model, making the service cost effective, easy to use and scalable [19]. The service highlights a specific retinal pathology, but the diagnosis of DR severity is made by an expert.

Saha and colleagues used artificial intelligence to assess ocular fundus images taken with various fundus cameras. The automated system proposed by the authors determines whether the quality of the images is acceptable or not. The clinical trial demonstrated a 97% agreement with a human evaluator. If an image is labelled as "reject", the ocular fundus will need to be photographed again [20].

Gulshan and colleagues developed an algorithm using deep learning for identifying cases of diabetic retinopathy and diabetic macular oedema in retinal fundus photographs. They used the EyePACS-1 dataset, which comprised of 9963 images taken from 4997 patients as well as the Messidor-2 dataset, containing 1748 images from 874 patients. The algorithm produced an area under the resulting operational curve of 0.991 (95% CI, 0.988-0.993) for the EyePACS-1 dataset and 0.990 (95% CI, 0.986-0.995) for the Messidor-2 dataset, proving to be a reliable predictor for detecting DR [21].

Voets et al attempted to reproduce the results of the deep learning AI algorithms published by Gulshan [21, 22]. However, they did not succeed in reproducing the original study results. Their AI algorithm yielded an area under the curve of the operational characteristics of 0.951 (95% CI, 0.947-0.956) on the Kaggle Eye PACS test set and 0.853 (95% CI, 0.835-0.871) on Messidor-2. The reported AUC of 0.99 on both test sets in the original study was not achieved. The authors therefore recommend the following improvements to the reporting of deep learning methods: (a) use publicly available data or provide detailed descriptions of the data, (b) publish the source code or all details of data pre-processing, and (c) publish all hyperparameters [22].

Rajalakshmi et al conducted a study to assess the efficacy of AI in diagnosing DR and detecting vision-threatening DR using fundus camera photographs on a Smartphone. Retinal images were assessed using Eye Art's verified AI-powered DR screening software. The automated classification's sensitivity and specificity were evaluated and compared with the assessments of ophthalmologists. The AI software demonstrated a sensitivity of 95.8% and specificity of 80.2% in detecting any signs of DR, and 99.1% sensitivity and 80.4% specificity in detecting DR [23].

Sahlstenet al developed a deep learning algorithm for identifying nonreferable DR/referable DR (NRDR/RDR) and nonreferable macular oedema/referable macular oedema (NRDME/RDME). In the first assessment of 7118 images, the algorithm devised by the authors exhibited a sensitivity of 0.896, specificity of 0.974, and AUC value of 0.987 [24].

Serener and colleagues conducted a study to compare the effectiveness of ResNet deep learning AI systems for diagnosing diabetic retinopathy (DR) using ocular fundus images from patients of various ethnic and geographic backgrounds. Results indicated that using datasets from Kaggle (USA) and Messidor (France) for training led to poor performance when testing ocular IDRID (India) images, resulting in an accuracy of 58.54%, sensitivity of 56.54%, and specificity of 72%.When using only Kaggle for training, an accuracy of 56.25%, sensitivity of 55.59%, and specificity of 57.43% were attained when E-Optha images from France were tested. The authors deem it crucial to obtain trained datasets from patients with similar ethnic and geographical backgrounds for improved diagnosis accuracy. Since different ethnicities exist around the world, a generalised dataset is necessary [25].

Katada at al26 conducted a study to compare the diagnostic performance of an AI machine learning system trained on 35,126 ocular fundus images from the US EyePACS database in detecting DR in ocular fundus images of Americans and Japanese. The AI model displayed 81.5% sensitivity and 71.9% specificity on American ocular fundus images. Similarly, it exhibited a sensitivity of 90.8% and a specificity of 80.0% in diagnosing 200 Japanese ocular fundus images from Keio University Hospital.The authors, as opposed to Ali Serener, reach the conclusion that an AI model trained on a US database can effectively diagnose DR on Japanese eye fundus images and can additionally serve as a cross-racial screening model in a telemedicine system [25,26].

KaiJin et al ascertain in their literature review that the utilisation of artificial intelligence (AI) within ophthalmology has the potential to address issues such as uneven distribution of medical resources and burden on professional ophthalmologists in nations like China [27]. The application of AI within ophthalmology appears promising, though its extensive clinical implementation remains distant.

Chawla et al conducted a total of 823 eye exams on 413 patients, examining recommended and non-recommended diabetic retinopathy cases with the aid of artificial intelligence technology. They found the prevalence of suspected glaucomatous optic disc changes to be 4.8% and 20.6%, respectively. Therefore, the authors suggest that screening programs should incorporate AI-based platforms capable of detecting multiple ophthalmic diseases, including glaucoma, to replace manual examinations [28].

Lim et al conducted a comparison of the diagnosis of more than mild DR (mtmDR) by EyeArt artificial intelligence software, retinal specialists, and general ophthalmologists. Results indicate that the Eye Art system had a significantly higher sensitivity in detecting mtmDR compared to retinal specialists or general ophthalmologists (97.3% vs 59.5% and 20.6%, respectively), in comparison to the reference clinical standard. The system has certain drawbacks such as a slightly lower specificity (86.3% compared to 98.9% and 99.8%, respectively), which could result in overtreatment. Nonetheless, a significant portion of false positives (i.e. overtreatments) manifested mild, nonproliferative mtmDR or other ocular pathologies requiring evaluation by an ophthalmologist [29].

Mathenge and colleagues conducted a study of the Rwanda Artificial Intelligence for Diabetic Retinopathy Screening (RAIDERS) programme in settings with limited resources. The study indicates that AI-assisted DR screening has shown potential to improve population coverage in low and middle-income countries. The findings from the RAIDERS trial offer proof for the incorporation of artificial intelligence (AI) in diabetic retinopathy (DR) screening, as a component of a viable national ophthalmology scheme to combat DR-associated blindness in sub-Saharan Africa [30].

A study by Mehra and colleagues investigated the effects of telemedicine screening for diabetic retinopathy (DR) in a primary care setting, utilising image analysis based on artificial intelligence (AI), reflex dilatation and secondary image re-reading. Of the 965 patients, 138 (14.3%) were classified as "positive" (above mild NPDR) and 827 (85.7%) as "negative" with a sensitivity of 100% and specificity of 89.2%. The researchers concluded that utilising AI to screen for diabetic retinopathy in a primary care environment produced outstanding outcomes, with no instances of false negatives [31].

Pei and colleagues investigated the screening efficacy of two AI-based systems (EyeWisdomDSS and EyeWisdomMCS) in 549 patients with type 2 diabetes mellitus using the assessments of two retinal specialists as the reference standard.32The EyeWisdomDSS system exhibited a sensitivity of 91.0% and a specificity of 81.3%, while the EyeWisdomMCS system correctly detected 76.2% of patients with DR and 92.4% of patients without DR. The EyeWisdom DSS was effective in screening for DR and the accuracy of the EyeWisdom MCS was higher in identifying patients without DR. This study highlights the potential benefits of using AI in healthcare. According to the authors, it is feasible and effective to perform AI-based DR screening in poor and densely populated areas of China.

Quellec et al. introduce an AI-powered approach named "ExplAIn" for identifying patients with no DR, mild NPDR, moderate NPDR, and severe NPDR. The algorithm efficiently detects and categorizes lesions in images with the ultimate image-level classification being an outcome of these multidimensional lesion segmentations [33].

Ruamviboonsuk and colleagues study presents a clinical deep learning systems integration for a primary care site, involving the National Diabetic Retinopathy Screening Program in Thailand. The system exhibited advantages in contrast to the diagnosis by local retinal specialists, as expressed by the authors. The reference standard was determined by a panel of three US certified retinal specialists. The deep learning system illustrated higher sensitivity (91.4% compared to 84.8%) and comparable specificity (95.4% compared to 95.5%). The authors' research is of great significance for the socio-economic advancement of the country and will be pursued further [34].

Xie and colleagues assessed the cost-effectiveness of two types of diabetes patient screening using deep learning: a semi-automated model to filter patients before assessment by humans, and a fully automated model with no human input. These were compared against screening by ophthalmologists. From the viewpoint of the health system, the semi-automated screening model was the most economical of the three, at £62 per patient per year.The automated model incurred an expense of £66 per patient annually whereas the human scoring model had an expense of £77 per patient each year. Upon switching to a semi-automated model, the Singapore healthcare system saved an estimated £489,000. This amount is equivalent to approximately 20% of the cost of current yearly screening [35].

Hayati and her team from Indonesia presented research on improving diabetic retinopathy (DR) classification using adaptive histogram correction with limited contrast (CLANE) through the employment of AI. The study demonstrated higher mean accuracy rates across several models when compared to the diagnostic accuracy from the original images: 91% for the VGG16 model, 95% for InceptionV3, and 97% for EfficientNet (87% for VGG16, 90% for InceptionV3, and 95% for EfficientNet). The findings from this thorough evaluation may prove advantageous in the detection of diabetic retinopathy through computer-aided diagnosis [36].

Monteiro put forward a fused method of training numerous individual deep learning models using a five-fold cross-validation technique and amalgamating their predictions to formulate a final outcome [37]. This composite model brings attention to each individual model's strengths and weaknesses, thereby enhancing the reliability of the results. A balanced DR Dataset comprising of 33310 retinal fundus images was employed for conducting experiments. The author has concluded that the proposed model surpasses the individual evaluation of all available DL deep learning models.

Conclusion

AI programmes undoubtedly have the potential to assist clinicians in timely DR diagnosis and referral to specialists for appropriate and timely treatment. AI software platforms have the potential to enhance the efficiency of ophthalmologists by reducing their workload, saving time and enhancing population coverage, in particular in economically deprived and inaccessible regions such as mountainous and steppe areas. Widespread implementation of these systems may overcome limitations pertaining to the unequal distribution of medical resources in densely populated developing nations and the workload of professional ophthalmologists, and minimize medical errors. We hope that such programs will be made available to the public as another accomplishment of human ingenuity [38,39].

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