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Efficacy of artificial intelligence-based screening for diabetic retinopathy in type 2 diabetes mellitus patients

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ABSTRACT

Aim: To explore the efficacy of artificial intelligence (AI)-based screening for diabetic retinopathy (DR) in type 2 diabetes mellitus (T2DM) patients.

Methods: Data were obtained from 549 T2DM patients who visited the Fundus Disease Center at Henan Provincial People's Hospital from 2018/10–2020/09. DR identification and grading were conducted by two retina specialists, EyeWisdom®DSS and EyeWisdom®MCS, with ophthalmologist grading as reference standard, efficacy of EyeWisdom was evaluated according to sensitivity, specificity, positive predictive value, and negative predictive value.

Results: Ophthalmologists detected 324 DR cases. Among them, there were 43 of mild non-proliferative DR (NPDR), 79 of moderate NPDR, 61 of severe NPDR, and 141 of proliferative DR (PDR). EyeWisdom®DSS detected 337 DR and EyeWisdom®MCS detected 264 DR. Sensitivity and specificity of EyeWisdom®DSS were 91.0%(95 %CI: 87.3%–93.8%) and 81.3% (95 % CI: 75.5%–86.1%), while EyeWisdom®MCS correctly identified 76.2%(95 %CI: 71.1%–80.7%) of patients with DR and 92.4%(95 %CI: 87.9%–95.4%) of patients without DR. EyeWisdom®DSS showed 76.5%(95 %CI: 69.6%–82.3%) sensitivity and 78.4%(95 %CI: 73.7%–82.5%) specificity for detecting NPDR and 64.5%(95 %CI: 56.0%–72.3%) sensitivity and 93.1%(95 %CI: 90.1%–95.3%) specificity for diagnosing PDR.

Conclusion: EyeWisdom®DSS is effective in screening for DR, and the accuracy of EyeWisdom®MCS was higher for identifying patients without DR. It is valuable to carry out AI-based DR screening in poorer regions.

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1. Introduction

According to data from the International Diabetes Federation, there were about 463 million diabetes mellitus (DM) patients worldwide in 2019, and it is predicted that this number will increase to 700 million by 2045 [1]. Diabetic retinopathy (DR) is one of the most common and serious complications of DM. It is the primary eye disease that causes blindness in the working population [2–4]. The reported prevalence of DR varies from 10% to 61% in people with DM in different countries [5]. However, research has shown that reasonable intervention and treatment of DR in the early stage can achieve good results in preventing the development of the disease and significantly reduce the blindness rate [6–8].

Unfortunately, people who live in counties, townships, villages, and marginal areas, often lack sufficient health knowledge. By the time DR is found in these individuals, it has often developed to a serious stage and caused irreversible visual impairment, which not only affects patients' quality of life but also increases the economic burden on society and the family, often leading to poverty in the latter case. Therefore, expanding the screening area of DR and carrying out targeted prevention and treatment of blindness can greatly reduce curable blindness. Regrettably, the number of ophthalmologists in China is insufficient, especially in primary medical institutions. According to data from the 21st National Ophthalmology Conference of the Chinese Medical Association held in 2016, 20% of county hospitals in China do not have an ophthalmology department. Even in institutions with such a department, there are few specialists in fundus diseases. The ratio of ophthalmologists to patients is 1:3000 in these areas [9], which is extremely unbalanced. Therefore, increasing the screening of DM patients to improve awareness, the treatment rate, and control rate of DR has become one of the main public health challenges in China [10–12].

Auxiliary measures based on artificial intelligence (AI) are efficient, cheap, and easy to operate for DR diagnosis [13]. EyeWisdom is an auxiliary diagnosis system for fundus diseases based on an AI algorithm developed by the company Zhiyuan Huitu (Vistel) in 2017. It mainly includes EyeWisdom®DSS software, a DR-specific auxiliary diagnosis system, and EyeWisdom®MCS software, a system with ophthalmic multi-disease screening as its core function [14]. EyeWisdom can screen for nearly 20 different eye diseases, such as DR, glaucoma, and age-related macular degeneration, based on the fundus photographs and disease history of subjects using an AI algorithm. It can not only directly provide suggestions for screening results, but it can also display nine typical DR lesions, such as microvascular tumor, retinal hemorrhage, hard exudation, and cotton wool spot, to help clinicians confirm the examination results. In addition, this fundus image analysis software is a cloud-based product, which can be used for real-time telemedicine combined with internet and 5G technology. It only takes 10 s from reading an image to outputting the results. The EyeWisdom AI algorithms have been trained in clinical practice and verified by retinal images obtained from the EyePACS database [15]. However, as yet, no report on the diagnostic and grading efficacy of EyeWisdom®DSS and EyeWisdom®MCS in patients with DM has been found.

Therefore, this study collected the disease history and fundus photographs of DM patients at the Fundus Disease Center in Henan Provincial People's Hospital from 2018/10–2020/09. The diagnostic efficacy of the EyeWisdom®DSS and EyeWisdom®MCS systems were evaluated according to the sensitivity, specificity, area under the curve (AUC), as well as the positive predictive value (PPV) and negative predictive value (NPV), with an ophthalmologist's diagnosis as a reference standard. This study was designed to improve the awareness rate and treatment rates of DR and reduce the blindness rate in primary medical institutions.

2. Methods

2.1. Participants

DM patients at the Fundus Disease Center in Henan Provincial People's Hospital from 2018/10/01–2020/09/30 were invited to participate in this study. Type 2 diabetes mellitus (T2DM) patients $\geq$ 18 years old for whom fundus photographs could be obtained were included in this research. The exclusion criteria were as follows: (1) T2DM patients with missing key variables, such as age, gender, and disease history; (2) patients whose fundus photographs were not clear enough due to small pupils, cataracts, or vitreous opacity that prevented ophthalmologists from making a diagnosis; (3) patients who suffered from heart, liver, kidney, and/or other important organ failure; (4) and those with malignant tumors. Demographic characteristics, disease history, fundus photographs, and images from optical coherence tomography examination (if available) were collected, which was performed by two authors (M.X. and R.H.) independently and consistency check was conducted. The study was approved by the Ethics Committee of Henan Provincial People's Hospital (registration number 58/2017), and written informed consent was obtained from all participants.

The sample size was calculated using formula (1) below based on the diagnostic test [16], where α = 0.05, allowable error δ = 0.08, and p is the sensitivity or specificity of the method to be tested. According to our pre-analysis, the sensitivity and specificity were 90.0% and 80.0%, respectively, for the DR-specific system (EyeWisdom®DSS), and 75.0% and 92.0%, respectively, for the multi-disease system (EyeWisdom®MCS). The minimum sample size of the DR group was 113, and that of the non-DR group was 97. A margin of 20% was used for the sample size to account for any invalid samples. Therefore, the minimum sample size was 136 for the DR group and 117 for the non-DR group.

$$n = \left(\frac{Z_\alpha}{\delta}\right)^2 (1-p)p \quad (1)$$

2.2. Acquisition of retinal images

Fundus examinations of DM patients were performed using the Zeiss non-mydriatic fundus camera (VISUCAM 224, Germany) by an ophthalmologist according to the unified

standards. This camera does not require mydriasis before use and provides a 45° field of view for each eye. Five fields were captured in each eye: macula centered, temporal side, nasal side, and the upper and lower quadrant of the retina.

2.3. Definitions and diagnostic criteria

DM was determined according to the Standards of Medical Care in Diabetes set in 2018 by the American Diabetes Association [17]. The diagnosis and grading of DR were determined by two ophthalmologists (H.D. and D.Q.) with more than five years of work experience according to International Clinical Diabetic Retinopathy (ICDR) criteria [18,19]. DR was divided into five stages as follows: (1) absence of DR: no obvious retinopathy and no abnormality; (2) mild non-proliferative diabetic retinopathy (NPDR): the early stage of retinopathy with only microaneurysms; (3) moderate NPDR: some of the blood vessels that nourish the retinas are blocked; (4) severe NPDR: one or more of the following: (i) more than 20 intraretinal hemorrhages in each of the four quadrants of the retina, (ii) clear venous beading in two or more quadrants, and (iii) significant intraretinal microvascular abnormality in one or more quadrants; and (5) proliferative diabetic retinopathy (PDR): retinal signals triggering the growth of neovascularization in which the new blood vessels are abnormal and fragile.

The kappa (κ) agreement between the two ophthalmologists was 0.91. When the diagnosis or grading results were inconsistent, the fundus photographs were adjudicated by a third retinal specialist (D.W.), whose diagnosis was accepted as the final judgment for subsequent analysis. Any patient diagnosed with DR in both eyes was considered one case, with the DR grade of the more serious eye accepted as the final diagnosis according to the ICDR severity grading system.

2.4. AI-based grading

The retinal photographs and medical history (after masking the patient's identity and diagnosis) were uploaded to the EyeWisdom platform for automatic diagnosis and grading. EyeWisdom is a software-based online cloud-computing platform. It has two systems: a DR-specific diagnosis system (EyeWisdom®DSS) and eye-related multi-disease diagnosis system (EyeWisdom®MCS). It can automatically analyze retinal images in conjunction with information about the patient's age, gender, and DM history, and then it provides information about the DR diagnosis and severity by automatically detecting the type, quantity, size, and location of retinopathy. In addition to the severity of DR, this software can also report the presence/absence of retinal hemorrhage, micro angioma, neovascularization, hard exudation, and fibroproliferative membrane. Images not clear enough to be diagnosed by EyeWisdom were excluded. The diagnosis of DR by EyeWisdom®DSS and EyeWisdom®MCS and the grading results of EyeWisdom®DSS were collected.

2.5. Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 23.0 (SPSS Inc, Chicago, IL). Qualitative data were described as frequencies. Sensitivity, specificity, PPV, and NPV were used to evaluate the diagnostic efficacy of EyeWisdom with the diagnosis of an ophthalmologist as a reference standard. Among these terms, PPV refers to the probability of disease when the test result is positive and NPV refers to the probability of absence of disease when the test result is negative. Kappa statistics were used to quantify and evaluate the consistency between AI analysis and the ophthalmologist's grading. All P-values were two-tailed, and the level of significance was set at $\alpha = 0.05$.

3. Results

3.1. Participant characteristics

Based on the inclusion criteria, 1768 retinal images from 563 DM patients were obtained; 14 DM patients (40 retinal images) were removed due to cataract or vitreous hemorrhage. A total of 549 DM patients aged 18–97 years old, for whom there were 1728 final images, were diagnosed by doctors and EyeWisdom. Of them, 272 (49.5%) were male and 277 (50.5%) were female. The mean age was 61.2 ± 11.8 years old. According to the ICDR standards, 225 (41%) were diagnosed as not having DR by the ophthalmologist. There were 324 (59.0%) DM patients diagnosed with DR, among whom 43 (7.8%) had mild NPDR, 79 (14.4%) had moderate NPDR, 61 (11.1%) had severe NPDR, and 141 (25.6%) had PDR. Based on the ICDR standards, typical fundus photographs of DR in different stages are shown in Fig. 1.

3.2. Comparison of ophthalmologist and AI DR diagnosis

EyeWisdom®DSS software detected 337 (61.4%) cases of DR in 549 DM patients, and EyeWisdom®MCS software detected 264 (48.1%) DR cases in these participants. Based on automatic grading by EyeWisdom®DSS, 68 (12.4%) patients had mild NPDR, 79 (14.4%) had moderate NPDR, 71 (12.9%) had severe NPDR, and 119 (21.7%) had PDR. The comparison of DR grading severity between the ophthalmologist and EyeWisdom®DSS software is shown in Fig. 2. In the 324 DR patients, 295 (91.0%) were correctly diagnosed with DR by EyeWisdom®DSS and 247 (76.2%) by EyeWisdom®MCS. For the 225 DM patients without DR, 83 (81.3%) were correctly diagnosed as not having DR by EyeWisdom®DSS, and 208 (92.4%) were correctly diagnosed by EyeWisdom®MCS. Fig. 3A shows the Venn diagram of the DR identified by the ophthalmologist versus AI and the overlap of DR observed in 373 patients. Fig. 3B shows the overlap of the absence of DR identified by the ophthalmologist versus AI. Fig. 3C–D show the overlap of NPDR and PDR identified by the ophthalmologist versus EyeWisdom®DSS software.

3.3. Efficacy of AI in the screening of DR in DM patients

The sensitivity, specificity, AUC, PPV, NPV, and kappa values for detecting DR, NPDR, and PDR using EyeWisdom software are shown in Table 1, in which ophthalmologist grading was taken as the reference standard. EyeWisdom®DSS correctly identified 91.0% (95% CI: 87.3%–93.8%) of patients with DR and 81.3% (95% CI: 75.5%–86.1%) of patients without DR, and

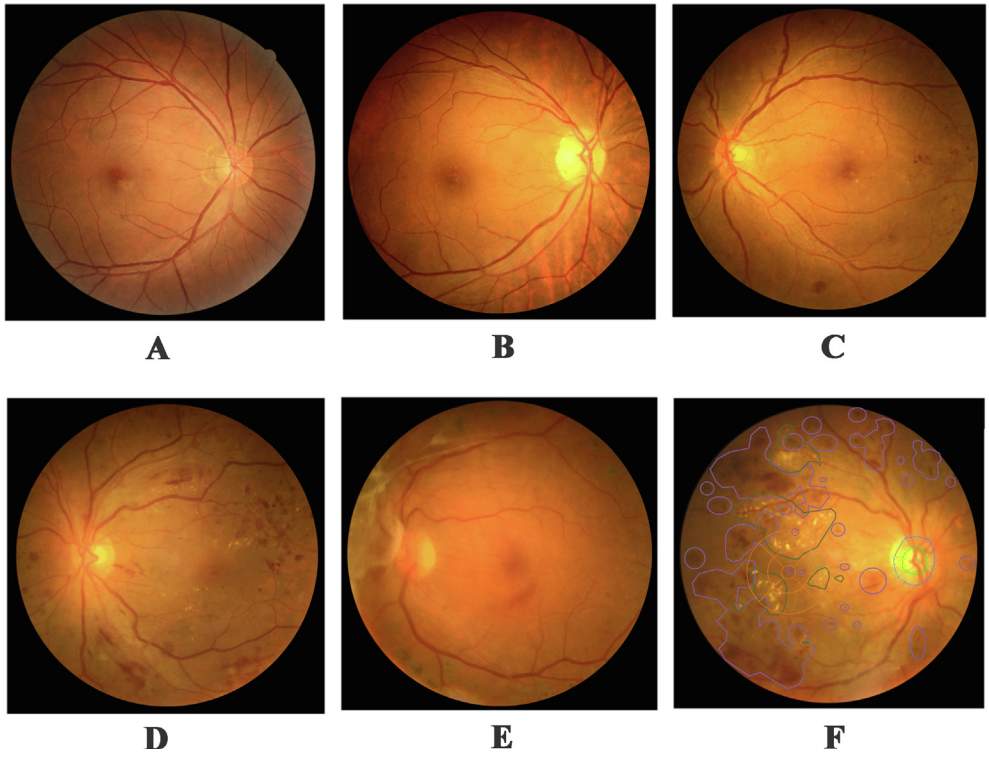

Fig. 1 – Typical fundus photographs of DR in different stages. **Typical fundus photograph showing the absence of DR. (B–E) Typical fundus photographs of mild NPDR (B), moderate NPDR (C), severe NPDR (D), and PDR (E). (F) Fundus lesion markings of severe NPDR identified by EyeWisdom®DSS. The purple outline marks retinal hemorrhage, green identifies hard exudation, and yellow shows macular fovea.**

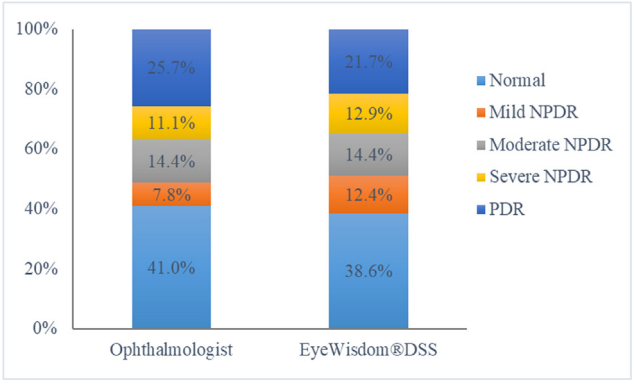

Fig. 2 – Comparison of ophthalmologist and EyeWisdom®DSS software DR severity grading.

EyeWisdom®MCS correctly identified 76.2% (95% CI: 71.1%–80.7%) of patients with DR and 92.4% (95% CI: 87.9%–95.4%) of patients without DR. EyeWisdom®DSS showed 76.5% (95% CI: 69.6%–82.3%) sensitivity and 78.4% (95% CI: 73.7%–82.5%) specificity for detecting NPDR and 64.5% (95% CI: 56.0%–72.3%) sensitivity and 93.1% (95% CI: 90.1%–95.3%) specificity in diagnosing PDR. The PPV of EyeWisdom®DSS for the detection of DR, NPDR, and PDR was 87.5% (95% CI: 83.4%–90.8%), 64.2% (95% CI: 89.7%–96.1%), and 74.5% (95% CI: 67.6%–83.6%), respectively. In addition, the NPV of EyeWisdom®DSS for the detection of DR, NPDR, and PDR was 86.3% (95% CI: 80.8%–90.5%), 86.8% (95% CI: 82.5%–90.2%), and 88.4% (95% CI: 84.9%–91.2%), respectively. The degree of agreement between EyeWisdom®DSS and the ophthalmologist grading for DR was 0.730 ($P < 0.001$), for NPDR it was 0.527 ($P < 0.001$), and for PDR it was 0.608 ($P < 0.001$) using the kappa statistics. The kappa value between EyeWisdom®MCS and ophthalmologist grading for DR was 0.660 ($P < 0.001$).

4. Discussion

This study evaluated the accuracy of EyeWisdom AI software for DR screening. We found that EyeWisdom®DSS has higher sensitivity and EyeWisdom®MCS has greater specificity. That is, the specific disease system was good at identifying patients and the multi-disease system was good at identifying normal participants, which suggested EyeWisdom can be established as an AI-based DR-screening model to be used in community and grassroots clinics in China in the future. The combination of these two systems may improve the awareness and treatment rate of DR, including avoiding or delaying its progression.

With the aging of the global population and increased prevalence of DM, the incidence of DR is also increasing [20,21]. A *meta*-analysis indicated that from 1990 to 2017 in the Chinese population, the pooled prevalence of DR, NPDR, and PDR was 1.14%, 0.90%, and 0.07%, respectively, and in patients with DM, the corresponding prevalence was 18.45%, 15.06%, and 0.99%, respectively [22]. A study conducted by Ruta et al., which was based on 72 articles from 33 developing and developed countries, showed the prevalence of DR varied

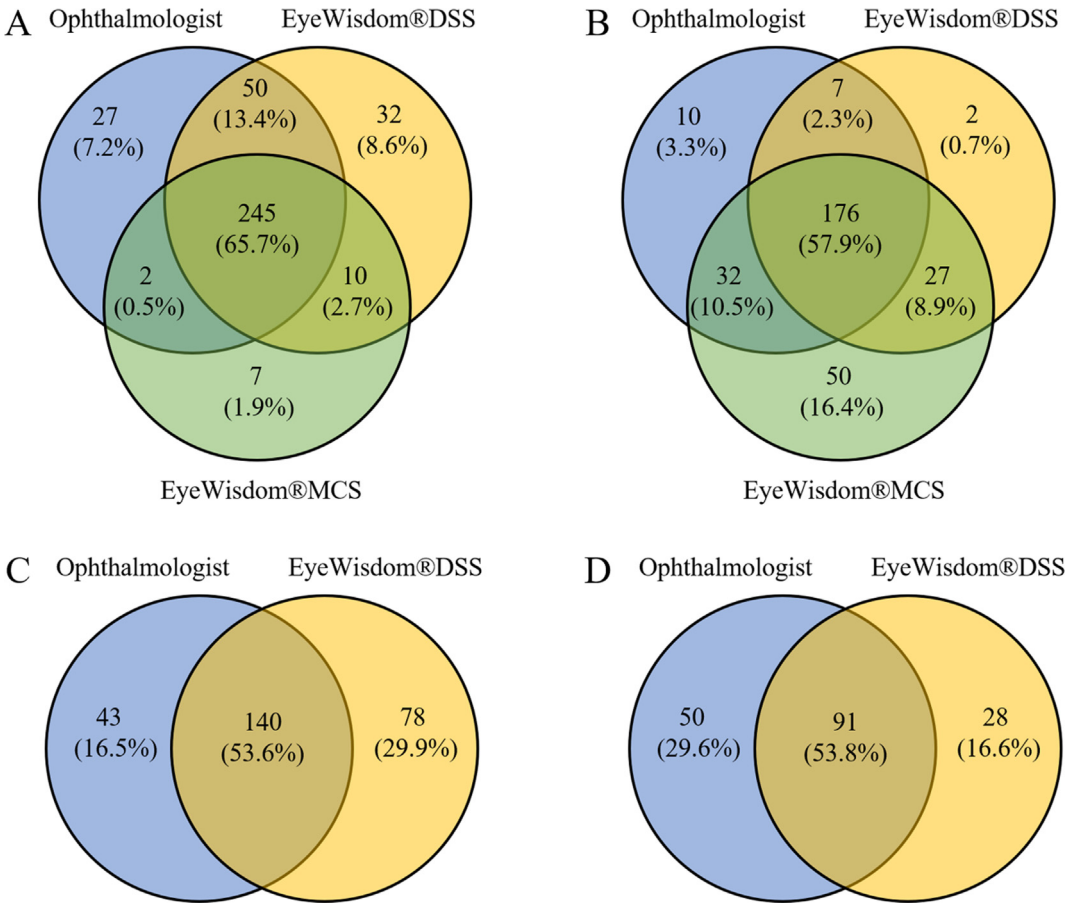

Fig. 3 – Overlap of DR and absence of DR identified by the ophthalmologist and AI. (A) Overlap of DR identified by the ophthalmologist versus AI (EyeWisdom®DSS and EyeWisdom®MCS). (B) Overlap of the absence of DR identified by the ophthalmologist versus AI (EyeWisdom®DSS and EyeWisdom®MCS). (C–D) Overlap of NPDR (C) and PDR (D). identified by the ophthalmologist versus EyeWisdom®DSS software.

from 10% to 61% in people with known type 2 diabetes mellitus (T2DM) and from 1.5% to 31% in people with newly diagnosed T2DM [5]. The prevalence of DR was 33.2% in the United States and 17.6% in India [5]. In this study, the prevalence of DR, NPDR, and PDR in DM patients was 59.0%, 33.3%, and 25.7%, respectively. The reasons for the difference in DR prevalence in different regions are multifactorial and include differences in demographic characteristics, research methods, and diagnosis and classification criteria of DR. In addition, DM patients in this study were all from the Fundus Disease Center at Henan Provincial People's Hospital. They cannot represent the general DM population that from the Department of Endocrinology. Therefore, most of these individuals were DM patients who had developed ocular symptoms or fundus lesions. This may explain the higher prevalence of DR, NPDR, and PDR in this study.

It should be noted that the onset of DR is insidious, and most patients have a long asymptomatic period before visual impairment. During this time, fundus lesions can be easily identified by fundus examination or retinal photography. Early detection is necessary for a good DR prognosis [23]. Therefore, DR screening for all DM patients is cost-effective in the long run and significant in terms of public health, especially in developing countries [24]. However, in the grassroots areas of China and other developing countries, the awareness and treatment rates of DR are very low due to a lack of medical resources, education, and experienced ophthalmologists. Existing DR-screening equipment has not been widely used due to the need for operation by professional ophthalmologists, its slow output, and the fact that it is inconvenient to move. In contrast, EyeWisdom, as an auxiliary AI diagnosis system for fundus diseases, has a number of advantages. If fundus photographs can be obtained, the system can provide diagnosis suggestions with only a computer. After simple training, the operator can complete the screening without needing professional ophthalmic knowledge. Therefore, this approach is not only suitable for large-scale screening of DR, glaucoma, and age-related macular degeneration, but it is also helpful for the long-term follow-up of DM patients. The system also enables remote guidance from ophthalmologists in tertiary hospitals, which could contribute to solving the problems related to diagnosis and treatment in poor areas.

The results of our study showed that the sensitivity of DR screening using EyeWisdom®DSS and the specificity of DR screening using EyeWisdom®MCS were high, reaching 91.0% and 92.4%, respectively. However, the efficacy of NPDR (76.5%) and PDR (64.5%) screening using EyeWisdom®DSS was relatively lower. For EyeWisdom®DSS, when the screen-

Table 1 – Efficacy of AI for detection of varying degrees of DR with ophthalmologist grading as reference standard (N = 549).

Retinopathy	Sensitivity (95% CI), %	Specificity (95% CI), %	AUC (95% CI)	PPV (95% CI), %	NPV (95% CI), %	Kappa	P
DR_{DSS}	91.0 (87.3, 93.8)	81.3 (75.5, 86.1)	0.862 (0.827, 0.897)	87.5 (83.4, 90.8)	86.3 (80.8, 90.5)	0.730	<0.001
DR_{MCS}	76.2 (71.1, 80.7)	92.4 (87.9, 95.4)	0.843 (0.809, 0.878)	93.5 (89.7, 96.1)	73.0 (67.4, 78.0)	0.660	<0.001
NPDR	76.5 (69.6, 82.3)	78.4 (73.7, 82.5)	0.776 (0.733, 0.819)	64.2 (57.4, 70.5)	86.8 (82.5, 90.2)	0.527	<0.001
PDR	64.5 (56.0, 72.3)	93.1 (90.1, 95.3)	0.788 (0.738, 0.839)	76.5 (67.6, 83.6)	88.4 (84.9, 91.2)	0.608	<0.001

DR_{DSS}: Diabetic retinopathy diagnosis by EyeWisdom®DSS; DR_{MCS}: Diabetic retinopathy diagnosis by EyeWisdom®MCS; NPDR: non-proliferative diabetic retinopathy; PDR: proliferative diabetic retinopathy; AUC: area under the curve; PPV: positive predictive value; NPV: negative predictive value.

ing result was positive, the probability of DR was 87.5%, and when the screening result was negative, the probability of participants not suffering from DR was 86.3%. For EyeWisdom®MCS, when the screening result was positive, the probability of DR was 93.5%, and when the screening result was negative, the probability of participants not suffering from DR was 73.0%. Our sensitivity was similar to that found in He *et al.*'s study [23], in which the sensitivity of AI software (Airdoc, Beijing, China) was 90.8%. Another study by Rajalakshmi *et al.* reported that EyeArt smartphone-based AI software showed 95.8% sensitivity and 80.2% specificity for detecting DR. The kappa agreement between EyeArt and the ophthalmologist grading for DR was 0.78 and for PDR it was 0.53 [25]. EyeWisdom has two systems: EyeWisdom®DSS has the advantage in detecting "DR" and EyeWisdom®MCS is good at detecting "no DR". Thus, it is necessary to build a new synthetic deep-learning AI system based on the algorithms of both EyeWisdom®DSS and EyeWisdom®MCS that can detect both "DR" and "no DR" effectively.

Undoubtedly, some limitations of this study should be noted. First, although EyeWisdom can diagnose and grade DR through an AI algorithm, it is not suitable for some patients. For example, it is not possible to obtain fundus photographs from some DM patients due to their small pupils or poor image quality from the opacity of cataracts. Second, EyeWisdom completes the diagnosis and grading according to the location and number of typical fundus lesions, such as retinal hemorrhage, micro angioma, and hard exudation. For retinal hemorrhage or neovascularization caused by other diseases, EyeWisdom cannot make a differential diagnosis. Third, the study participants were DM patients at the Fundus Disease Center, most of which had developed eye-related symptoms or retinopathy. Therefore, the prevalence and diagnostic efficacy found in this study may not be representative for all DM patients. Finally, the sample size was relatively small and the patients were from a single hospital; therefore, future studies should be conducted with larger samples and field settings.

Measures can be taken to address these limitations in the future. For example, the AI algorithm can be optimized to enable the system to make a differential diagnosis by taking into account more detailed information, such as disease history indicators, duration of disease, and pathological characteristics. For patients with a smaller pupil, manual photography after mydriasis and then transmission of the image to EyeWisdom®DSS and EyeWisdom®MCS may be suitable. Where mydriasis cannot be photographed, scanning laser ophthalmoscopy is currently used for DR diagnosis.

In conclusion, the prevalence of DR, NPDR, and PDR was high in patients with DM. On the one hand, EyeWisdom®DSS is more proficient at identifying DR, but its DR-classification accuracy is relatively poor. EyeWisdom®MCS, on the other hand, is better at identifying the absence of DR. Although the classification efficacy of EyeWisdom is poor, it has the benefits of economy, simple operation, convenient image transmission, and remote guidance. With the development of the Internet and 5G technology, using AI to diagnose DR will undoubtedly save significant manpower and financial resources in countryside or rural district and help to make population screening for DR more affordable [26,27]. Therefore, the system can not only provide a diagnostic platform for community clinics and countryside areas in developing countries, but it can also help establish a large-scale AI-based screening model for DR. It can also play an important auxiliary role in improving the awareness, treatment, and monitoring of disease progression of patients in developing countries, especially in rural areas.

Declaration of Competing Interest

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

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Author contribution

Z.L. and X.P. contributed to the conception of the study. X.P. and X.Y. contributed to the data interpretation, data analysis and manuscript writing. Y.Y. and H.Z. contributed to interpretation, discussion, reviewed/edited the manuscript. M.X. and R.H. contributed to the data collection. Y.W. contributed to the grammar of the manuscript. All authors read and approved the final manuscript.

REFERENCES

[1] International diabetes federation diabetes atlas, 2019, 9th Edition [Internet]. Accessed on 13 October 2020. Available from: http://www.diabetesatlas.org/.
[2] Bawankar P, Shanbhag N, K. SS, Dhawan B, Palsule A, Kumar D, et al. Sensitivity and specificity of automated analysis of single-field non-mydriatic fundus photographs by Bosch DR Algorithm-Comparison with mydriatic fundus photography (ETDRS) for screening in undiagnosed diabetic retinopathy. PLoS One 2017;12(12):e0189854.
[3] Lian F, Wu L, Tian J, Jin M, Zhou S, Zhao M, et al. The effectiveness and safety of a danshen-containing Chinese herbal medicine for diabetic retinopathy: a randomized, double-blind, placebo-controlled multicenter clinical trial. J. Ethnopharmacol. 2015;164:71–7.
[4] Sivaprasad S, Gupta B, Crosby-Nwaobi R, Evans J. Prevalence of diabetic retinopathy in various ethnic groups: a worldwide perspective. Surv. Ophthalmol. 2012;57(4):347–70.
[5] Ruta LM, Magliano DJ, Lemesurier R, Taylor HR, Zimmet PZ, Shaw JE. Prevalence of diabetic retinopathy in Type 2 diabetes in developing and developed countries. Diabet. Med. 2013;30:387–98.
[6] Sadda SR. Assessing the severity of diabetic retinopathy: early treatment diabetic retinopathy study report number 10. Ophthalmology 2020;127(4):S97–8.

[7] Tan F, Chen Qi, Zhuang X, Wu C, Qian Y, Wang Y, et al. Associated risk factors in the early stage of diabetic retinopathy. Eye Vis (Lond). 2019;6(1):23.
[8] Arcadu F, Benmansour F, Maunz A, Willis J, Haskova Z, Prunotto M. Deep learning algorithm predicts diabetic retinopathy progression in individual patients. NPJ Digit Med. 2019;2:92.
[9] Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog. Retin. Eye Res. 2018;67:1–29.
[10] Huang OS, Tay WT, Tai ES, Wang JJ, Saw SM, Jeganathan VS, et al. Lack of awareness amongst community patients with diabetes and diabetic retinopathy: the Singapore Malay eye study. Ann. Acad. Med. Singap. 2009;38:1048–55.
[11] Teng Y, Cui H, Zhang QS, Teng YF, Su Y, Yang MM, et al. Prevalence of diabetic retinopathy among the elderly in rural southern Shuangcheng city, Heilongjiang province. Chin. J. Epidemiol. 2010;31:856–9.
[12] Bakkar MM, Haddad MF, Gammoh YS. Awareness of diabetic retinopathy among patients with type 2 diabetes mellitus in Jordan. Diabetes Metab. Syndr. Obes. 2017;10:435–41.
[13] Ting DSW, Cheung C-L, Lim G, Tan GSW, Quang ND, Gan A, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. JAMA 2017;318(22):2211.
[14] Zhiyuanhuitu Vistel [Internet]. Accessed on 10 October 2020. Available from: https://vistel.cn/.
[15] Cuadros J, Sim I. EyePACS: an open source clinical communication system for eye care. Stud. Health Technol. Inform. 2004;107:207–11.
[16] Hajian-Tilaki K. Sample size estimation in diagnostic test studies of biomedical informatics. J. Biomed. Inform. 2014;48:193–204.
[17] Li Y, Teng D, Shi X, Qin G, Qin Y, Quan H, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study. BMJ 2020;369:m997.
[18] Seino Y, Nanjo K, Tajima N, Kadowaki T, Kashiwagi A, Araki E, et al. Report of the committee on the classification and diagnostic criteria of diabetes mellitus. J. Diabetes Investig. 2010;1(5):212–28.
[19] Wilkinson CP, Ferris FL, Klein RE, Lee PP, Agardh CD, Davis M, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. Ophthalmology 2003;110(9):1677–82.
[20] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract. 2010;87(1):4–14.
[21] Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res. Clin. Pract. 2014;103(2):137–49.
[22] Song P, Yu J, Chan KY, Theodoratou E, Rudan I. Prevalence, risk factors and burden of diabetic retinopathy in China: a systematic review and meta-analysis. J. Glob. Health 2018;8 (1). https://doi.org/10.7189/jogh.08.010803.
[23] He J, Cao T, Xu F, Wang S, Tao H, Wu T, et al. Artificial intelligence-based screening for diabetic retinopathy at community hospital. Eye (Lond). 2020;34(3):572–6.
[24] Rajalakshmi R, Arulmalar S, Usha M, Prathiba V, Kareemuddin KS, Anjana RM, et al. Validation of smartphone based retinal photography for diabetic retinopathy screening. PLoS One 2015;10(9):e0138285.
[25] Rajalakshmi R, Subashini R, Anjana RM, Mohan V. Automated diabetic retinopathy detection in smartphone-based fundus photography using artificial intelligence. Eye (Lond). 2018;32(6):1138–44.
[26] Xie Y, Gunasekeran DV, Balaskas K, Keane PA, Sim DA, Bachmann LM, et al. Health economic and safety considerations for artificial intelligence applications in diabetic retinopathy screening. Transl. Vis. Sci. Technol. 2020;9(2):22.
[27] Fenner BJ, Wong RLM, Lam W-C, Tan GSW, Cheung GCM. Advances in retinal imaging and applications in diabetic retinopathy screening: a review. Ophthalmol. Ther. 2018;7 (2):333–46.