Smartphone Eye Examination: Artificial Intelligence and Telemedicine

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Abstract

Background: *The current medical scenario is closely linked to recent progress in telecommunications, photodocumentation, and artificial intelligence (AI). Smartphone eye examination may represent a promising tool in the technological spectrum, with special interest for primary health care services. Obtaining fundus imaging with this technique has improved and democratized the teaching of fundoscopy, but in particular, it contributes greatly to screening diseases with high rates of blindness. Eye examination using smartphones essentially represents a cheap and safe method, thus contributing to public policies on population screening. This review aims to provide an update on the use of this resource and its future prospects, especially as a screening and ophthalmic diagnostic tool.*
Methods: *In this review, we surveyed major published advances in retinal and anterior segment analysis using AI. We performed an electronic search on the Medical Literature Analysis and Retrieval System Online (MEDLINE), EMBASE, and Cochrane Library for published literature without a deadline. We included studies that compared the diagnostic accuracy of smartphone ophthalmoscopy for detecting prevalent diseases with an accurate or commonly employed reference standard.*
Results: *There are few databases with complete metadata, providing demographic data, and few databases with sufficient images involving current or new therapies. It should be taken into consideration that these are databases containing images captured using different systems and formats, with information often being excluded without essential detailing of the reasons for exclusion, which further distances them from real-life conditions. The safety, portability, low cost, and reproducibility of smartphone eye images are discussed in several studies, with encouraging results.*
Conclusions: *The high level of agreement between conventional and a smartphone method shows a powerful arsenal for screening and early diagnosis of the main causes of blindness, such as cataract, glaucoma, diabetic retinopathy, and age-related macular degeneration. In addition to streamlining the medical workflow and bringing benefits for public health policies, smartphone eye examination can make safe and quality assessment available to the population.*

Keywords: *smartphone-based fundus imaging, mobile phones, artificial intelligence, retinal imaging, smartphone, telemedicine*

Introduction

Exploration of the eye fundus has always aroused interest, and experimental observation of cats' eyes while submerged in water is considered to have been pioneer in this area. Following the description made in 1910 by Allvar Gullstrand (Nobel Prize, 1911), fundus cameras gradually evolved, maintaining many of these original concepts.[1] The first images captured date from 1886[2] to 1891.[3] More than 130 years have therefore gone by since those images and their prominent corneal reflex and faintly visible optic disk.[4]

In the 1970s, Pomerantzeff et al[5,6] and Ducrey et al[7] designed a wide-angle camera with separation of the light source to obtain photographs in a field of $\sim 148°$ from equator to equator. With a fiber optic source close to the cornea or sclera for transillumination of the eyeball, this method alleviated previous problems associated with intraocular illumination.[8,9]

Camera systems have evolved significantly in obtaining sharp, wide-field images.[2,9] Conventional fundus cameras offer excellent quality images, with or without mydriasis, but their volume, portability logistics, availability, high acquisition and maintenance costs, as well as dependence on specialized professionals, make them unviable for use with the population at large, especially in developing countries. In these scenarios, direct ophthalmoscopy ends up being the most widely used method, especially by physicians who are not ophthalmologists.[10,11] Despite this, considerably low levels of confidence in retinal assessment using this tool have been reported.[12]

Recently, more user-friendly, intelligent, and portable tools, for both the posterior and anterior segments, have expanded the technological spectrum.[13] The greater the public sector constraints, the greater the benefits offered through these options.[4,14] Recent progress in access to telecommunications, together with the deployment of handheld devices and smartphone-based imaging systems, has resulted in advancement that facilitates diagnosis, photodocumentation, telemedicine, and artificial intelligence (AI).[15,16] There are currently 3.8 billion smartphones worldwide. This means that 66.9% of people have their own device.[17]

The smartphone has become commonplace as both an irreplaceable and rapid source of information because of its accessibility and portability.[15] Hundreds of applications for use in ophthalmology are available, including for assistance during patient care such as checking visual acuity, refraction, chromatic tests, visual fields, amblyopia assessment, and tear film.[18–22] Its use for eye imaging is of growing interest, especially in expanding screening for diseases with high blindness rates, such as diabetic retinopathy, retinopathy of prematurity (ROP), glaucoma, and age-related macular degeneration.[23–25]

The objective of this review was to provide an update on the use of this resource and its perspectives, especially as a screening and ophthalmologic diagnostic tool.

Discussion

THE SMARTPHONE AS A DIAGNOSTIC TOOL

Obtaining fundus imaging with this technique has improved and democratized the teaching of fundoscopy, but in particular, it contributes greatly to screening for diseases with high rates of blindness.[15,23] For example, significant global growth of myopia by the year 2025 has been projected (~ 1 billion with high myopia), reinforcing the need for these improvements in accessibility and prevention.[10,26]

Ophthalmoscopy using smartphones (smartphone fundoscopy [SF]) essentially represents a cheap and safe method, thus contributing to public policies on population screening.[27–30] Diverse health care professionals can access and handle this tool with adequate reproducibility. In a randomized prospective study, Kim and Chao[31] assessed medical students with regard to ease of learning ophthalmoscopy using direct and smartphone techniques. After only 1 h of teaching instruction, the optic nerve was clearly correctly identified in 82.3% of cases with smartphone use versus 48.5% with direct ophthalmoscopy. Their study found greater ease and confidence in using SF. Dunn et al[32] also studied the ease of use of this method by second-year medical students, with encouraging results. Jansen et al[33] found no differences between technicians and ophthalmologists, none of whom had previous experience in SF, with regard to learning the method, thus emphasizing the high accessibility of the resource.

On the contrary, Kohler et al[29] obtained slightly discordant results when comparing both techniques with 137 students. The mean number of attempts to visualize retinal structures was 2.7 (standard deviation [SD] ±2.3) with direct ophthalmoscopy versus 4.5 (SD ±2.9) with the smartphone (*Figs. 1 and 2*). Omari et al.[34] assessed the use of SF in the emergency room of an academic center, and observed no difference between medical residents and attending reviewers' results, and the correct diagnosis was >78%.

The images obtained, including those from eye selfies, can be assessed remotely, either synchronously or asynchronously. Primary health care settings with limited resources, due to either the absence of specialized physicians or lack of equipment, can strongly benefit from SF with uncontestable cost-effectiveness and reduction of disparities.[14,35–38] The most recent generations of digital cameras enable external and fundoscopy images to be obtained without the need to use condenser lenses.[39] Logistical difficulties, technical errors, poor communication, and privacy issues are limitations of its use through telecommunications.[15]

In particular, in the coronavirus disease 2019 (COVID-19) era, increasing and practical use of this option has been seen.[40,41] He et al[42] compared SF with handheld NMFP RetinaVue 100 (Welch Allyn) in a prospective cross-sectional surveillance and diagnostic accuracy study among 79 adult neurological inpatients. They observed 14% of relevant fundoscopic signs, and the agreement was slightly lower for SF.

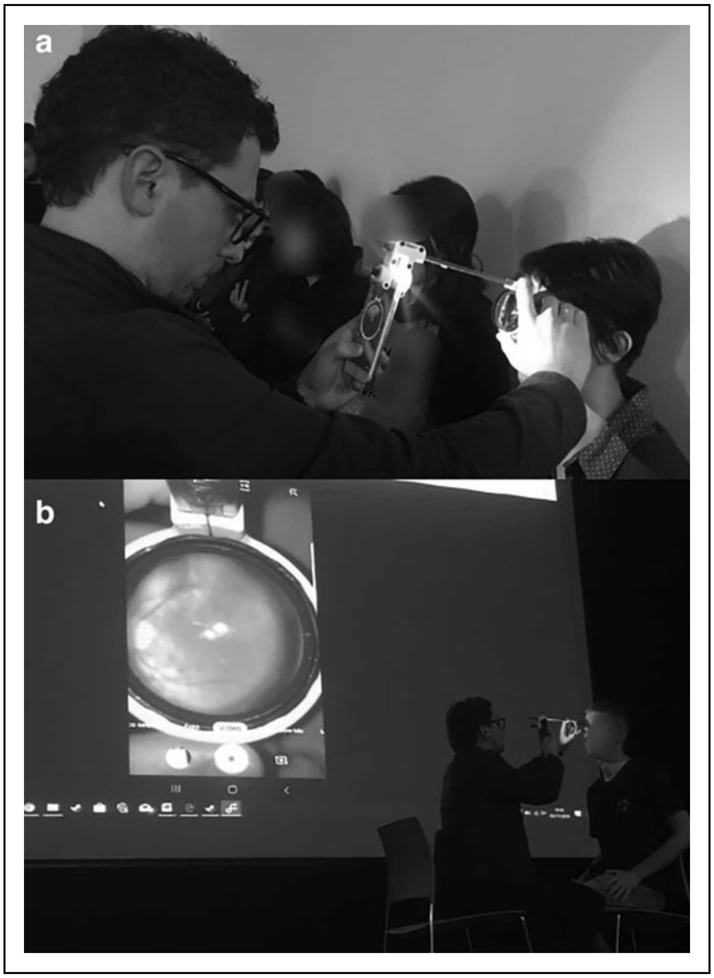

Fig. 1. Smartphone on fundoscopy: basic technique **(a)** and first-year medical students demonstrating the examination technique live, with simultaneous transmission to the auditorium screen **(b)**.

Fig. 2. Selfie fundoscopy. An option to automonitorization far from the medical services. The examination is done using the aid of a mirror.

In this scenario, patients can have follow-up without travelling to specialized centers. Thus, there is a reduction in the number of unnecessary consultations, an improvement in scheduling logistics, and greater patient adherence.[43] In addition, exchanges between young doctors in rural areas and specialists from tertiary hospitals and universities are made possible.[15] A systematic review showed teleophthalmology to be a cost-effective alternative to eye examinations in general.[23] It can best be seen as an extension to the existing eye care services, rather than a replacement[15] (*Fig. 3*).

However, some aspects have not yet been fully completed. Some versions already use applications designed for tracking changes based on AI.[4,16,44] There are SF devices, such as “iExaminer” and “D-Eye,” which offer magnified images of good quality.[10] Importantly, there are, to date, no increased photobiological or photochemical risks with the use of smartphones and condenser lenses.[45]

A systematic review and meta-analysis investigated the agreement between images obtained through smartphones and conventional methods (fundoscopic examination and retinal cameras) in 4,219 eyes. Regardless of the smartphone brand, the lens used (20 or 28 diopters), or the adapter, agreement between methods was substantial, with a Kappa coefficient of 77.77% (95% confidence interval [CI]: 70.34–83.70).

The area under the receiver operator characteristic curve (AUC) was 0.86%, with an 80% sensitivity and specificity cut-off point.[14] Murtaza et al[46] showed similar data, with detection of ophthalmologic changes in 74.3% of the cases evaluated using smartphones versus 77.1% using traditional retinal cameras. Image quality was poorer for very elderly, black, and pseudophakic patients. Low patient co-operation was also associated with loss of image quality.[14]

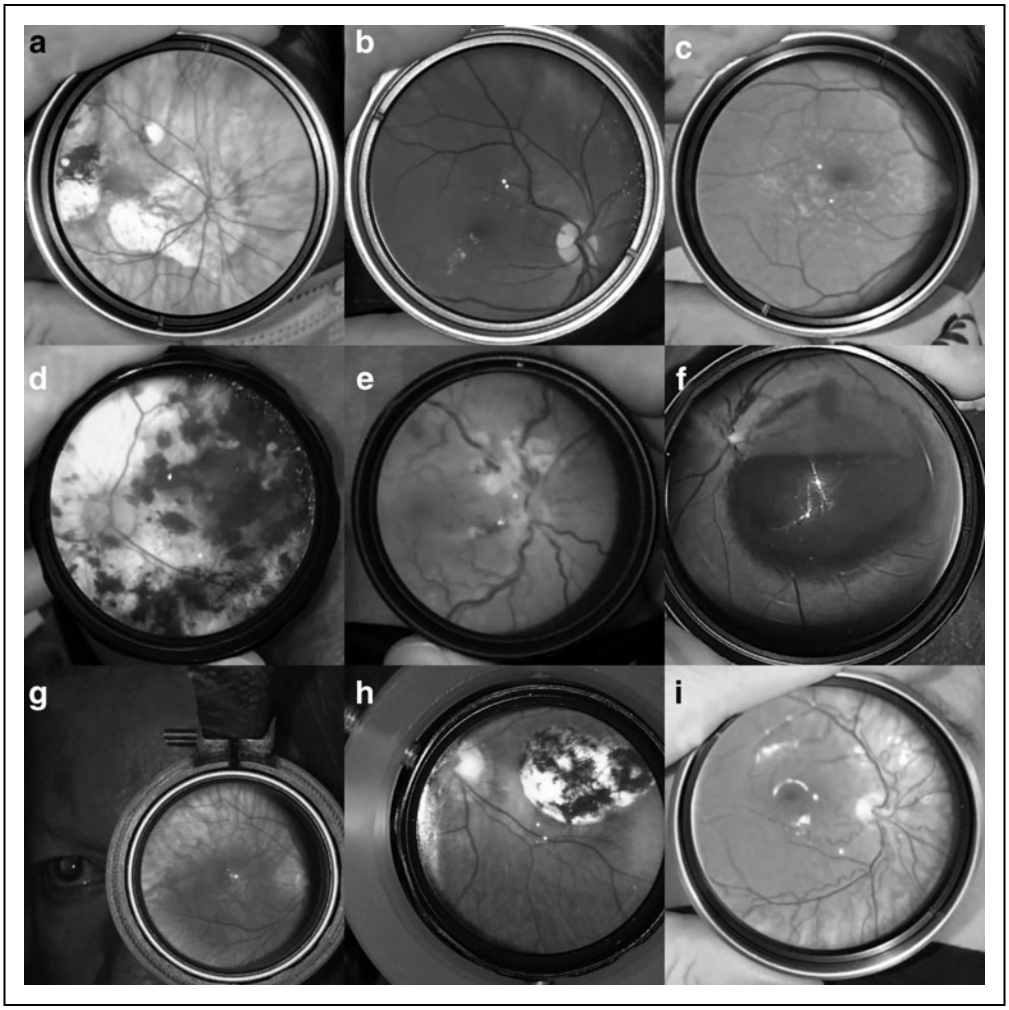

Fig. 3. Different diagnoses: **(a)** myopic degeneration, **(b)** diabetic macular edema, **(c)** age-related macular degeneration, **(d)** traumatic retinopathy, **(e)** hypertensive retinopathy, **(f)** preretinal hemorrhage, **(g)** albinism, **(h)** toxoplasmic retinochoroiditis, **(i)** retinopathy of prematurity.

ANTERIOR SEGMENT

Cataracts are one of the leading causes of visual impairment, accounting for up to 65.2 million cases of visual impairment or blindness worldwide. Currently, biomicroscopy is the method used to diagnose lens opacities, but variation between examiners can influence classification. Especially in rural areas where unequal distribution of specialists and resources persists, this method still faces difficulties.[47]

Algorithms using AI in the context of the anterior segment are still little explored. Lack of robust equipment and external validation continues to be important limitations. Algorithms may be able to perform automated cataract detection and classification. Images based on slit-lamp photography are being used[47,48] (*Fig. 4*).

In a multicenter study in China, Wu et al[49] assessed a universal AI platform for collaborative cataract management. They used 37,638 mydriatic and nonmydriatic slit-lamp images of 10,257 cases available through the Chinese Medical Alliance for Artificial Intelligence (CMAAI) (30,132 images for training agents and 7,506 for the validation test). The AI agent achieved an "area under the receiver operator characteristic curve" (AUC) >99% for cataract diagnosis in all tests. The agent achieved an AUC >90% for reference cataract detection, even in the case of the nonmydriatic images.

Askarian et al[50] using different smartphone camera sensors and chroma variations could diagnose diseased eyes with 96.6%, 93.4% specificity, and 93.75% sensitivity. Their method is affordable, rapid, easy to use, and versatile for bedside telemedicine. Images from a smartphone could be a useful and noninferior tool in areas with limited health care facilities, especially to add telehealth consultations.[51,52]

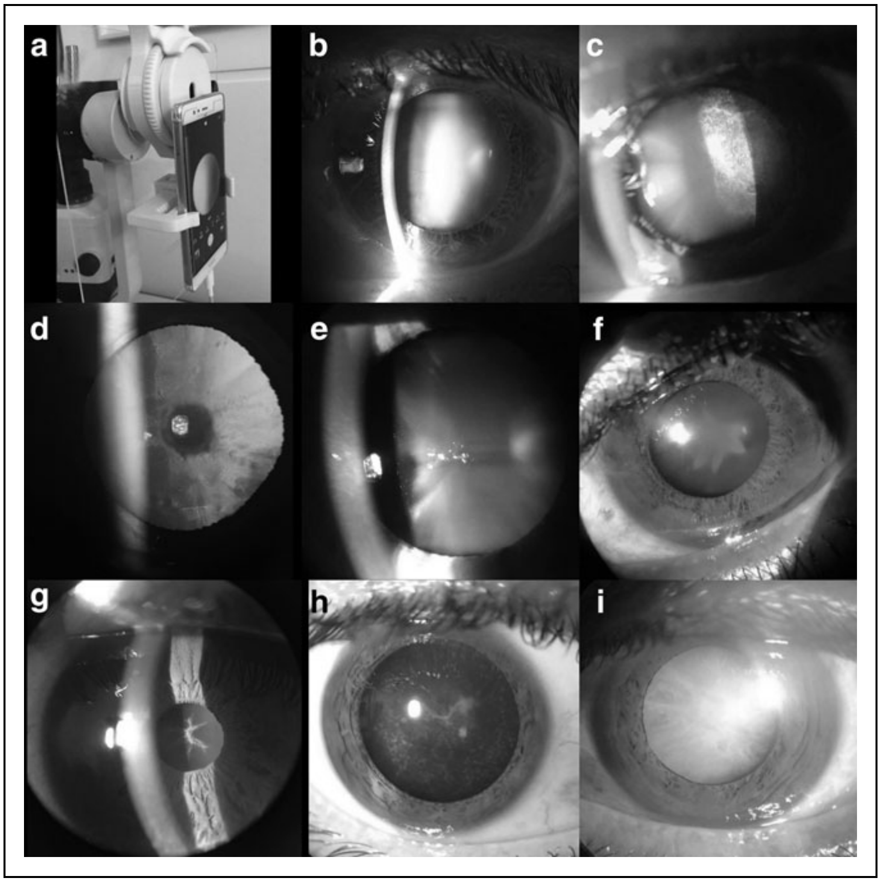

Fig. 4. Smartphone and cataract: **(a)** slit-lamp adapter; **(b)** nuclear cataract; **(c)** posterior subcapsular cataract; **(d)** posterior polar cataract; **(e)** Christmas tree cataract; **(f)** traumatic cataract; **(g)** chlorpromazine-induced cataract; **(h)** congenital cataract; and **(i)** dense white cataract.

Increasing use of retinal imaging involving AI, especially in diabetic retinopathy, is encouraging in posterior segment disorders.[53] Studies with automated systems involving cataract classification based on the sharpness of fundus images are emerging with encouraging results.[54,55] Syarifah et al[56] and Dong et al[57] used deep learning based on images to detect and classify cataracts. Fundus image visibility was used to indicate four classes of lens opacity severity (normal, mild, moderate, and severe).

The 7,951 images were preprocessed using the "maximum entropy method," and subsequently features were extracted using the Caffe-based deep learning network. The Support Vector Machine (SVM) and Softmax (form of machine learning algorithm) are used for cataract classification, obtaining classification accuracy of up to 84.7%. When validated in internal testing with 2,355 images, the authors report 94.07% correct cataract detection and 90.82% correct disease severity level classification.[57]

Ran et al[58] studied an algorithm through the Deep Convoluted Neural Network for initial feature extraction associated with the Random Forest Network (machine learning model) for predicting presence of cataracts. The presence of the disease was also assessed by experienced ophthalmologists based on visualization of the fundus structures of 5,409 images. The system provided a 97.4% AUC, 97.26% sensitivity, and 96.92% specificity for cataract detection.

Use of AI, especially in relation to cataracts, provides encouraging results, but improvements are still required. Besides the difficulty of external validation, definition of "ground truth" as a reference is based on an entirely subjective method based on assessment of the fundus photograph's "haziness" level.[47] Portable slit lamps attached to smartphones aid in anterior segment diagnostic examinations.[59] The reproducibility of images of cortical and posterior subcapsular cataracts appears to be higher than that in other sites.[60]

In addition to algorithms for cataract diagnosis and classification, deep learning has been helping the process of selecting and calculating intraocular lens (IOL) "power formulas."[47,61,62] The "Ladas Super Formula" was developed based on existing formulae (Hoffer Q, Holladay-1, Holladay-1 with Koch adjustment, Haigis, and SRK/T formula). Although there is little mathematical detail in the literature, the method is believed to be able to specify the most optimal biometric components of each existing formula, such as axial length and corneal refractive power.

Based on an algorithm trained on $\sim$12,000 eyes with measurements obtained from the Haag-Streit Lenstar, the Hill-Radial Basis Function (RBF) method was able to estimate the power of the IOL. These algorithms still require adaptations, but it is believed that eyes with atypical biometric profiles, such as extremely short and long axial lengths, may be the greatest beneficiaries of this technology.[47]

Scantling-Birch et al[63] reviewed the apps available for toric IOL surgery. They observed that the Toric Calculator for iPhone and iToric Patwardhan applications achieved similar levels of misalignment reduction when compared with digital systems.

Dutt et al[13] designed a smartphone slit lamp for tele-ophthalmology use with an adjustable slit beam and different background lights and illumination angles. They provided a demonstration of a telemedicine and ergonomic—user-friendly device that is very easy for nonspecialists to use. Rampat et al[48] demonstrated that the use of guidelines such as CONSORT-AI, SPIRIT-AI, and STARD-AI will guide the AI-related trials for anterior segment diseases and refractive evaluations. Goel et al[52] in a noninferiority survey study concluded that smartphone camera was noninferior to the slit-lamp camera devices.

Confocal specular microscopy is an important tool for corneal endothelial analysis.[64] In view of its high cost and low accessibility in more remote areas, smartphone-based specular imaging and automated analysis is being tested. Mantena et al[65] validated this tool with results comparable with the standard method. Capable of quantitatively assessing the corneal endothelium, a smartphone connected to a slit lamp was used to acquire images using the specular reflection technique. The image processing algorithm on the device found no significance between the two methods regarding endothelial cell density and percentage of hexagonal cells. The coefficient of variation was significant.

GLAUCOMA

Glaucoma, alongside diabetic retinopathy and cataract, is among the leading causes of visual impairment and blindness. Considering its silent course, it is believed that >50% of individuals are not aware that they have it until they reach advanced stages of the disease.[66] Russo et al[67] assessed agreement between optic disk results of patients with ocular hypertension and primary open-angle glaucoma using SF and fundus biomicroscopy.

No statistical differences were observed between the mean estimates of vertical disk cupping in both techniques, suggesting that smartphone ophthalmoscopy is a suitable technology to aid in screening for the disease. Accurate agreement between the two methods was observed in 21 of 29 eyes with primary open-angle glaucoma, and in 52 of 78 eyes of patients with ocular hypertension.

Bastawrous et al[68] assessed 2,152 optic disks in Kenya. High-quality images were observed in 73.7% of cases, regardless of the system used. Kappa coefficient of 69% evidences excellent agreement between the methods, allowing adequate remote classification of the images obtained. Studies using smartphones are also emerging for the assessment of post-trabeculectomy patients.[69]

Ting et al[70] assessed 71,896 retina images of 14,880 patients for possible glaucoma. Sensitivity was 96.4% (95% CI: 81.7–99.9), and specificity was 87.2% (95% CI: 86.8–87.5) with an AUC of 0.942. Muhsen et al[71] in a prospective clinical-based validation study performed on 90 patients from a tertiary hospital observed a limited accuracy and agreement between expert ophthalmologist and smartphone-based D-Eye fundoscopy.

In addition, new tools coupled to the smartphone have emerged, including the observation of blebs, tonometry, gonioscopy, and perimetry. Morphological features of the bleb, such as vascularization and microcysts, can be analyzed with adequate clarity.[69] Wu et al[72] developed a prototype smartphone-based tonometer and demonstrated grossly equivalent IOP measurements related to different tonometers (Goldmann, ICare, pneumotonometry, and Tono-Pen). Pujari et al[73] described ways to get gonioscopy images using smartphone and gonioscopic lenses. Pradham et al[74] showed a fairly good agreement between a smartphone-based head mounted perimeter with Humphrey Field Analyzer. They also highlighted that the portable system was very well accepted and could be a potential tool.

Li et al[75] also assessed the performance of the deep learning algorithm to detect glaucomatous optic neuropathy and obtained very encouraging results. They included 48,116 color fundus photographs for software development and validation, and trained 21 ophthalmologists to classify the photographs. AUC was 0.986 with 95.6% sensitivity and 92% specificity. Coexistence of high myopia or pathological myopia was associated with false-positive and false-negative results. It is possible that the better long-term approach would be to use AI for predicting outcomes.

Nakahara et al[76] validated the use of a deep learning algorithm to automatically screen glaucoma from smartphone-based images. Bragança et al[77] using the panoptic ophthalmoscope and smartphone built a new public dataset that offers images entirely obtained with this technique. They analyzed 1,000 volunteers with a deep learning approach with an accuracy of 90% to identify glaucoma from fundus images. Coan et al[78] in a recent review of the use of two-step AI frameworks for glaucoma detection showed accuracy between 85% and 100%, and highlighted the necessity of more high-quality datasets.

RETINAL DISEASES

Diabetic retinopathy. It is believed that one in three people with diabetes have diabetic retinopathy.[79] Given this condition, early detection methods are emphatically even more necessary in the current scenario.[70] Traditional fundus imaging systems are known to be expensive, offering little portability and often requiring patients to be in vertical position when they are examined.[4,9] These characteristics greatly reduced their use in primary health care and mobile care services.[80] Risk of diabetic retinopathy can be reduced by 95% through early screening, detection, and treatment.[10]

In diabetic patients, good performance in retinal imaging with SF has been proven in several studies.[80–90] A systematic review with meta-analysis involving 1,430 diabetic patients highlighted the diagnostic accuracy of the technique, especially in more advanced cases. Indirect ophthalmoscopy and slit-lamp biomicroscopy were the reference standards commonly used as comparisons in these studies. Sensitivity and specificity in diagnosing diabetic retinopathy, regardless of the level of severity, were 87% (95% CI: 74–94) and 94% (95% CI: 81–98), respectively. For proliferative disease, sensitivity and specificity reached 92% (95% CI: 79–97) and 99% (95% CI: 96–99), respectively.[80]

Rajalakshmi et al[81] analyzed 602 eyes of diabetic patients using both techniques (conventional Carl Zeiss Fundus camera and smartphone). There was no difference between the techniques concerning their ability to detect the different stages of retinopathy. The conventional camera showed nonproliferative diabetic retinopathy in 43.9% of the patients and proliferative retinopathy in 15.3%. The smartphone method detected nonproliferative disease in 40.2% and proliferative disease in 15.3% of cases.

In Italy, Russo et al[89] analyzed 240 eyes of diabetic patients and found very similar results between the techniques. Compared with fundus biomicroscopy, the sensitivity and specificity of SF in detecting clinically significant macular edema were 81% and 98%, respectively. For proliferative disease, the rates were as high as 89% and 100%.

In a study conducted in India with 381 diabetic eyes, Wintergest et al[90] analyzed different smartphone-based approaches to fundus imaging (three direct approaches and one indirect approach). Devices based on direct ophthalmoscopy including Peek Retina (Peek Vision Ltd., London, UK, adapter version from 2017), D-EYE (D-EYE S.r.l.; Padova, Italy, adapter version from 2016), a do-it-yourself solution developed by the Sankara Eye for Samsung Galaxy S4 Smartphones (Samsung Electronics, Seoul, South Korea) were used in these techniques. The indirect approach used the Paxos Scope adapter (Digisight Technologies, Inc., now Verana Health, Inc., San Francisco, CA, adapter version from 2017).

In accordance with the requirements of the Paxos Scope application, iPhones (6th generation; Apple, Inc., Cupertino, CA) were used jointly with the Pan Retinal 2.2 lens (Volk Optical, Inc., Mentor, OH) for indirect ophthalmoscopy. Smartphone imaging using indirect ophthalmoscopy produced better image quality ($p < 0.01$). However, examination time was longer (111 vs. 68–87 s, $p < 0.0001$).

ROP and others. Screening for ROP using smartphones is also attracting interest. With the aid of an accessory lens, peripheral images captured were considered satisfactory for staging and determining the need for treatment.[33,91–93] In a comparison with the standard fundoscopy technique, Wintergers et al[36] analyzed 26 eyes with this disease. The level of detail observed was similar between the techniques, while a longer examination time was found for the smartphone method (109.0 ± 57.8 vs. 75.9 ± 36.3 s, $p < 0.01$).

Inter-rater reliability (Cohen's squared kappa) for the classification of plus disease and stage of ROP using the smartphone method was 0.84 and 0.86, respectively. With the standard fundoscopy technique, these values were 0.76 and 0.90. Determination of the ROP zone was in agreement with ophthalmoscopy in 80% of eyes for the smartphone method and in 82% of eyes for the conventional method.

Sivaraman et al[94] demonstrated that SF provided a wide fundus view of 50–65° with a single shot, but mosaic of 4–5 images from different zones can offer $\sim 100°$ with a pupil of 5 mm. Singh et al[95] described a novel technique using the smartphone mounted on virtual-reality headset that allows one to capture useful peripheral retinal images with indentation. Patel et al[96] analyzed 43 children (mean age 6.7 years) with different diseases such as retinoblastoma, Coats, and commotio retina, and the mean time to get a 90° field of view was 2.3 ± 1.1 min. They used the RetinaScope device with the aid of an iPhone 5s smartphone (Apple) and a 54-D ophthalmic lens (OI54-A; Ocular Instruments, Bellevue, WA).

There was 96% agreement between the imaging diagnostic and the clinical diagnostic. This device was well tolerated and increases the possibilities for pediatric ophthalmology. Lin et al[97] compared RetCam versus SF in 71 premature babies, and concluded that SF could capture adequate retinal images but was unable to judge the zone and stage of ROP.

Detection of ROP through AI was studied by Brown et al[98] using 5,511 retinal images. In all, 14.6% (805) patients with preplus disease and 3.1% (172) with plus disease were detected. With regard to the diagnosis of plus disease, the algorithm achieved 93% sensitivity and 94% specificity. For preplus disease, the rates were 100% and 94%, respectively.

Two applications, MDEyeCare and CRADLE, developed for smartphone-based leukocoria detection were analyzed in 34 eyes with retinoblastoma by Khedekar et al.[99] Without the need for pupil dilation and anesthesia, the method is based on the red reflex and is especially useful for physicians who are not ophthalmologists. The MDEyeCare application was able to detect leukocoria at the early stages of retinoblastoma in 50% of cases in group B and in 83% in group C. At the late stages of the disease (groups D and E), 100% of the tumors were detected. The CRADLE application was able to detect leukocoria only at the advanced stages of the disease.

Associated with AI. AI software applied to SF images has shown adequate performance in detecting prevalent anterior and posterior segment diseases.[38,43,47,48,54,64,65,100–104] The concept of AI dates from 1956 and since then has gradually been enhanced, so that in some situations in ophthalmology it achieves accuracy of 98–100%.[55]

AI still has obstacles to overcome before it can be universally adopted. For example, many databases have been formed with images from films, the quality of which varies greatly and which are now in disuse. In addition, collection of images, which need to be very broad and very comprehensive, has mostly been derived from clinical trials, which is known to be far removed from image collection conditions in real clinical life. There are few databases with complete and public metadata, providing demographic data, and few databases with sufficient images involving current or new therapies.

Information is lacking on who made the diagnosis, this being essential for system reliability, and attempts at external validation, or validation of negative and positive predictive values, are scarce, even though these data are the mainstay of any trial. It should be taken into consideration that these are databases containing images captured using different systems and formats, with information often being excluded without essential detailing of the reasons for exclusion, which further distances them from real-life conditions. It is also noteworthy that there is a lack of uniformity and cooperation between institutions in the creation of common, freely accessible databases, with the essential issues of preservation of privacy and data security having remained undefined so far.[105–108]

Examples of AI algorithms for screening diabetic retinopathy include Google AI, EyeArt, and IDxDR.[109–112] They found 89.5% sensitivity (95% CI: 82.3–94.0) and 92.4% specificity (95% CI: 86.4–95.9). In the case of referable diabetic retinopathy, sensitivity was 97.9% (95% CI: 92.6–99.4); specificity was 85.9% (95% CI: 76.5–91.9). Despite the small number of studies covered by the analysis, the results demonstrated a significant negative predictive value (99.9–100.0%).[113] A meta-analysis conducted by Tan et al[80] also found similar results, showing that smartphone ophthalmoscopy can perform well in detecting diabetic retinopathy.

In their cross-sectional study, Sosale et al[114] used AI on images of 900 subjects taken with "the Remidio NM fundus-on-phone camera" (iPhone 6) to detect diabetic retinopathy. They used the Medios Technologies, Singapore, AI algorithm. It can be used offline. Regardless of the stage of the disease, sensitivity and specificity of the AI algorithm were 83.3% (95% CI: 80.9–85.7) and 95.5% (95% CI: 94.1–96.8), respectively. With regard to detection of diabetic macular edema or moderate or worse nonproliferative diabetic retinopathy, AI sensitivity and specificity reached 93% (95% CI: 91.3–94.7) and 92.5% (95% CI: 90.8–94.2), respectively.

Malerbi et al[115] analyzed the accuracy of a deep learning device (PhelcomNet) linked to a handheld retinal camera (Phelcom Eyer). They assessed a total of 679 images. The algorithm's sensitivity and specificity was 97.8% (95% CI: 96.7–98.9) and 61.4% (95% CI: 57.7–65.1), respectively. False-negative cases were classified by trained ophthalmologists as moderate nonproliferative diabetic retinopathy.

AI software applied to SF images and also to optical coherence tomography (OCT) is showing adequate performance in detecting and management of prevalent retinal diseases.[116,117] OCT integrated into a smartphone is complex due to the specific wavelengths to be emitted. Different projects destined to have easy, portable, and cheap equipment exist, and the information linked to the AI will become more precise in the management of certain retinal diseases.

The handheld equipment available discussed by Chopra et al[118] include the Envisu C2300 OCT (Leica Microsystems, Germany), the iVue system by Optovue, Inc., and the Heidelberg Spectralis Flex Module (Heidelberg Engineering, Heidelberg, Germany). The portability of the equipment allows imaging of patients in different positions and locations, such as intensive care units and operating rooms.[119] However, in addition to the steep learning curve, movement and heaviness of the equipment interfere.

The first autonomous AI-based diagnostic system for detecting diabetic retinopathy in primary care has been commercially approved based on a prospective study with 900 participants. Sensitivity and specificity of 87.2% and 90.7%, respectively, were achieved, demonstrating the promising capacity of AI in the diagnosis and prevention of diabetic vision loss.[109]

Ting et al[70] used deep learning to detect diabetic retinopathy and age-related macular degeneration in a set of 71,896 retinal images from 14,880 patients. The software showed "area under the receiver operator characteristic curve" (AUC) of 0.936 with 90.5% sensitivity (95% CI: 87.3–93) and 91.6% specificity (95% CI: 91.0–92.2) for detection of reported diabetic retinopathy. Sensitivity and specificity ratios observed at advanced stages of the disease were 100% (95% CI: 94.1–100) and 91.1% (95% CI: 90.7–91.4), respectively, with an AUC of 0.958. For age-related macular disease, they found 93.2% sensitivity (95% CI: 91.1–99.8) and 88.7% specificity (95% CI: 88.3–89.0) with an AUC of 0.931.

Refractive errors. Among refractive errors, myopia continues to be a growing cause of visual impairment worldwide. Current technology offers the smartphone-based mobile refractometer available through the "GoCheck Kids-Pediatric Vision Screening Solution."[16,37,120] In a study evaluating the application, Peterseim et al[120] found 76.0% sensitivity and 67.2% specificity in the detection of risk factors for amblyopia, with positive predictive values of 57% and negative predictive values of 83.0%. This technology may help in the identification of risk factors for amblyopia, especially in children who do not cooperate during measurement of visual acuity.

Jeganathan et al[121] compared the portable refractor with subjective (manifest and cycloplegic) refraction in 87 subjects with mean age 51.9 ± 18.3 years in a cross-sectional study. They observed small, but clinically significant differences from subjective refraction. Even though the smartphone autorefractor seems to be valuable where access to a specialist is limited.

Luo et al[122] developed an app to estimate the myopic refractive error. In total, 113 myopic subjects with astigmatism no greater than −1.75 diopters were enrolled. They observed the consistency and repeatability of the app when compared with clinical and autorefractor measurements.

Hasrod et al[123] carried out NETRA measurements on subjects with and without cycloplegia, and suggested the use of this portable instrument for geographical regions with eye and vision care limitations. Ee and Samsudin[124] reported a cross-sectional study comparing NETRA smartphone-based and automated refraction with subjective refraction in 204 subjects, and observed significant myopic overestimation of the automatized tools.

Similar refraction results were shown by Joseph et al[125] with the use of the device called ClickCheckTM compared with subjective and autorefraction with high level of agreement for spherical power measurement. Debert et al[126] used a flash concentrator case and a software for simultaneous smartphone photorefraction. This resource appears to be a cost-effective alternative, including amblyopia detection.

Conclusions

Important progress has been made with technology in the last decade, especially in the field of ophthalmology. New portable and easy-to-handle fundus cameras are revolutionizing primary care programs. Images obtained from smartphones have high concordance with traditional methods, and are a powerful arsenal for early screening and diagnosis. Their exponential growth in addition to teleophthalmology appears to be connecting previously remote regions.[66,116,117,127]

New AI systems can assist in screening for the most prevalent causes of blindness, especially in rural and low-resource areas. The smartphone ophthalmoscopy can be considered promising in this scenario, for both general practitioners and specialists, as a viable alternative to conventional screening approaches. Besides speeding up the medical workflow and bringing benefits for public health policies, this technology can provide the population with safe and quality ophthalmic assessment.[10,63]

AI will help overcome the barriers that prevent access to ideal case management and concretely improve overall visual health problems. SF and AI algorithms pave the way for in-home testing. However, like any other new technology it will take a long time for AI to gain support and be implemented in health care systems. One of the main challenges is the lack of data standardization and interoperability.

Health care data are often stored in different formats and systems, making it difficult to integrate and analyze using AI. This can lead to errors and inaccuracies in AI algorithms, which can have serious consequences for patient care. Another challenge is the ethical and legal implications of using AI in health care. For example, there may be concerns about the privacy of patient data, as well as issues surrounding the liability of AI algorithms for medical decisions.

Furthermore, there may be resistance from health care professionals to adopt AI technologies due to concerns about job displacement and the need for retraining. Despite these challenges, there are also many potential benefits to using AI in ophthalmology. For example, AI can be used to improve the accuracy and speed of diagnosis, particularly for conditions such as diabetic retinopathy and age-related macular degeneration. It can also be used to monitor disease progression and predict treatment outcomes.

Algorithms still miss certain subsets in different populations and require continuous financial investments.[75,117] In the future, it will be important to address the challenges associated with AI implementation in health care and to develop AI algorithms that are accurate, reliable, and transparent. In addition, there may be opportunities to use AI to develop personalized treatment plans for patients based on their individual characteristics and medical history.

Authors' Contributions

C.S.M., A.A., and M.B.P. have made substantial contributions to the conception of the work, the acquisition/analysis, and interpretation of data; have drafted the work; have approved the submitted version; have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature. M.A.P.V. have made substantial contributions to the conception of the work, the acquisition/analysis and interpretation of data; have drafted the work; substantively revised it; have approved the submitted version; have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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