Diabetic Retinopathy Screening in Urban Primary Care Setting with a Handheld Smartphone-based Retinal Camera.

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Research Article

Abstract

Aims: To evaluate diabetic retinopathy (DR) screening with a portable handheld smartphone-based retinal camera and telemedicine in an urban primary health care setting; to evaluate the learning curve for image acquisition, performed by healthcare personnel without previous experience on retinal imaging.

Methods: Prospective study that enrolled patients with type 2 diabetes mellitus (T2DM) followed at a primary healthcare unit in São Paulo, Brazil. After a brief training in image acquisition, there was further continuous feedback during the remote image reading process. Each patient underwent two fundus and one anterior ocular segment images per eye, after mydriasis. Patients were classified according need of referral.

Results: A total of 627 adult individuals with T2DM underwent retinal evaluation. The population was composed by 63.2% female individuals, age median of 66 years-old, diabetes duration 10.7 ± 8.2 years and A1c 7.7 ± 1.9% (61 ± 20.8 mmol/mol). The most prevalent associated comorbidities were arterial hypertension (80.3%) and dyslipidemia (50.2%). Referral decision was possible in 81.2% patients. Most patients had absent or non-referable DR; the main ocular media opacity detected was cataract. After the 7th day of image acquisition, the daily rate of patients whose images allowed clinical decision was maintained above 80%. A higher A1c was associated with referable DR.

Conclusion: A low-cost DR screening strategy with a handheld device and telemedicine is feasible and has the potential to increase coverage of DR screening in underserved areas; the possibility of mobile units is relevant for DR screening in the context of Covid-19 pandemic.

Introduction

Visual loss secondary to diabetic retinopathy (DR), a leading cause of severe visual loss worldwide, can be prevented with timely screening, detection, and treatment; however, even in high-income countries, access to yearly eye examinations is limited, leaving a substantial number of patients at risk [1]. In middle to low income countries, the rate of individuals with diabetes who have access to eye examinations is remarkably low [2]. In Brazil, Primary Health Care is developed through forms of teamwork composed of a physician, a nurse, nursing assistants and community agents of health, aiming to assist populations defined by Basic Health Units ("Unidade Básica de Saúde" - UBS). In turn, the UBS is responsible for support and infrastructure; since there is no availability of an ophthalmologist in the medical staff of most UBSs, diabetic retinopathy (DR) screening is performed in secondary care units [3]; hence, the waiting time for an appointment is often increased, causing DR monitoring and timely treatment to be extremely difficult.

Teleophthalmology programs have facilitated the identification of DR cases by utilizing digital retinal imaging [4]; additionally, teleophthalmology based on mobile imaging units can ameliorate DR screening and decrease the possibility of poor compliance or lost follow-up appointments [5]. The combination of teleophthalmology with portable devices may further increase access to eye care in underserved

populations. The importance of the teleophthalmology strategy lies on decreasing the burden on the health system, referring to specialized care only those individuals with treatable conditions, and allowing timely treatment to prevent diabetic blindness. Hence, image quality is paramount to the success of the screening program, as low-quality images will not yield diagnosis, making necessary an evaluation by the specialist.

Hand-held cameras are increasingly available for diabetic retinopathy screening, having several advantages over traditional tabletop cameras, such as increased portability and decreased cost, with the potential of improving DR screening rates [1]. For optimal image quality, training in image acquisition and ocular media transparence are needed.

The present study was designed to evaluate diabetic retinopathy screening with a portable retinal camera and telemedicine in a primary health care urban setting. The learning curve for image acquisition, performed by healthcare personnel without previous experience on retinal imaging, was also evaluated.

Materials And Methods

This study enrolled 627 individuals aged over 18 years-old with a previous type 2 diabetes mellitus (T2DM) diagnosis who were treated in a UBS on the outskirts of the city of São Paulo. Non-inclusion criteria were not adopted. The study was conducted in compliance with the Declaration of Helsinki, in accordance with the institutional ethics committees (#3050387 and #3141417). After signing informed consent, participants were assessed for demographic, clinical and biochemical features and had the anterior and posterior ocular segments of both eyes photographed after mydriasis.

Clinical and demographic data analysis show that the population was consisted by 63.2% female, age median of 66 years-old, diabetes duration 10.7 ± 8.2 years and A1c $7.7 \pm 1.9\%$ (61 ± 20.8 mmol/mol). The most prevalent associated comorbidities were arterial hypertension (80.3%) and dyslipidemia (50.2%).

A smartphone-based hand-held device (Eyer, Phelcom Technologies, São Carlos, Brazil) was used for retinal image acquisition according to a previous protocol used in the Brazilian multicenter study of diabetic retinopathy [6] and photographs of the anterior and posterior ocular segments were obtained for both eyes, after mydriasis induced by 1% tropicamide eye-drops. Two images of the posterior segment, one field centered on the fovea and the other field centered on the optic disc of each fundus were captured. The professionals responsible for image acquisition were a team of four nurses involved in diabetes care in the own basic health unit, without previous experience in this kind of procedure. They underwent a four-hour training about image protocol and acquisition by an ophthalmologist, and, thereafter, they started performing retinal images and relied on the continuous remote feedback given by the specialist as images were interpreted. Image acquisition occurred from February 6th to March 14th, 2020 comprising a 5-week period, in non-consecutive days.

Remote image reading was performed at EyerCloud platform (Phelcom Technologies, São Carlos, Brazil) by the same retinal specialist (FKM). First, the photographs of patients' retinas were evaluated by quality

and classified as gradable or ungradable images. Subsequently, diabetic retinopathy classification was performed for those with gradable images, and patients with ungradable images had their anterior ocular segment images assessed regarding the presence of cataracts or other media opacities. Whenever the severity of cataract precluded fundus evaluation, the patient would be considered as referable for ophthalmologic evaluation. When ocular media had enough transparence to allow DR grading, each patient was categorized according to the most affected eye as follows: non-referable (absent or mild to moderate non-proliferative diabetic retinopathy without diabetic maculopathy) or referable (severe non-proliferative diabetic retinopathy; proliferative diabetic retinopathy; presence of macular edema in at least one eye) [7]. The images with poor quality for reasons other than cataract, and also images from patients who did not comply with the proposed protocol, for example, by lack of image fields or image taken of non-representative fields, were considered as protocol failure; such patients were also referred for ophthalmological evaluation.

To evaluate the image acquisition learning curve, a specific analysis was performed regarding each day of exam, and the daily rate of patients successfully evaluated by teleophthalmology, regarding the presence of cataracts, DR classification and presence of maculopathy, was calculated. Furthermore, information concerning the duration of exam per patient was collected.

Statistical analysis:

Statistical analyses were performed using the SAS/STAT software. An ANOVA One-Way model and *Fisher's exact test* were applied to compare variables, and the non-parametric Kruskal-Wallis test was employed for the comparison between patients' groups; p values <0.05 were considered statistically significant.

Results

Six hundred and twenty-seven individuals with T2DM underwent retinal evaluation by the smartphone-based hand-held device. The photographs allowed a clinical decision in 509 (81.2%) patients, who either had their diabetic retinopathy graded (439) or presented with ocular media opacities that supported their referral to the specialist (70). In the remaining 118 patients (18.8%), images were ungradable for causes other than ocular media opacities, such as inadequate technique or frames that did not correspond to the proposed protocol; those patients were referred. Patients who were referred because of media opacities comprised 61 cases of cataracts and 9 cases of vitreous, corneal, or posterior capsule opacities. Among the 439 gradable patients, DR classification was as follows: 333 with no DR, 40 with non-referable DR and 66 with referable DR. Overall, a total of 373 patients had no indication for specialist referral because of DR and/or ocular media opacities (Figure 1).

Except for A1C, all other clinical and demographic variables were not different regarding DR classification, as shown in Table 1.

The learning curve of image acquisition was evaluated according to the rate of patients whose images allowed clinical decision on daily basis. All images for the present study were collected along 16 non-consecutive days; from the 7th day onward, the rate of patients whose images allowed clinical decision was maintained above 80%, as seen in Graphic 1. Exam duration per patient had an average time of 2.5 *+* 1.7 minutes (median 2.0, range 0–15 minutes).

In a sub-analysis, the patients were divided into 2 groups: those with images that allowed a management and those whose images did not yield management; clinical and technical variables were compared between these groups. Patients whose images did not yield were older (p = 0.04) and exam duration for image acquisition was longer (p<0.001); other parameters as gender, A1c and duration of diabetes did not reach statistical significance.

Discussion

After a brief training and a short learning curve, healthcare professionals without previous experience on retinal imaging acquisition performed well, attaining a rate of over 80% of examined patients whose exams allowed clinical decision; the short time of exam spent per patient was also compatible with a successful screening strategy. The training, the imaging protocol and the remote reading showed that image acquisition with a portable device associated to teleophthalmology is a feasible strategy for DR and cataract screening in patients with diabetes who dwell in a urban area and are followed in a primary health care setting.

DR screening programs have been implemented with success over the last decades in several countries, resulting in lower rates of diabetic blindness [8–11]. Adequate image quality is a major factor on which the success of the screening strategy is dependent upon [12], and we hereby present favorable results and a high rate of clinical yield attained after a brief training and subsequent continuous remote feedback; of note is the previous lack of experience of the trained team. The sustainability and cost-effectiveness of screening programs are also fundamental for its implementation and success; to the best of our knowledge, ours is the first report on the performance of low-cost, portable hand-held devices for DR screening in a urban setting in Brazil, a continent-sized country with very heterogeneous socioeconomic realities and an uneven distribution of ophthalmologists [13], home to the fifth biggest diabetic population in the world [14] and also to the largest public free and chronically underfinanced healthcare system [15]. Multiple socioeconomic barriers prevent access to eye examination in the poor regions of Brazil [2]. Recently, several authors have proposed teleophthalmology to increase access, with favorable cost-effectiveness results and a reduced burden to specialized services [13,16].

In the present study, we propose a decision tree based not only on DR grading, but also on the presence of ocular media opacities. By evaluating anterior segment images, the reader is able to judge if cataracts are the reason for ungradable fundus images, and this is a clinically relevant information, as cataracts are a significant public health issue and an important cause of blindness in developing countries [17], also being an important cause for referral in patients with diabetes. The presence of cataracts is usually

considered a flaw in the screening of DR by teleophthalmology as it frequently precludes DR classification [18]; some screening protocols propose the exclusion of patients with cataracts [19]. We believe that grouping cataract and referable DR patients is effective in providing proper healthcare for those individuals; cataract referral and treatment in patients with diabetes should follow a special protocol because of the increased risk of ocular complications in such patients.

The patients enrolled for diabetic retinopathy screening with a portable retinal camera adequately represent the population with DM2 treated in primary health care, characterized by the predominance of the elderly, mostly women, diabetes duration over 10 years and regular glycemic control. Arterial hypertension and dyslipidemia were the most prevalent comorbidities associated with DM [20]. We observed that patients with referable DR had higher A1c than those with DR absent or non-referable, while other clinical and demographic variables were similar. The association between poor glycemic control and severity and progression of retinopathy is well established in the literature, in addition to diabetes duration, nephropathy, hypertension, and dyslipidemia [7]. Further, DR has been related to the development of macrovascular complications of diabetes, specifically, cerebrovascular, cardiovascular and peripheral complications [21]. Ours results also pointed out to the imaging protocol having a poorer diagnostic yield in older patients, who have also experienced a longer duration of the exam. Ocular characteristics such as impaired pupil dilation may have played a role, even though the images acquisition has been done after pharmacological mydriasis.

This study strengths are its "real life" approach, since it was performed during ongoing healthcare by a team of nurses in a primary care setting, and the feasibility of a protocol that involves a handheld device and a telemedicine approach, offering the perspective of DR screening with mobile units and home evaluation, potentially increasing access in underserved areas while offering a safer alternative to individuals with diabetes, considering the vulnerability brought by the ongoing Covid—19 pandemic. Regarding study limitations, is should be pointed out that only patients who dwell in a urban area were evaluated; furthermore, other ophthalmological evaluation modalities, such as visual acuity measurement, slit-lamp examination or optical coherence tomography, were not available, thus limiting the conclusions on diabetic maculopathy.

Conclusion

Our data point to the feasibility of a low-cost DR screening strategy which involves training of non-specialized healthcare personnel, a handheld device and telemedicine. Such protocol is compatible with the Family Health Strategy, with the potential to increase the coverage of DR screening in underserved areas; the possibility of mobile units is also relevant as an alternative for DR screening in the context of the Covid—19 pandemic. A major challenge is to provide timely treatment for detected cases of sight-threatening DR and cataract.

Declarations

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Table

Table 1. Clinical and demographic variables among patients classified as having DR absent, DR non-referable and DR referable

	DR absent	DR non-referable	DR referable
Age (years)	65.1 ± 11.5	66.5 ± 9.4	63.1 ± 12.2
Gender M/F (%)	36.5/63.5	23.8/76.2	46/54
DM duration (years)	10.8 ± 8.4	9.3 ± 6.7	10.8 ± 7.5
A1c (%)	7.6 ± 1.7	7.4 ± 1.4*	9.2 ± 2.4[#&]
A1c (mmol/mol)	60 ± 18.6	57 ± 15.3*	77 ± 26.2[#&]
Hypertension (%)	80.9	80.9	76.5
Dyslipidemia (%)	49	52.7	56.2

Data showed as mean ± standard deviation; DR: diabetic retinopathy, M:male; F: female; DM: diabetes
mellitus; A1c: glycated hemoglobin; DR: diabetic retinopathy; *DR absent compared to DR non-referable:

p=0.914, [#]DR absent compared to DR referable: p=0.0062; [&]DR non-referable compared to DR referable: p=0.0335; ANOVA.

Figures

627 individuals with T2DM were enrolled

118 exams (18.8%): images did not allow clinical decision
causes:
inadequate technique (n=66)
inadequate frames (n=44)
poor mydriases (n=1)
miscellaneous (n=7)

509 exams allowed clinical decision (81.2%)

70 exams: ocular media opacities precluded DR grading
causes:
cataract (n= 61); vitreous opacity (n=3); corneal opacity (n=3) and posterior capsule opacity (n=3)

439 exams were gradable

DR absent (n=333)

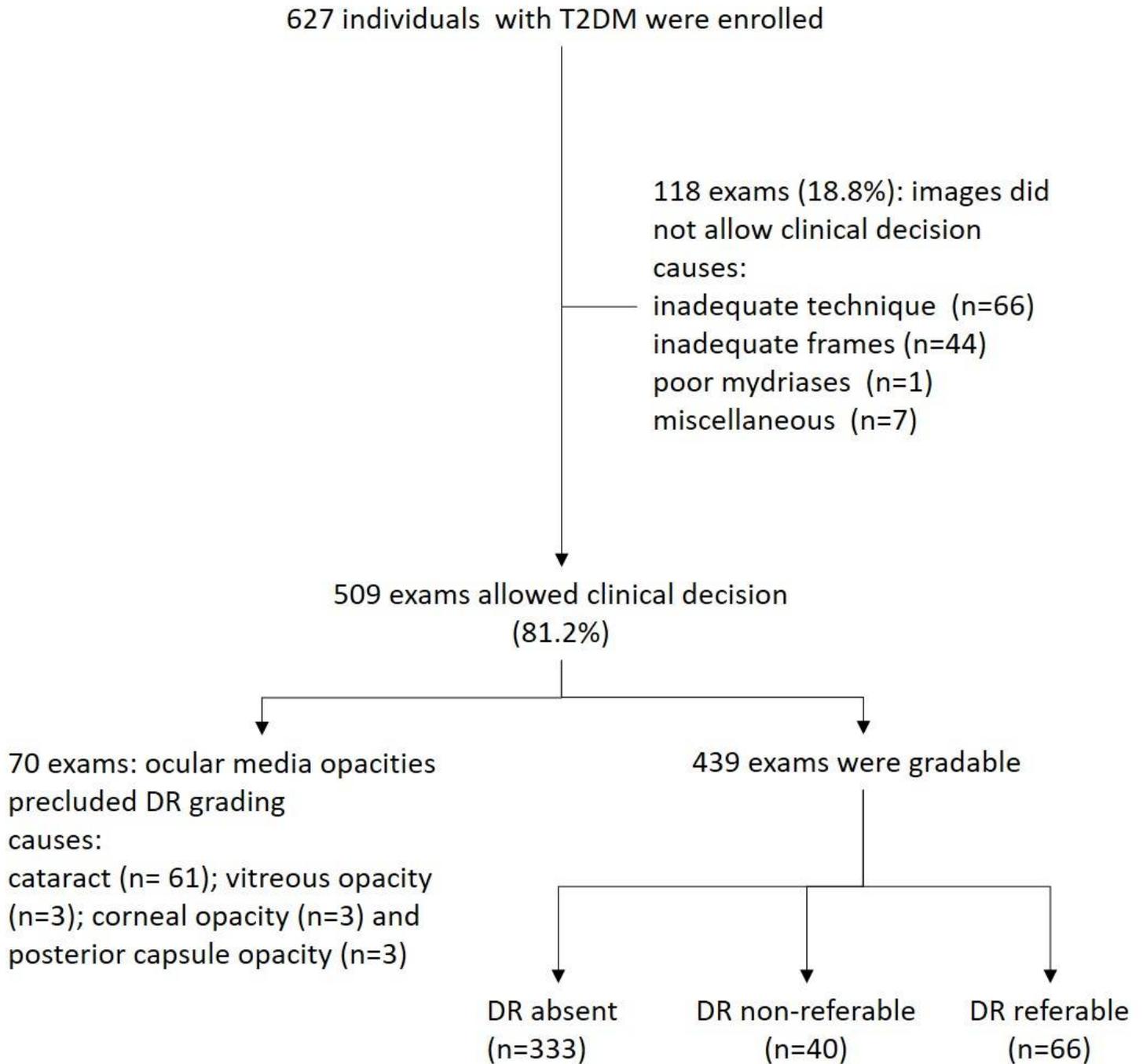DR non-referable (n=40)

DR referable (n=66)

Figure 1

T2DM: type 2 diabetes mellitus, n: number of patients; DR: diabetic retinopathy.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Graphic1DRScreeningUrban.docx