Screening for diabetic retinopathy: the first telemedical approach in a primary care setting in France

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SUMMARY

Objectives: Diabetic retinopathy (DR) remains a major cause of visual impairment in France, due to insufficient regular annual screening. Fundus photography is a sensitive alternative to ophthalmoscopy for DR screening. The aim of our study was to report the first telemedical approach to this screening in a primary care setting in France.

Methods: A DR screening centre equipped with a nonmydriatic camera was opened in the 18th district of northern Paris and placed at the disposal of general practitioners (GPs) of the Réseau de Santé Paris Nord (North Paris Health Network). These GPs were invited to send their diabetic patients who had no known DR and had had no fundus examination for more than one year to this screening center. Retinal photographs were taken by an orthoptist without pupillary dilation and sent for grading through the Internet to the Lariboisière Hospital Ophthalmology Department.

Results: During an 18-month period, 912 DR screening examinations were performed in 868 diabetic patients referred to the DR screening center by 240 GPs. Patients’ mean ± SD age was 59.9 ± 11.1 years. Of these 868 patients, 260 (30%) said they never had an ophthalmological examination. Diabetic retinopathy was detected in 197 patients (22.7%). The proportion of patients for whom fundus photographs of one or both eyes could not be assessed was 10.1%. 159 patients (18.3%) required referral to an ophthalmologist.

Conclusion: Nonmydriatic photography, combined with teletransmission to a reading centre, proved to be a feasible valid method for the detection of DR. This screening method allowed the identification of patients requiring prompt referral to an ophthalmologist for further complete eye examination.

Key-words: Diabetic retinopathy • Screening • Fundus photography • Telemedicine.


RÉSUMÉ

Dépistage de la rétinopathie diabétique : la première approche de la télémédecine en médecine générale en France

Objectifs : La rétinopathie diabétique (RD) représente une cause majeure d’altération de la fonction visuelle en France, liée à une insuffisance de dépistage annuel régulier. La photographie du fond d’œil est une alternative de bonne sensibilité à l’ophtalmoscopie pour le dépistage de la RD. L’objectif de notre étude était de rapporter la première approche de télémédecine pour ce dépistage dans un contexte de médecine générale en France.


Résultats : Au cours d’une période de 18 mois, 912 examens de dépistage de la RD ont été réalisés chez 868 patients diabétiques adressés au centre de dépistage par 240 généralistes. L’âge des patients étaient de 59.9 ± 11.1 ans (SD). Parmi ces 868 patients, 260 (30 %) ont déclaré n’avoir jamais bénéficié d’examen ophtalmologique. Une rétinopathie diabétique a été décelée chez 197 patients (22.7 %). La proportion de patients chez qui la photographie du fond d’œil de l’un ou l’autre œil a pu être évaluée a été de 10,1 %. 159 patients (18,3 %) ont nécessité l’avis d’un ophtalmologiste.

Conclusion : La photographie non mydriatique, combinée à la télétransmission à un centre de lecture, apparaît donc comme une méthode valide réaliste pour la détection de la RD. Cette méthode de dépistage permet d’identifier les patients nécessitant un avis ophtalmologique rapide pour examen plus complet.

Mots-clés : Rétinopathie diabétique • Dépistage • Photographie du fond d’œil • Télémédecine.

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Although laser photocoagulation effectively prevents complications of diabetic retinopathy (DR), this disease is still a major cause of visual impairment and blindness in most developed countries [1]. This is mainly because DR is diagnosed and treated too late, when complications have already developed. In an effort to detect DR at an early stage, before visual loss, international and national guidelines for DR screening have been formulated, which recommend annual fundus examination for all diabetic patients [2-5], and the effectiveness of such recommendations has been demonstrated [6, 7].

In France, there are 2 to 2.5 million diabetic patients, and the estimated number of undiagnosed cases is almost as large. About 30% of them have diabetic retinopathy, and 10% have a sight-threatening form of diabetic retinopathy [1, 8]. The need for screening already exceeds the capacity in private practices and hospital departments, with waiting periods of more than 6 months in some French regions. Moreover, screening requirements are expected to increase over the next decade, due to the increasing prevalence and incidence of diabetes [8]. In France, the results of a recent survey of patients with type 2 diabetes by the CNAMTS (Caisse Nationale d’Assurance Maladie des Travailleurs Salariés — National Health Insurance Fund) showed that in 1999, only 40% of these patients had had an ophthalmological examination during the previous year [9]. This situation did not improve significantly during 2000 and 2001. In view of the increasing prevalence of type 2 diabetes in the general population, and of the significantly disproportionate decrease in the number of ophthalmologists in France, this situation is not expected to improve for the next 15 years.

DR screening in France, is usually performed using fundus examination after pupillary dilation by an ophthalmologist. Colour fundus photography using a nonmydriatic camera is an alternative DR screening method which is at least as sensitive as ophthalmoscopy [11-15]. In addition, new nonmydriatic cameras allow the acquisition of high-quality digital fundus photographs without the need for pupillary dilation, and these photographs can be transmitted through the Internet to distant experts [15]. The development of high-speed networks allow the transmission of good quality photographs, making consultations from distant locations possible. Thus, telemedicine seems particularly relevant to screening for DR [16]. The equipment of peripheral centers with nonmydriatic cameras, combined with telemedical linkage to a reference center where ophthalmologists can grade the images, will make DR screening by experts accessible to a much wider population, while saving doctors’ time. Such a project has already been set up in Paris, with the installation of a nonmydriatic retinograph in the Diabetology Department of the Hôpital Bichat. There fundus photographs of diabetic patients are taken routinely by a nurse, and transmitted electronically to the Ophthalmology Department at the Hôpital Lariboisière for interpretation. We report here the results of the first telemedical approach to screening for diabetic retinopathy in a French primary care setting.

Patients and methods

This first telemedical approach to screening for DR was developed within the Réseau de Santé Paris Nord (North Paris Health Network), which includes a group of healthcare professionals from five north Paris districts. A DR screening centre equipped with a Topcon TRC-NW6 nonmydriatic camera was opened in one of these districts (the 18th) and placed at the disposal of general practitioners (GPs) of the North Paris Health Network. These GPs were invited to send their diabetic patients who had no known DR and had no fundus examination for more than one year to this screening center. Patients had access to the center by appointment during the center’s long working hours.

Patients were screened for DR by an orthoptist. The clinical information recorded included their identification, address, and date of birth, their GP’s address, the type and duration of their diabetes, and the date and results of their last fundus examination. The detection protocol included measurement of visual acuity, and the taking of fundus photographs by an orthoptist. In all, the screening examination lasted about 15 minutes. Digital photographs were obtained without pupillary dilation from a nonmydriatic funduscope camera (model TRC-NW6; Topcon, Rotterdam, The Netherlands).

Photography

The Topcon TRC-NW6S camera is a nonmydriatic digital retinal camera which allows nine 45° retinal colour photographs to be taken of the posterior pole and peripheral retina without pupillary dilation, using semi-automatic guidance for peripheral fixation. It is connected to a digital camera (Fuji, S2-PRO, FUJI, Tokyo, Japan). Images are captured in true colour (24 bits) at a resolution of 1490 × 960 pixels.

Retinal photographs were taken with this camera in a well-darkened room. Field alignment and focusing of the retinal image were easy, using overlapping and alignment of spots on the monitor view. The photographer viewed each digital image immediately, and repeated the image acquisition process if the original image was unsatisfactory. Five 45° non-stereoscopic images of 5 overlapping fields were taken for each eye: one image was centred on the macula, including the optic disc, and one each on the nasal, temporal, superior and inferior fields. The original image size was 1.5 M. To be transferred through the Internet network, it was compressed using the Joint Photograph Experts Group (JPEG) compression method. After reduc-
tion by a 1:10 compression ratio, the final mean file size of a single image after compression was 140 KB.

The original images were stored on a conventional personal computer. The compressed images and clinical data were sent through the Internet for storage in a medical server which provided a secure environment (Lincoln). All the data were protected by a 128 bit-encryption. OPHCARE (Lincoln, Boulogne-Billancourt, France) is a secured Internet application developed for DR screening, and located on the server. It allows the storage of clinical data and fundus photographs, the publishing of a standardized report, and statistics. Safe access to the application is ensured by the use of a password. The OPHCARE program was conducted in accordance with the French law on computerized information and civil liberties (CNIL, Commission Nationale Informatique & Liberté).

Grading of retinal images

The stored images were downloaded by the ophthalmologists at the ophthalmological reference center (Hôpital Lariboisière) and displayed on a 21-inch monitor (resolution: 1280 x 1024 x 24 bits). To increase grading accuracy, the images were enhanced by contrast, brightness, and zoom facilities when necessary, using Topcon image processing software (Optilink, Topcon, Rotterdam, the Netherlands).

The quality of each photograph was scored on the following 5-grade scale [15-17].

— Grade 1: excellent
— Grade 2: good definition of most retinal detail, easy to assess
— Grade 3: definition limited, difficult to assess
— Grade 4: only gross detail visible
— Grade 5: not gradable.

Diabetic retinopathy was classified, according to the ALFEDIAM classification, a modified version of the ETDRS classification [5], as follows: five grades of severity were established: No diabetic retinopathy (No DR); mild non-proliferative DR: occasional microaneurysms or haemorrhages; moderate non proliferative DR with moderate intraretinal microvascular anomalies and/or definite venous beadings; and proliferative DR with newvessels on the disc or elsewhere on the retina. Macular œdema was diagnosed from the presence of hard exudates within one disc diameter of the foveola.

The conclusion reached after retinal image grading indicated the recommendation for follow up. The patient had to be referred to an ophthalmologist in case of moderate nonproliferative DR or worse, in case of cataract or associated ocular pathology, or of ungradable photographs. The duration of retinal image grading was less than 5 minutes per patient. All photographs were graded during the two days after they were taken.

The screening report was printed by the orthoptist at the Screening Site, and sent by mail to the GPs and patients. If necessary, the report could be sent to the GPs via the Internet.

The report’s content included the diagnosis of DR, if detected, the severity of DR, and advice to consult an ophthalmologist for further eye fundus examination in the following cases: moderate non proliferative DR or worse, according to the ALFEDIAM classification [18], diagnosis of macular edema, or ungradable photographs.

Results

The DR screening center opened on February 1st, 2002. A campaign of information was conducted via meetings with North Paris GPs and mailing. Posters were sent to all GPs and pharmacists. Flyers containing information on DR were sent to GPs for display in their waiting rooms.

Between February 1st 2002 and July 31st 2003, 912 DR screening examinations were performed for 868 diabetic patients (487 men and 381 women), referred to the DR screening center by 240 GPs. Forty-four patients came twice at a one-year interval.

Table I
Year of previous ophthalmological examinations and percentages of patients examined, in a total cohort of 868.

<table>
<thead>
<tr>
<th>Previous ophthalmological examination</th>
<th>Never</th>
<th>&lt;2000</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>260</td>
<td>117</td>
<td>128</td>
<td>218</td>
<td>128</td>
<td>17</td>
<td>868</td>
</tr>
<tr>
<td>Percentage</td>
<td>(30)</td>
<td>(13.4)</td>
<td>(14.7)</td>
<td>(25.1)</td>
<td>(14.7)</td>
<td>(2)</td>
<td>(100)</td>
</tr>
</tbody>
</table>

868 patients were screened for diabetic retinopathy in 912 examinations. Five patients were one-eyed. The duration of retinal image grading was less than 5 minutes per patient. All photographs were graded during the two days after they were taken.

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Table II
Quality of retinal photographs, as assessed by the graders.

<table>
<thead>
<tr>
<th>Image Quality</th>
<th>RIGHT EYE</th>
<th>LEFT EYE</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>643</td>
<td>577</td>
<td>1220</td>
</tr>
<tr>
<td>3</td>
<td>197</td>
<td>250</td>
<td>447</td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>52</td>
<td>94</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>30</td>
<td>58</td>
</tr>
<tr>
<td>TOTAL</td>
<td>910</td>
<td>909</td>
<td>1819</td>
</tr>
</tbody>
</table>

868 patients were screened for diabetic retinopathy in 912 examinations. Five patients were one-eyed.
Patients’ mean age $\pm$ SD was 59.9 $\pm$ 11.1 years (range: 17 to 91). Sixty-nine patients had type 1 diabetes and 799, type 2 (503 non insulin-dependent, 28 insulin-requiring and 268 requiring diet alone). The mean $\pm$ SD duration of diabetes was 8.65 $\pm$ 8.2 years (range: 0 to 53).

Among these 868 patients, 260 (30%) said they had never had an ophthalmological examination or did not remember having one. The year of previous examination and percentages of patients examined are given in Table I. Almost 40% of patients had an examination between 2001 and 2003, but only 224 patients of the entire cohort of 868 (25.8%) knew the results of their examination and said they had no DR.

**Quality of photographs**

Table II indicates the quality of the photographs, as assessed by the graders. Retinal photographs were ungradable in 58 eyes (3.2%) and of low quality (grade 4) in 94 eyes (5.2%). The causes of poor image quality in these 152 eyes were lens opacities in 47 and small size of the pupil in 105. The proportion of patients for whom photographs of one or both eyes could not be assessed was 10.1%. Image quality was correlated with patients’ age. The mean age of the 92 patients with ungradable or low quality images was 69.5 $\pm$ 11.1 years, vs 58.8 $\pm$ 11.1 for the 776 patients with grade 1, 2 or 3. The difference between the age of the two groups was highly significant ($p < 0.0001$, Mann-Whitney test). None of the patients under 40 had ungradable images; among patients over 40, the percentage of ungradable images increased with age, and reached 20% after 70 years.

Diabetic retinopathy was detected in 197 patients (22.7%). Of these, 72 (8.3%) had moderate nonproliferative or more severe DR in at least one eye. Proliferative DR was observed in 2 patients. Macular edema was detected in 18. Twenty-eight patients (3.2%) had a serious form of DR requiring laser treatment (severe nonproliferative or proliferative DR, or macular oedema). Fourteen of them said they never had an ophthalmological examination and 10 had had an examination more than one year previously.

After the screening examination, 159 patients (18.3%) were referred to an ophthalmologist. The causes for referral were DR in 75 patients, cataract and/or ungradable photographs in 66, and other causes in 18 (Tab III).

Of the 240 GPs who sent patients to the screening center, 125 were located in the 18th district or in adjacent districts. The location of GPs in relation to the DR screen-
Discussion

We report here the first telemedical experience of screening for diabetic retinopathy in a primary care setting performed in France. Nonmydriatic retinal photographs were taken by an orthoptist at a screening center located in the 18th district of Paris, and transmitted for grading to the Ophthalmology Department of a large Paris hospital.

The accuracy of photographs or digital images and their appropriateness for diagnosing or monitoring DR have been evaluated in several studies [11-18]. Screening for DR is now usually performed with a nonmydriatic camera, which has the theoretical advantage of avoiding pupillary dilation, thanks to its infrared focusing system. In addition, these cameras do not require skilled photographers. However, they have been criticised for the quality of the photographs they produce [17], a drawback that may limit their efficacy and reliability as a screening tool. And until recently, the use of a nonmydriatic camera has been recommended when screening for DR, provided it is combined with pupillary dilation [18]. Several new nonmydriatic cameras are being commercialized due to the growing demand, but must be rigorously evaluated before being used without pupillary dilation. When comparing the results of fundus photography using the TRC-NW6 nonmydriatic Topcon digital camera to the reference standard of ETDRS retinal photographs, we obtained a sensitivity of 92 to 100% for the detection of moderate to severe forms of DR, thus demonstrating that this camera could be used without dilation to screen for DR [15]. Our present results confirm its good performance.

In our study, the quality of retinal images correlated closely with age, as previously reported [19] since 77.7% of our patients with low quality images were aged 60 or more. DR screening using nonmydriatic photography is therefore less effective in older patients, although 77% of our patients over 70 still had gradable photographs. Note, however, that an optimal technique of image acquisition, performed in darkness by a trained orthoptist, was crucial to obtain these good results.

As stated above, the screening procedure was performed by an orthoptist. In France, orthoptists are indeed allowed by national decree to take retinal photographs (Ministry of Health, Official Decree n° 2001-591, Paris 2001). Note that nurses are also allowed by national decree to screen for any sensorial disorders (Ministry of Health, Official Decree n° 2002-194, Paris 2002). The nonmydriatic camera can easily be handled by a non ophthalmologist and its use only requires about two weeks of training. The screening procedure comprised recording of the medical data necessary for retinal grading, measurement of visual acuity and the taking of retinal photographs. Measurement of visual acuity is recommended to improve the performance of screening for DR, because the combination of decreased visual acuity and low image quality can also indicate a diagnosis of cataract. In addition, measurement of visual acuity has been advocated as an additional inexpensive tool when screening for diabetic maculopathy, because diagnosis of macular thickening may be difficult on nonstereoscopic images, and low visual acuity may be a good indicator of macular edema [20].

In the present series, five photographs of each eye were taken. Until now, the most widely used methods of screening for DR included two or three 50 or 45° retinal photographs [21-23]. As the TRC-NW6 Topcon camera allows 9 photographs of the posterior pole and peripheral retina to be taken, we decided to use a pattern of 5 overlapping fields, although that did not seem to increase the sensitivity of DR detection [15]. In addition, the risk involved in increasing the number of photographs is that their quality will decline, due to the pupillary constriction induced by repetitive flashes. Therefore, a method including 3 retinal photographs of each eye seems appropriate for DR screening.

Although telemedicine seems particularly relevant to this screening, it involves additional difficulties. In order to fasten the transmission of digital retinal images, compression techniques are required, and information may be lost during such compression. Here, we used a JPEG compression ratio of 1:10, which reduced the image size from 1.5 MB to 150 KB, without altering their gradability. It has indeed been shown that when the original retinal image size is 1.5 MB, a JPEG compression ratio of 1:20 to 1:12 is suitable for DR screening [24, 25]. In addition, the storage and transmission of medical data through the Internet requires a secure environment, to preserve clinical confidentiality. To fulfill these requirements, all our data were stored in a medical server and protected by a 128 bit-encryption.

Photographs were graded by two trained ophthalmologists. To be optimal, this grading must be performed on a high resolution screen. Grading of retinal photographs is a rapid procedure, as an average of 15 patients can easily be graded per hour, whereas hardly more than 15 can be screened in half a day by dilated eye examination. Screening for DR using retinal photography is therefore a safe and sensitive method, which allows physicians to save time for managing patients with DR.

During this first telemedical approach, 912 DR screening examinations were performed in 868 diabetic patients. Although diabetes had been diagnosed a mean 8.65 years before the study, 30% of the patients said they had never had an eye fundus examination or did not remember hav-
ing one. In addition, less than a quarter had had their eye fundus examination performed within the last year as recommended by the ANAES and ALFEDIAM (20.2%). In comparison, 39.1% and 41.5% of the diabetic patients from the CNAMTS study had been reimbursed for an ophthalmologic consultation in 1998 and 1999 respectively [9]. This rate rose to 43% in 2001 in the ENTRED study [26]. Nevertheless, it cannot be stated that eye fundus examination was always performed in these studies, as the exact content of the ophthalmologic consultation was not specified in either case. This may explain why only 20% of the population in the present study had had a fundus examination before enrolment. Most patients who had not had regular DR screening were screened thanks to our screening project. The results suggest that screening for DR using retinal photography may improve DR screening. However, it was difficult to determine whether the improvement of DR screening in our study was due to our use of a nonmydriatic camera or to the information and sensitization of GPs to the need for an annual screening examination for all diabetic patients. A further study in which the results of DR screening using eye fundus photography were compared to the results of conventional screening by an ophthalmologist has been performed and should help to answer this question (the DODIA study, Massin et al. submitted).

Here, DR screening showed that the prevalence rate of DR in the 868 patients studied was 22.7%, with a 8.3% rate for moderate to severe forms. Although this prevalence was lower than that observed in epidemiological studies [27], it was to be expected, because the patients previously diagnosed as having DR had been excluded. Twenty-eight patients (3.2%) had a vision-threatening form of DR requiring laser treatment (severe nonproliferative or proliferative DR, or macular oedema). With these results, the screening system achieved its main goal, which is to diagnose undetected forms of DR requiring prompt referral to an ophthalmologist.

Retinal photography also allowed the detection of ocular pathologies other than DR in 18 patients. Glaucoma could be suspected from the appearance of the optic disc (cup/disk ratio). It is indeed important to screen diabetic patients for glaucoma, although the latter has not been proven to be more prevalent in diabetic patients than in the general population [28]. However, all diabetic patients were given information at the screening centre, including recommendations for regular ophthalmological examination in order to check their visual acuity and intraocular pressure, and the possible presence of cataract.

During the 18-month experience reported here, the activity of the screening centre was moderate, as only 912 examinations were performed. This may be partly because it was a first and brief experience, and the activity of the screening centre will no doubt increase with time. An average of 3000 screening procedures per year can be expected to be performed with a single nonmydriatic camera. Two hundred and forty GPs participated in the study. Note that more than half the GPs of the 18th Paris district, where the screening center was located, sent at least one patient.

**Conclusion**

The taking of fundus photographs without pupillary dilatation, and their teletransmission to a reading center is a feasible valid method for the detection of DR. It also seems a valid method of improving DR screening, and of overcoming the growing difficulties expected in the future due to an increased number of diabetic patients and reduced number of ophthalmologists. The participation of orthoptists, after adequate training and accreditation, will help to extend the benefits of screening for DR to a much wider population. The process of increasing the number of orthoptists, with the object of further encouraging their participation in patient care, has already begun.

Screening with eye fundus photographs is of course not designed to be the only method of detecting retinopathy, and cannot replace the ophthalmologist in the overall management of diabetic eye complications. It should rather be proposed as an additional alternative method of improving DR screening. This method has been compared to classical screening based on fundus examination by an ophthalmologist, and the results are presented in a further study (Massin et al., submitted). The extension to additional centers of this program of screening by fundus photographs is under way. However, this extension will require quality assurance which must be integrated into the process. All the staff involved in such a program will be expected to take part in quality assurance, as appropriate. Standards will have to be set by the various professional groups involved in the program. Lastly, a major obstacle to the spread of this new method of screening in France is the lack of quotation by the National Health Service of the grading of photographs, a problem which should be solved as a priority.

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