Screening of diabetic retinopathy: Effect of field number and mydriasis on sensitivity and specificity of digital fundus photography

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Abstract

Purpose. – To evaluate the sensitivity and specificity of one- and three-field, nonmydriatic and mydriatic, and 45° digital colour photography compared with mydriatic indirect ophthalmoscopy for diabetic retinopathy (DR) screening.

Methods. – A group of 79 patients (158 eyes) were included in this prospective study. Colour fundus photographs were taken with a Topcon TRC-NW6S digital camera, using four different techniques—single-field nonmydriatic; three-field nonmydriatic; single-field mydriatic; and three-field mydriatic—followed by dilated ophthalmoscopy. Two independent ophthalmologists classified blinded photographs according to the presence or absence of specific diabetic retinal findings. The sensitivity, specificity and agreement (kappa analyses) of the four methods were calculated for the presence or absence of DR and for all diabetic retinal findings.

Results. – The sensitivity and specificity of digital photography compared with ophthalmoscopy for detection of DR were, respectively: 77 and 99% using single-field nonmydriatic; 92 and 97% using three-field nonmydriatic; 90 and 98% using single-field mydriatic; and 97 and 98% using three-field mydriatic. The degrees of agreement for the four methods were 0.82, 0.90, 0.90 and 0.95, respectively. For specific retinal findings, sensitivity was greater for detection of hard exudates, nerve fibre layer haemorrhage and venous beading, and lower for detection of microaneurysms, dot-blot haemorrhage, cotton wool spots and intraretinal microvascular anomalies.

Conclusion. – The three-field strategy without pupil dilation represents a good compromise, with reasonable sensitivity and good comfort (short examination duration, able to drive after photography) favouring patient compliance with the screening programme.

Résumé

Dépistage de la rétinopathie diabétique : effets du nombre de champs et de la mydriase sur la sensibilité et la spécificité de photographies numériques du fond d’œil.

Objectifs. – Évaluer la sensibilité et la spécificité du dépistage de la rétinopathie diabétique par rétinocaméra numérique en comparant quatre stratégies (un champ non mydriatique, trois champs non mydriatiques, un champ mydriatique, trois champs mydriatiques) à l’ophthalmoscopie au verre à trois miroirs.

Méthodes. – Un total de 79 patients (158 yeux) a été inclus dans cette étude prospective. Des photographies numériques du fond d’œil ont été réalisées avec un rétinographe Topcon TRC-NW6s, suivant quatre techniques successives : un champ non mydriatique, trois champs non mydriatiques, un champ mydriatique, trois champs mydriatiques. Un examen biomicroscopique au verre à trois miroirs a ensuite été réalisé. Les clichés ont été interprétés en insu par deux ophtalmologistes, de façon à déterminer la présence ou l’absence d’une rétinopathie diabétique et de ses différents signes d’atteinte rétinienne. La sensibilité, la spécificité et l’agrément (coefficient Kappa) des quatre méthodes pour le dépistage de la rétinopathie diabétique et de chacun de ses signes ont été calculés.

Résultats. – La sensibilité et la spécificité des photographies numériques étaient respectivement de 77 et 99 % avec un cliché non mydriatique, 92 et 97 % avec trois clichés non mydriatiques, 90 et 98 % avec un cliché mydriatique, 97 et 98 % avec trois clichés mydriatiques. Les degrés d’agrément (coefficient k) étaient respectivement pour les quatre méthodes de 0.82, 0.90, 0.90 et 0.95. La sensibilité du rétinographe est globalement...
1. Introduction

Diabetic retinopathy (DR) is the leading cause of blindness in most developed countries [1]. However, blindness due to diabetes is preventable: good glycaemic control and timely intervention with laser photocoagulation can effectively prevent severe complications of DR [2]. To identify patients who require laser photocoagulation, an efficient screening programme needs to be established [3]. The conventional method is to perform a fundus examination with pupil dilation using slit-lamp biomicroscopy at least once a year. However, in most countries, many diabetic patients are never screened for DR and suffer visual loss because of the inadequacies of the screening programmes [4,5]. In fact, the need for screening exceeds the capacity of ophthalmologists. Moreover, the number of diabetic patients is expected to increase worldwide while the number of ophthalmologists is expected to decrease in some countries, including France [6,7]. For this reason, fundus photography without pupil dilation was proposed as an alternative means of DR screening [8–10]. Organizations and consensus conferences have produced screening procedural guidelines, and most have recommended a two-field strategy (macular and nasal) without pupil dilation [11].

Numerous studies have determined the efficacy of 45° digital one- and three-field methods, and either mydriatic or nonmydriatic fundus photographs for DR screening [8–10,12,13], but few have compared the effectiveness of these strategies for specific diabetic retinal findings (such as haemorrhage, microaneurysms or cotton wool spots) [14]. The aim of this study was, therefore, to examine and compare a range of available strategies to determine the most effective screen for specific DR findings.

2. Patients and methods

2.1. Patients

Seventy-nine consecutive diabetic patients were recruited into this prospective study. Patients were excluded if they had received previous ophthalmological treatment such as laser photocoagulation or vitrectomy, or been seen by an ophthalmologist for a retinal fundus examination within the last 12 months. Verbal consent was obtained from the participants after having received both oral and written information about the prospective study.

2.2. Study protocol

A Topcon TRC-NW6S nonmydriatic camera (Topcon, Tokyo, Japan) with 800 × 600 pixel density linked to a Sony CCD camera (Sony, Tokyo, Japan) was used. IMAGE Net 2000 software was used to process the images, which were viewed on a 21-inch monitor (1280 × 1024 × 24 bits). The first (right) eye was photographed after five minutes of adaptation to the dark in a darkened room. A trained photographer (ophthalmologist or nurse) took three undilated 45° retinal photographs: one centred on the fovea; one centred on the nasal retina with the temporal edge of the optic disc at the edge of the field; and one centred on the temporal retina, with the fovea at the nasal edge of the field. A semiautomatic guidance system (target fixation) allowed peripheral photographs to be taken. After five minutes of dark adaptation, the left eye was photographed using the same system. Two drops of tropicamide 1% were then instilled into each eye. After 30 min, three 45° photographs of the eye were taken, following the same protocol as for the right eye. Finally, all subjects underwent a careful eye examination, performed by an ophthalmologist using a three-mirror lens, and the entire fundus was also scanned.

All digital images were read by two trained, blinded readers (ophthalmologists). Each image was reviewed for the presence or absence of microaneurysms, nerve fiber layer haemorrhage, dot-blot haemorrhage, cotton wool spots, hard exudates, intraretinal microvascular anomalies, venous beading, and neovascularization of the disc and/or elsewhere. A diagnosis of diabetic retinopathy was made if one or more specific signs were observed in each eye. Grading of the fundus examination was recorded using the same protocol as for the digital photographic examination.

2.3. Statistical methods

The sensitivity and specificity of the findings with the different digital imaging modalities were calculated for each eye. The reference standard was based on mydriatic ophthalmoscopy. Kappa statistics were used to measure reproducibility between the readings of the digital photographs and the fundus examinations. Kappa statistics represent the observed level of agreement adjusted for the level of agreement that would have been expected by chance alone. Kappa values less than 0.4 were interpreted as poor agreement, 0.4–0.75 were inter-
Table 1
Sensitivity, specificity, underestimation, overestimation, exact agreement and kappa statistics for each of the four studied strategies (reference standard: mydriatic indirect ophthalmoscopy)

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Under (%)</th>
<th>Over (%)</th>
<th>Exact agreement (%)</th>
<th>Kappa statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-field nonmydriatic</td>
<td>76.92</td>
<td>99.16</td>
<td>5.70</td>
<td>0.63</td>
<td>93.67</td>
<td>0.82</td>
</tr>
<tr>
<td>Three-field nonmydriatic</td>
<td>92.31</td>
<td>97.48</td>
<td>1.90</td>
<td>1.90</td>
<td>96.20</td>
<td>0.90</td>
</tr>
<tr>
<td>One-field mydriatic</td>
<td>89.74</td>
<td>98.32</td>
<td>2.53</td>
<td>1.27</td>
<td>96.20</td>
<td>0.90</td>
</tr>
<tr>
<td>Three-field mydriatic</td>
<td>97.44</td>
<td>98.32</td>
<td>0.63</td>
<td>1.27</td>
<td>98.10</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Under, underestimation (false negatives); Over, overestimation (false positives).

3. Results

3.1. Patient characteristics

A total of 158 eyes from 79 patients (men/women = 0.89) with diabetes underwent digital photography and fundus examination. Of these patients, 24 had type 1 diabetes, 49 had type 2 and six had other forms of diabetes (two with mature-onset type diabetes of the young, and four with gestational diabetes). Average age was 52.4 years (range 16–89). The average duration of diabetes was 8.5 years for type 1 diabetes, 17.2 years for type 2 diabetes and 4.3 years for other forms. According to the reference standard of slit-lamp biomicroscopy, 40 eyes (25.3%) had DR and 118 eyes (74.7%) did not.

3.2. Retinopathy detection rates by different strategies

The rates of nongradable photographs were 11.4, 13.3, 2.5 and 3.8% with one-field nonmydriatic, three-field nonmydriatic, one-field mydriatic and three-field mydriatic screening, respectively. Detection of DR, and the sensitivity, specificity, overestimation (false positives), underestimation (false negatives) and agreement (kappa statistics) of the four photographic strategies are presented in Table 1. Sensitivity ranged from 76.9 (one-field nonmydriatic) to 97.4% (three-field mydriatic), specificity ranged from 97.5% (three-field mydriatic) to 99.2% (one-field nonmydriatic) and agreement ranged from 0.82 (one-field nonmydriatic) to 0.95 (three-field mydriatic). Statistically significant differences were observed in the sensitivity of the detection of DR between one-field nonmydriatic and three-field nonmydriatic ($P<0.001$), one-field mydriatic and three-field mydriatic ($P<0.01$), one-field nonmydriatic and one-field mydriatic ($P<0.01$), three-field nonmydriatic and three-field mydriatic ($P<0.05$), and one-field nonmydriatic and three-field mydriatic ($P<0.001$) photographs. There was no significant difference in sensitivity between three-field nonmydriatic and one-field mydriatic photographs ($P=0.90$).

Detection of specific retinal findings, and the sensitivity, specificity and agreement (kappa statistics) of the four photographic strategies are presented in Table 2. Sensitivity ranged from 54 to 92% for microaneurysms, 59 to 71% for nerve fiber layer haemorrhage, 50 to 68% for dot-blot haemorrhage, 50 to 100% for cotton wool spots, 57 to 74% for hard exudates, 57 to 71% for intraretinal microvascular abnormalities and 100% for venous beading. No patient showed retinal or disc neovascularization. Specificity values were above 96% for microaneurysms, nerve fiber layer haemorrhage, intraretinal microvascular anomalies, dot-blot haemorrhage, cotton wool spots, hard exudates and venous beading.

4. Discussion

Our results suggest that colour digital photography is both sensitive and specific in the detection of DR in an at-risk population. Overall, compared with indirect ophthalmoscopy, the four strategies tested showed high levels of sensitivity and specificity. Sensitivity ranged from 77 to 97%, specificity ranged from 97 to 99%, and agreement ranged from 0.82 to 0.95.
to 0.95. However, there were differences among the four strategies themselves. Single-field digital photography was not as sensitive as three-field examination and, although sensitivity and agreement were significantly higher with a mydriatic strategy, the use of three fields per eye gave the best results ($P < 0.01$). We therefore hypothesize that larger fundus areas are photographed using a mydriatic and a three-field strategy, and that the rate of unreadable photos decreases with a mydriatic approach, as has been previously suggested [12].

The reference standard chosen for this study was indirect ophthalmoscopy, using slit-lamp biomicroscopy performed by an ophthalmologist. In fact, the reference standard used in research protocols is seven-field stereoscopic photography, but the method is complicated, time-consuming and unsuitable for large-scale screening. Nevertheless, indirect ophthalmoscopy is used as the reference standard in many studies [8,9]. The present study used one- and three-field strategies, and the rate of unreadable photographs increased with three fields. Also, a comparison of one- and two-field strategies may be more relevant, as Perrier et al. reported an increase of 6.2% in the rate of poor image quality with three or four fields compared with two fields [13].

A number of studies have compared digital fundus photography and ophthalmoscopy, but the results have been mostly influenced by the DR stage of the referred patients [8–10,12–14]. Our results are comparable to those previously reported. Murgatroyd et al., one of the largest earlier studies comparing 45° digital photography with ophthalmoscopy, reported sensitivities of 83, 86 and 90% with one-field nonmydriatic, one-field mydriatic and three-field mydriatic screening, respectively [12]. Their methodology was similar to that used in the present study, but we had a higher proportion of gradable photographs, possibly because our patients were younger. This may also explain why we achieved a higher sensitivity for the detection of DR.

The purpose of the present study was also to assess the effectiveness of digital photography in detecting diabetic retinal features. Analysis of the sensitivity rates for specific retinal findings showed higher rates in the detection of hard exudates, nerve fiber layer haemorrhage and venous beading. On the other hand, microaneurysms, dot-blot haemorrhage and cotton wool spots were less likely to be detected. Thus, we hypothesize that size and/or the contrast definition of retinal findings may have influenced the ability to detect them. This would explain why microvascular changes such as hard exudates or nerve fiber layer haemorrhage were visualized more clearly.

In conclusion, digital retinal colour photography offered sensitivity, specificity and exact agreement values that were good enough to recommend it for DR screening. Also, as expected, mydriasis improved image quality, sensitivity and specificity. Nevertheless, although it may not apply to all diabetic lesions, we consider that nonmydriatic photographs are the optimal screening strategy for DR. Dilating the pupils can cause discomfort to patients as it increases the duration of the examination and makes it impossible to drive, leading to poorer compliance. However, pupil dilation may be used when image quality is poor, such as in older patients with advanced cataract or senile myosis. In such cases, retinal findings such as venous beading and nerve fiber layer haemorrhage are more likely to be detected.

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**References**


