Two-Field Photography Can Identify Patients With Vision-Threatening Diabetic Retinopathy

A screening approach in the primary care setting

Catharina Stellingwerf, MD
Peter L.L.J. Hardus, PhD
Johanna M.M. Hooymans, PhD

OBJECTIVE — To compare the effectiveness of two 45° photographic fields per eye in the screening for diabetic retinopathy with the routine ophthalmologist’s examination and to study the effectiveness of visual acuity measurement in the detection of diabetic macular edema.

RESEARCH DESIGN AND METHODS — Type 1 and 2 diabetic patients without a known history of more than minimal retinopathy (n = 469) had a routine examination by an ophthalmologist, including visual acuity measurement, indirect retinoscopy, and biomicroscopy. At the same time, two-field nonstereoscopic retinal photographs were made of both eyes and assessed in a masked fashion by a retinal specialist. The results were compared.

RESULTS — The prevalence was 4.3% for vision-threatening retinopathy and 24% for any retinopathy. The sensitivity of two-field photography in identifying diabetic patients with sight-threatening retinopathy was 93% (specificity 99%) and sensitivity for detecting any retinopathy was 83% (specificity 88%). The percentage of referrals to an ophthalmologist was 6.2%. All patients with macular edema detected by biomicroscopy were classified as having vision-threatening retinopathy on the photographs.

CONCLUSIONS — Two-field retinal photography is a promising alternative to the routine ophthalmologist’s examination in the screening for diabetic retinopathy. Visual acuity measurement is not a sensitive tool for the detection of macular edema. Screening for diabetic retinopathy using two-field retinal photography is feasible in a primary care setting and can substantially lower the number of ophthalmic referrals.

Diabetes Care 24:2086–2090, 2001

Diabetic retinopathy is currently the leading cause of blindness in the western world in people aged 20–65 years (1). Several studies indicate that severe visual loss by diabetic retinopathy is caused to a large extent by lack of adequate screening (2). When not discovered before vision loss occurs, the disease usually progresses severely, and at that point, laser treatment is rarely effective in restoring vision (3,4). Therefore, it is vital to detect retinopathy in time to prevent the permanent and destroying effects of this disease. Regular fundus examinations in mydriasis are recommended for all patients with diabetes (5).

Screening in the Netherlands is typically retinoscopy through dilated pupils performed by an ophthalmologist. An alternative is retinal photography. The retina is photographed through a dilated pupil, and the photographs are evaluated by an expert. This method of screening is very suitable for use in a primary care setting. Screening in a primary care setting could dramatically reduce the number of premature referrals to an ophthalmologist. It will favor accessibility of the screening and increase compliance.

The gold standard for evaluating diabetic retinopathy is the grading of stereoscopic photographs of seven fields (6). Several studies have demonstrated that a reduced number of photographic fields can provide sufficient information in clinical trials and epidemiological studies (7,8). However, for screening purposes, this was not evaluated (9).

In the present study, the grading results of two central nonstereoscopic 45° photographic fields were compared with the findings from indirect retinoscopy and slitlamp biomicroscopy performed by an ophthalmologist. In a small study, the agreement of this technique and seven-field stereo photography was satisfactory (8).

Standard photography does not provide stereopsis. Therefore, macular thickening, which is important for the diagnosis of clinically significant macular edema, will be missed. Visual acuity is considered as an aid for detecting macular edema (10), in addition to the retinal photographs. We evaluated the effectiveness of visual acuity measurements in the diagnosis of macular edema.

RESEARCH DESIGN AND METHODS — Consecutive patients were recruited from a university hospital practice and a general practitioner laboratory over a 2-year period. Patients were eligible for inclusion if they had type 1 diabetes (based on autoimmunity) for at least 5 years or type 2 diabetes (based on insulin resistance) regardless of the duration of the diabetes. For the diagnosis of
diabetes, the following World Health Organization criteria were used: fasting blood glucose of >6.1 mmol/l or blood glucose of ≥11.1 mmol/l 2 h after a glucose load. If patients had been examined previously, they were excluded if they had grade 3 retinopathy (see Table 1) or more retinopathy in one or both eyes on their previous visit. In the general practitioner laboratory, only type 2 diabetic patients were screened.

### Visual acuity

Best visual acuity was measured on both eyes using a Snellen chart. In the university practice, visual acuity was measured after refraction; in the general practitioner laboratory, distance correction glasses were worn for testing if the patient normally used them, and a pinhole was also used with the glasses.

### Examination

Both eyes were inspected using biomicroscopy of the anterior segment to determine the presence of iris neovascularization or significant cataract. Mydriasis was achieved by 0.5% tropicamide and 2.5% phenylephrine; if the pupil diameter was still <6 mm after 20 min, another drop of each medicine was instilled. The grade of diabetic retinopathy was determined by indirect retinoscopy and by slitlamp biomicroscopy. In addition, when clinically significant macular edema was present on biomicroscopy, it was noted. Macular edema was defined according to the Early Treatment Diabetic Retinopathy Study (ETDRS) (11): 1) thickening of the retina within 500 μm of the fovea and/or 2) hard exudates within 500 μm of the fovea if associated with thickening of the adjacent retina and/or 3) zone(s) of retinal thickening of one disc area or larger, any part of which is within one disc diameter of the fovea. This examination was done by one of six graduated ophthalmologists from the University Hospital of Groningen. The patients in the general practitioner laboratory were examined by one of the authors (C.S.). This examination, which includes indirect retinoscopy and biomicroscopy, will henceforth be called retinoscopy.

### Photography

Two nonstereoscopic 45° photographs of each eye were made through dilated pupils as follows: the photograph was centered on the fovea, with the nasal edge of the optic disc at the edge of the photograph and a nasal field with 1 disc diameter at the temporal edge of the optic disc. An ophthalmic photographer or a doctor’s assistant performed the photography; the doctor’s assistants were trained for 1 week by an ophthalmic photographer. We used a Canon CF-60 UV retinal camera with Ektachrome professional ISO 64 film (Kodak) and had them processed in a photo laboratory.

### Grading

The images were graded by a retinal specialist in a masked fashion using an upright slide magnifier. The quality of the photographs was assessed as “good” (lesions discernible with difficulty), “fair” (lesions discernible with difficulty), or “insufficient” (presence of lesions not discernible). Grades 1–5 were allocated only if the quality was at least “fair” for both eyes and sufficient retinal area could be assessed on the photographs; if this was not the case, grade 6 was allocated.

Retinopathy was assessed according to a modified Airlie House Classification system (12) (Table 1). A level of severity for each person was assigned according to the degree of retinopathy present in the more affected eye. We modified the method for the use of retinoscopy. We considered retinopathy grade 3.5 or higher in at least one eye as a reason for referral to an ophthalmologist, and we defined this retinopathy as vision-threatening. Ungradable photographs of one or both eyes were also considered as a reason for referral.

### Results

Of the 469 diabetic patients included, 231 were men and 238 were women. Their age (mean ± SD) was 51 ± 17.7 years. Of these subjects, 311 had type 2 diabetes, and 158 had type 1 diabetes; 47% used only insulin, 43% used only oral antidiabetic medication, 1% used both, and 9% were treated only with diet. More patients had findings of no retinopathy with retinoscopy than with photographs (76 vs. 70%) (Table 2). From six (1.3%) patients, the photographs of one eye (two patients) or both (four patients) were notgradable. In the

### Table 1—Definitions of retinopathy grades

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No retinopathy</td>
</tr>
<tr>
<td>1.5</td>
<td>Only intraretinal hemorrhages</td>
</tr>
<tr>
<td>2</td>
<td>Only microaneurysms</td>
</tr>
<tr>
<td>3</td>
<td>Microaneurysms and intraretinal hemorrhages, maximum 20 red dots</td>
</tr>
<tr>
<td>3.5</td>
<td>Grade 3 plus hard exudates or &gt;20 red dots</td>
</tr>
<tr>
<td>4</td>
<td>Grade 3 plus &gt;1 cotton wool spot or intraretinal microaneuripathy or venous beading</td>
</tr>
<tr>
<td>5</td>
<td>Neovascularization or fibrosis in the optic disc (and/or elsewhere in the retina), preretinal hemorrhage, and/or vitreous hemorrhage</td>
</tr>
<tr>
<td>6</td>
<td>Not gradable</td>
</tr>
</tbody>
</table>

### Table 2—Grade of diabetic retinopathy with retinoscopy and retinal photographs

<table>
<thead>
<tr>
<th>Grade</th>
<th>Retinoscopy</th>
<th>Retinal photography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1</td>
<td>Type 2</td>
</tr>
<tr>
<td>1</td>
<td>97 (61)</td>
<td>258 (83)</td>
</tr>
<tr>
<td>1, 5</td>
<td>5 (3.2)</td>
<td>19 (6.1)</td>
</tr>
<tr>
<td>2</td>
<td>27 (17.1)</td>
<td>16 (5.1)</td>
</tr>
<tr>
<td>3</td>
<td>16 (10.1)</td>
<td>10 (3.2)</td>
</tr>
<tr>
<td>3, 5</td>
<td>6 (3.8)</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td>4</td>
<td>5 (3.2)</td>
<td>2 (0.64)</td>
</tr>
<tr>
<td>5</td>
<td>2 (1.3)</td>
<td>1 (0.32)</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>158 (100)</td>
<td>311 (100)</td>
</tr>
</tbody>
</table>

Data are n (%).
Two-field photography in diabetic retinopathy screening

Table 3—Test statistics for the detection of retinopathy by retinal photography compared with retinoscopy

<table>
<thead>
<tr>
<th></th>
<th>Vision-threatening retinopathy</th>
<th>Any retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1</td>
<td>Type 2</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>92.3</td>
<td>100</td>
</tr>
<tr>
<td>Specificity</td>
<td>98.6</td>
<td>99.3</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>85.7</td>
<td>77.8</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>99.3</td>
<td>100</td>
</tr>
<tr>
<td>Agreement (weighted κ)</td>
<td>0.70</td>
<td>0.71</td>
</tr>
</tbody>
</table>

Data are %, unless otherwise indicated.

In addition, we analyzed the groups of type 1 and 2 diabetic patients separately. The prevalence of vision-threatening retinopathy was 2.3% in the group of type 2 diabetic patients. The sensitivity of the retinal photograph grading was 100% (specificity 99%). In the group of type 1 diabetic patients, the prevalence of vision-threatening retinopathy was higher, i.e., 7.6%. The specificity for detecting these patients using retinal photographs was 92% (specificity 98%). Vision-threatening retinopathy was not detected with retinal photographs in one patient, and he was assessed as having grade 3 retinopathy; peripheral exudates were missed on the photographs.

The agreement between the gradings with retinoscopy and those with retinal photographs was good, with a weighted κ of 0.71. Exact agreement between assessment using retinoscopy and retinal photographs was 80.8%. For 13.8% of the patients, a higher grade of retinopathy was found with the photographs, and in 5.8% of the patients, more abnormalities were seen with retinoscopy. We checked whether the agreement between the gradings with retinoscopy and retinal photographs would be better when not taking into account the distinction made between intraretinal hemorrhages and microaneurysms. The weighted κ for retinoscopy compared with retinal photography was 0.71 in the original grading and 0.73 for the grading without this distinction.

Visual acuity was <0.8 in one or both eyes in 120 (25.6%) patients. Macular edema was detected with slitlamp biomicroscopy in only nine of these patients. The sensitivity of visual acuity measurement for the detection of macular edema is therefore quite low (7.5%). Lowering the visual acuity limit to values <0.8 did not improve sensitivity. However, specificity was high (99.0%). In the other patients, cataracts, macular degeneration, glaucoma, or amblyopia could explain the subnormal visual acuity. All of the patients with macular edema determined by retinoscopy had diabetic retinopathy grade 3.5 or higher on the retinal photographs. One patient had iris neovascularization in one eye; he had grade 5 retinopathy determined by both retinoscopy and photographs.

Conclusions

The minimum sensitivity required for screening methods for diabetic retinopathy is often considered to be 80% (13). For both type 1 and type 2 diabetic patients, the sensitivity of two-field retinal photography was far above 80%; in fact, the sensitivity was 95% for the detection of vision-threatening retinopathy in this group of patients with a low prevalence of vision-threatening retinopathy. Few photographs were of insufficient quality for grading, both in the university hospital and in the general practitioner laboratory, where doctor’s assistants who had had only a short training in retinal photography made the photographs. In this predominantly Caucasian population, the acceptable photographic rate was better than in other studies using 45° photography. It may be that in a Northern European population, ocular characteristics favor this technique, whereas other ethnic groups and populations may have larger numbers of patients with poor dilation or lens or media opacity. Forty-five degree photographs are more susceptible than 30° photographs to anything that degrades image quality because of the smaller details and difficulty in detecting lesions at the edges of the fields.

In their review of the effectiveness of screening tests for diabetic retinopathy, Hutchinson et al. (14) showed that mydriatic 45° retinal photographs read by different health care professionals mostly reach a sensitivity >80%. This could not be reached by using direct or indirect ophthalmoscopy, even when used by experienced ophthalmologists. The number of photographs per eye was not evaluated.

We chose mydriatic photography because it has higher sensitivity in the detection of vision-threatening retinopathy than the nonmydriatic method (14).

We compared two-field 45° retinal photography to slitlamp biomicroscopy and indirect ophthalmoscopy as a standard. In clinical trials, seven-field stereophotography graded by more than one independent grader is the most reliable noninvasive gold standard (15). However, slitlamp biomicroscopy in combination with indirect ophthalmoscopy is the preferred and widely accepted method.

Referrals

A total of 23 subjects (4.9%) with retinopathy grade 3.5 or higher in at least one eye and 6 subjects (1.3%) with ungradable photographs for at least one eye needed (if not included in this study) referral to an ophthalmologist. The referral rate based...
used by ophthalmologists when screening for diabetic retinopathy. It is a sensitive method for detecting vision-threatening diabetic retinopathy (11). Thus, it is a logical reference standard for a screening procedure to be evaluated. Harding et al. (16) photographed three overlapping 45° fields per eye and used slitlamp biomicroscopy as a reference standard as well. They found an 89% sensitivity for the detection of vision-threatening diabetic retinopathy.

The agreement in our study between two-field photography and slitlamp biomicroscopy is good, and it is better than that found by Verhoeven et al. (17), who made one photograph per eye (κ = 0.41), but was comparable with results by Schachat et al. (18), who graded the individual characteristics of diabetic retinopathy using photography and biomicroscopy (κ = 0.56–0.79). The agreement between two-field and seven-field stereo-photography was reasonable to good in the study of Aldington et al. (8) (κ varied from 0.44 to 0.77).

Unfortunately, there is little uniformity in the grading systems used when screening for diabetic retinopathy. The definition of vision-threatening retinopathy often differs as well in the studies published. The grading we chose was based on the grading used in the larger studies, like the ETDRS and the U.K. Prospective Diabetes Study (UKPDS). We followed the suggestions for modification for screening purposes made by Klein et al. (12), which does not grade the severity of specific lesions separately. This grading differentiates between intraretinal hemorrhages and microaneurysms, which can be difficult to distinguish with retinoscopy or on retinal photographs. The agreement we found when not taking into account this distinction was almost the same, which means that in our series, the confusion of hemorrhages and microaneurysms was small.

Harding et al. (16) noted that macular edema in particular was missed on the photographs. In our series, all of the patients with macular edema diagnosed on retinoscopy were graded on retinal photographs as having vision-threatening retinopathy and were referred to an ophthalmologist. Because macular edema can be missed on photographs, visual acuity measurement is often recommended in addition to photography in the screening for diabetic retinopathy. In a primary care setting, however, best-corrected visual acuity can be difficult and time-consuming to measure. In addition, it is not very specific; it will detect cataracts and age-related macular degeneration, which is not the purpose of the screening. Finally, macular edema is preferably detected and treated before visual acuity loss occurs (19). In our study, visual acuity measurement had low sensitivity in the detection of macular edema. All of the techniques using nonstereoscopic retinal imaging have limitations in the detection of macular edema. Besides slitlamp biomicroscopy, oral fluorescein could be an alternative, because this screening method has good sensitivity in detecting macular edema. However, it is much more time-consuming than retinal photography and has a small risk of allergic reaction, which is a drawback when using the technique on a large scale.

An alternative method for the detection of macular edema is to use the presence of hard exudates on the photographs within one disc diameter of the fovea as a parameter. This parameter was shown to be sufficiently sensitive for the detection of macular edema because 98% of the patients with reduced vision (<6/9) due to macular edema have an exudate in at least one eye (13). Bressnick et al. (9), who used the ETDRS database (with a high prevalence of vision-threatening retinopathy), showed that the sensitivity for detecting clinically significant macular edema is 94% for the criterion of any hard exudate within one disc diameter of the center of the macula. To make the screening as sensitive as possible without losing too much specificity, we propose referring to an ophthalmologist those patients with at least one hard exudate in at least one eye (grade 3.5 and higher). In our series, we can conclude that although retinal thickening caused by macular edema could be overlooked on retinal photographs, all of the patients with macular edema had other characteristics of vision-threatening retinopathy as well and were referred to an ophthalmologist. With this referral policy, visual acuity measurement may therefore not be indicated. Because this study had only 23 patients with vision-threatening retinopathy, a larger study will be necessary on this issue.

Although the purpose of screening for diabetic retinopathy is the detection of vision-threatening retinopathy, the detection of minimal background retinopathy is not unimportant. Most guidelines recommend screening patients without any retinopathy twice yearly, whereas patients with slight signs of retinopathy are screened yearly. Like other studies (6,19), we found a higher prevalence of background retinopathy with retinal photographs than with retinoscopy. Probably, small abnormalities like one or two microaneurysms are more easily detected on retinal photographs than with retinoscopy. It is likely that the retinal photographs have a greater sensitivity in the detection of any retinopathy. Thus, retinal photography is an even more powerful tool for the screening of diabetic retinopathy.

Conventional retinal photography is partly being replaced by digital imaging. The instantaneous availability and the rapid transfer of the images are some of the advantages of digital processing over 35-mm film processing. At present, however, 35-mm photographs reach a higher sensitivity in the detection of any retinopathy and vision-threatening retinopathy because they have a higher resolution (20–22). In addition, the equipment necessary for digital imaging and processing is not yet available to most ophthalmology or diabetes practices, whereas 35-mm cameras are readily available.

Screening for diabetic retinopathy can be done effectively with two nonstereoscopic retinal photographs per eye. It is a very sensitive tool for detecting retinopathy in both type 1 and type 2 diabetic patients. When applied in the primary care setting, it can substantially lower the number of ophthalmic referrals. However, before widespread application can be recommended, a larger multicenter study should be conducted. Using the presence of hard exudates as a parameter for the presence of macular edema is more effective than using visual acuity screening. Further study is required on this issue.

Acknowledgments—This work was supported by grants from the University Hospital of Groningen.

References
2. Klein R. Barriers to prevention of vision
Two-field photography in diabetic retinopathy screening