# ORIGINAL ARTICLE

# Validation of the Electronic Mailing of Retinographs of Diabetic Patients in Order to Detect Retinopathy in Primary Care

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**Objective.** Evaluate concordance in biomicroscopy evaluation of diabetic retinopathy degree among ophthalmologists. Validation of e-mail transmission of digital fundus photographs of type 2 diabetes patients as a method of diabetic retinopathy detection.
**Design.** Descriptive study.
**Setting.** Urban, primary health centre, and hospital.
**Participants.** Type 2 diabetic patients selected of consecutive form when going to the primary health center (n=352).
**Main measurements.** Parallel observer-blind evaluation of degree of retinopathy through biomicroscopy performed by ophthalmologists, against digital photographic images sent by e-mail taken by the family doctors. Concordance in the biomicroscopy among ophthalmologists was previously tested.
**Results.** Retinopathy was revealed in 25.70% of the retinographs; 10.44% was mild, 12.05% moderate, and 3.21% severe. Weighted kappa was 0.876 for biomicroscopy concordance. Sensitivity in detecting retinopathy is 76.6% and specificity 95.2%; 92.7% and 99.5% for ophthalmologist-derivable retinopathy. Sensitivity was 66.7% for non-mydriatic retinograph without dilation, 76.9% with elective dilation, and 85% with the mydriatic.
**Conclusions.** Concordance in evaluation of retinopathy degree through biomicroscopy was "very good." This allows using a single ophthalmologist's exploration as a reference model. E-mail transmission of the photograph of the back of the eye in type 2 diabetic patients as a retinopathy detection method is feasible. Regardless of the type of retinograph used, the photographs should be taken on the dilated eye, as this significantly improves sensitivity.

**Key words:** Diabetes mellitus type 2. Diabetic retinopathy. Diagnostic thechniques ophthalmological. Reference standard. Evaluation studies.

## VALIDACIÓN DE LA TRANSMISIÓN POR CORREO ELECTRÓNICO DE LA RETINOGRAFÍA DE PACIENTES DIABÉTICOS PARA DETECTAR RETINOPATÍA EN ATENCIÓN PRIMARIA

**Objetivo.** Evaluar la concordancia de la biomicroscopia de los pacientes diabéticos tipo 2 entre oftalmólogos, y analizar la validez de la transmisión por correo electrónico de la fotografía del fondo de ojo de pacientes diabéticos tipo 2, para detectar retinopatía diabética.
**Diseño.** Observacional, descriptivo.
**Emplazamiento.** Centro de salud y hospital urbanos.
**Participantes.** Pacientes diabéticos tipo 2 seleccionados de forma consecutiva al acudir al centro de salud (n = 352).
**Mediciones principales.** Valoración en paralelo, de forma ciega para los observadores, del grado de retinopatía mediante biomicroscopia realizada por oftalmólogos, frente a imagen fotográfica digital realizada por el médico de familia enviada por correo electrónico. Previamente se comprobó la concordancia entre oftalmólogos en la biomicroscopia.
**Resultados.** El 25,70% de las retinografías mostraron retinopatía: el 10,44%, leve; el 12,05%, moderada, y el 3,21%, severa. El análisis de la concordancia en la biomicroscopia mostró un valor kappa ponderado de 0,876. La sensibilidad para detectar retinopatía es del 76,6% y la especificidad del 95,2%; que son del 92,7% y el 99,5%, respectivamente, para retinopatía derivable al oftalmólogo. La sensibilidad fue del 66,7% con el retinógrafo no midriático sin dilatación, del 76,9% con dilatación electiva y del 85% con el retinógrafo midriático.
**Conclusiones.** La concordancia, mediante biomicroscopia, ha sido «muy buena» y permite utilizar la exploración de un solo oftalmólogo como patrón de referencia. Es factible la transmisión telemática de la fotografía del fondo de ojo de pacientes diabéticos tipo 2 como método para detectar retinopatía. Las fotografías deberían realizarse dilatando, independientemente del tipo de retinógrafo empleado, ya que mejora significativamente la sensibilidad.

**Palabras clave:** Diabetes mellitus tipo 2. Retinopatía diabética. Técnicas diagnósticas oftalmológicas. Estándares de referencia. Estudios de evaluación.

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# Introduction

Diabetic retinopathy (DR) is a highly prevalent, chronic and progressive disease. It is the second cause of blindness in Spain and the second in people of working age.[1] Even in its most aggressive forms, loss of acute vision symptoms are not normally present, so when there is a decrease it is usually too late for effective treatment. For this reason early detection is vital.

Laser photocoagulation prevents or delays vision loss in a good number of patients.[2] Photographs of the back of the eye are more reliable than ophthalmoscope for diagnosis.[3] Studies have validated the digital image as the most ideal method for DR screening.[4]

In the Andalusian Health System the diagnosis and follow-up of type 2 diabetic patients is carried out in primary care centres. In those centres, the health network allows digital images taken, to be sent by e-mail to a reference centre to be stored and studied by ophthalmologists for classification and treatment of DR. Studies are required to assess the real use of this method and, its practicality in providing full cover for the diabetic population, and its direct relationship at the 2 care levels and, its potential to reduce costs with a greater benefit for patients and the system.

To achieve this, we proposed the following objectives: to evaluate the concordance of biomicroscopy between ophthalmologists. To analyse the validity of digital photographs (received by e-mail) read by ophthalmologists and family doctors to detect DR, and to look at the benefits for patients.

# Methods

## Design
Observational, descriptive. Parallel blind assessment, of the degree of DR measured with a biomicroscope and comparing this with a digital photographic image.

## Population and Sample
Type 2 diabetic patients, who had not received photocoagulation, consecutively selected on arriving at a clinic.
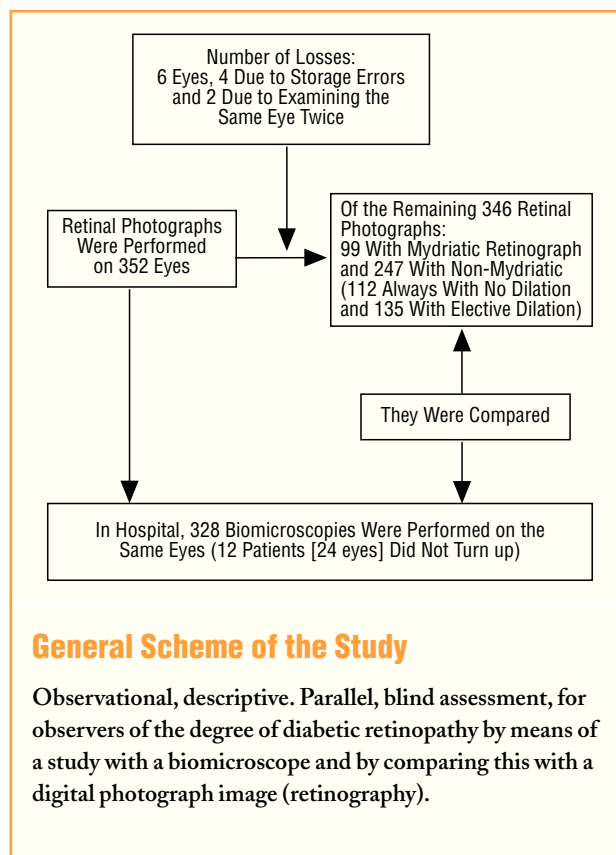
The sample size for the kappa index is N=196 (15% disagreement ratio, precision 5%, and a 95% confidence level).[5] For validation, for a 95% negative predictive value, precision 5% and a 95% confidence level, N=73.

It was increased to Na=91, according to Na=N [1/(1−R)], for losses.[6]

## Measured Variables
Degree of DR in the digital photograph and biomicroscopy, according to the modified Early Treatment Diabetic Research Study (ETDRS) classification,[7] measured by an ophthalmologist. Macular oedema was excluded as stereoscopic photographs could not be taken.

Diagnosis of DR in the photograph by the family doctor.

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Number of Losses:
6 Eyes, 4 Due to Storage Errors and 2 Due to Examining the Same Eye Twice

Retinal Photographs Were Performed on 352 Eyes

Of the Remaining 346 Retinal Photographs:
99 With Mydriatic Retinograph and 247 With Non-Mydriatic (112 Always With No Dilation and 135 With Elective Dilation)

They Were Compared

In Hospital, 328 Biomicroscopies Were Performed on the Same Eyes (12 Patients [24 eyes] Did Not Turn up)

## General Scheme of the Study

**Observational, descriptive. Parallel, blind assessment, for observers of the degree of diabetic retinopathy by means of a study with a biomicroscope and by comparing this with a digital photograph image (retinography).**

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## Data Collection and Variable Measurement Techniques
In a first group of participants, a family doctor, previously trained in ophthalmology, took 3 photographs (JPEG format) of each eye with a Topcon® TRC-50 EX mydriatic retinograph, under mydriasis with tropicamide with or without phenylephrine, and of the, macular, nasal and upper temporal fields.[8] With the second group, a Topcon® NW100 non-mydriatic retinograph was used, with first ones always without dilation and the following ones dilated with tropicamide when, in their opinion, the quality of the photograph was not good. In both cases, 3 photographs, nasal, central, and temporal (immovable fixed points in this retinograph), were taken.

The photographs were sent by e-mail to the Juan Ramón Jiménez Hospital, using the program Outlook 2000®, over the Andalusia Regional Government Corporate network.

The eye fundus (3 photos) was divided into 6 fields: papilla, macula, upper, lower, temporal, and nasal; it was considered "not assessable" when more than 3 were of poor quality.

The patients were sent to the ophthalmologist with 3 weeks to avoid any progression of the DR causing discordances.

Biomicroscopy was performed independently by 2 ophthalmologists with a slit lamp and a non-contact lens (VOLK Super 66)® or a contact lens (Ocular MAINSTER Standard Focal/Grid®), if the version was inappropriate.

## Data Analysis
Weighted linear and quadratic kappa index, was used to assess the agreement of the biomicroscopy between ophthalmologists. For the strength of the agreement the Landis and Koch[9] scale was used. To test the validity, sensitivity (Se), specificity (Sp), the po-

sitive predictive value (PPV), and the negative predictive value (NPV), for all the standards and confidence intervals (CI) were measured.

Version 11.0 of the SPSS program and version 6.0 of EpiInfo program was used.

## Results

There were 352 retinal photographs performed; 99 with a mydriatic retinograph (MYD), 247 non-mydriatic (NO-MYD): 112 always with no dilation (NOMYD-ND) and 135 with elective dilation (NOMYD-D). Six eyes (1.7%) eyes were lost, 4 due to storage errors and 2 due to duplication of the examination in the same eye. There were no losses in the electronic transmission.

The mean age and standard deviation of the patients was 65.4±9.9 years.

The ophthalmologist considered 28% of the examinations non-assessable (17.2% of those performed with MYD, 38.4% of the NOMYD-ND, and 27.4% of the NOMYD-D) (P=.0027). Cataracts were more common in the non-assessables (63.42%) than in the assessables (15.32%) (P<.001).

Similarly with other problems of transparency (5.8% compared to 4.9%; P=.005). A family doctor made 291 examinations, of which 23.71% were non-assessable compared with 50.9% which made 55 (P=.004).

Of the retinal photographs read by ophthalmologists, 25.7% had DR: 10.4% mild (MiDR), 12% moderate (MoDR), and 3.2% severe (SDR).

The family doctor considered 13.6% of the retinal photographs non-assessable. Of the assessable ones, 36.5% had DR.

Overall, 328 biomicroscopies were performed, as 12 of the patients (24 eyes) did not turn up, 3 of them had lesions in both eyes, and in 1 the lesion was MoDR. Four were non-assessable (1 due to a detached retina, 2 due to cataracts, and 1 with no diagnosis). Of the 28.7% who had a lesion: 12.65% were MiDR; 13.9%, MoDR; 1.8%, SDR; and 0.3% very severe (VSDR). The mean time between the retinograph and the biomicroscopy was 15.6 days, and ranged between 2 and 68 days.

The agreement in biomicroscopy between ophthalmologist was "very good" (linear weighted kappa =0.80; 95% CI, 0.73-0.88, and quadratic weighted kappa =0.88; 95% CI, 0.65-0.95).

Table 1 shows the validity results of digital photographs read by the ophthalmologists and family

doctors as a method for detecting DR and referable DR (grade ≥MoDR), and in Table 2, that of the ophthalmologists differentiated by retinal photographs. Significant differences were found in sensitivity in favour of MYD (P=.009), compared to NOMYD-ND.

## Discussion

The agreement in biomicroscopy was "very good." It enables the examination by an ophthalmologist to be like a reference test.

The time between the 2 tests was not seen to influence the differences, since it was too short for the lesions to progress. We found the sensitivity to be slightly less than the 80% recommended by the British Diabetic Association[10] and a specificity slightly higher than the recommended 95%. With NOMYD-SD, the sensitivity is clearly lower, although specificity is maintained. This decrease in sensitivity is found by the majority of authors. When the eyes which had had poor quality photographs were subsequently dilated, we found a great improvement in the sensitivity, although lower than MYD dilating to 100% and with higher temporal field. In this case, the sensitivity and specificity are similar to those of Baeza Díaz et al,[11] using 3 fields and dilation if the examination quality was poor, or Murgatroyd et al,[12] who used 3 fields with dilation, and somewhat higher than that of other authors such as Harding et al[13] and Lawrence,[14] with 3 fields, or Scanlon et al,[15,16] Olson et al[17], or Stellingwerf et al,[18] with 2.

The negative predictive value was taken as a reference for the sample size, since, on having an effective treatment for DR, it is important to avoid the patients with a lesion being diagnosed as healthy. In our case it was very good and similar to that found by Stellingwerf et al[18] and lower than that of Baeza Díaz et al.[11]

**TABLE 1** **Analysis of the Digital Photograph Assessments Made by Ophthalmologists and Family Doctors as a Method of Detecting Retinopathy in General and Referable in Particular (Degree Equal to or Greater Than Moderate)**

| | Diabetic Retinopathy | | Diabetic Retinopathy ≥Moderate | |
| | Ophthalmologist | Family Doctor | Ophthalmologist | Family Doctor |
| --- | --- | --- | --- | --- |
| Sensitivity | 76.6% (64.3-85.9) | 78.37% (67.3-87.1) | 92.7% (79-98.1) | 95.2% (82.9-99.2) |
| Specificity | 95.2% (90.7-97.9) | 78.64% (72.4-84) | 99.5% (96.6-100) | 81.5% (75.9-86.1) |
| Positive predictive value | 86% (74.2-93.7) | 56.86% (46.7-66.6) | 97.4% (84.9-99.9) | 47.6% (36.7-58.7) |
| Negative predictive value | 91.3% (86.1-95.1) | 91.01% (85.8-94.6) | 98.4% (95.1-99.6) | 99% (96-99.8) |

**TABLE 2** **Analysis of the Validity of Digital Photography Read by Ophthalmologists by Retinograph Type (Mydriatic, Non-Mydriatic With Elective Dilation and Non-Mydriatic With No Dilation)**

| | Mydriatic | Non-Mydriatic With Elective Dilation | Non-Mydriatic With No Dilation |
| --- | --- | --- | --- |
| Sensitivity | 85% (62.1-96.8) | 76.9% (56.4-91) | 66.7% (41-86.7) |
| Specificity | 96.4% (85.1-98.9) | 93.4% (84.1-99.2) | 98% (89.1-99.9) |
| Positive predictive value | 85% (62.1-96.8) | 83.3% (62.6-95.3) | 92.3% (64-99.8) |
| Negative predictive value | 94.6% (85.1-98.9) | 90.5% (80.4-96.4) | 88.9% (77.4-95.8) |

Although 28% of the examinations were non-assessable, it would be 5.8% if we discard those who had cataracts or opacities, which is around the 5% recommended by the British Diabetic Association.[10] If we analyse by methods, the losses decrease with dilation, and this difference is statistically significant. Murgatroyd et al,[12] achieved a reduction in non-assessables from 26% to 5% by dilating the eyes to 100%. The difference found between the MYD and NOMYD could be due to 3 different causes: the first could be the dilation of the eyes to 100% instead of 50.74% and, also a higher dilation by using 2 drops of tropicamide and phenylephrine if 1 was not sufficient. The second could be the greater temporal field which cannot be done with NOMYD. This would have less influence because, although some authors, such as Baeza et al,[11] found slight improvements in the sensitivity for retinopathy, others, such as Perrier et al[19] and Baeza et al themselves, did not find any when they studied referable retinopathy. Also, the third field does not reduce the losses. The third reason could be the difference in technical quality of the retinal photographs. That from the MYD was higher than the NOMYD used, which was a portable apparatus with poorer software.

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## What Is Known About the Subject

- **Diabetic retinopathy is highly prevalent disease which does not usually present with loss of acute vision; its early detection is essential.**

- **Back of the eye photographs are more reliable than ophthalmoscope for the diagnosis of diabetic retinopathy.**

- **The health service internet allows digital images taken in primary care health centres to be sent, stored and studied by ophthalmologists.**

## What This Study Contributes

- **Retinal photographs of type 2 diabetic patients sent by e-mail is feasible as a method for the detection and monitoring of retinopathy.**

- **The retinograph must be the non-mydriatic type and the photos taken dilated with tropicamide.**

- **The person taking the retinal photographs should do as many as possible and be trained well to avoid losses and the high number of false positives.**

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On the other hand, many disadvantages were observed: MYD required much more time to learn than NOMYD and it resulted in one of the 3 doctors refusing to use it; the time required, 12 examinations were made with NOMYD for every 5 with MYD, with the need for more health staff, and lastly, the inconvenience for the patients, longer waiting time in clinic and then a much longer and uncomfortable pupil dilation.

The reading of the digital photograph by a family doctor is very safe when detecting a significant DR. Good sensitivity was found, 95.2%, and a very good NPV of 99% when MoDR or higher was assessed, which ensures that patients with DR are not diagnosed as healthy. However, the specificity of 81.5% and a PPV of 47.6% to detect MoDR or higher, raises doubts on if the high number of false positives in a disease like DR, which could mean telling patients that they do not have it, counteracts the benefits that practically no lesion escaped. In any case, it is clear that training in reading, the only objective difference between these and the ophthalmologist, is essential.

As regards benefits to the patients (and for the health system), half of them would have avoided going to the ophthalmologist and almost all of them that had to go had a DR (16.8%≥MoDR) or opacities.

To send the digital photograph of the back of the eye of type 2 diabetics by e-mail, as a method of detecting and monitoring DR, is viable and on setting it up the following recommendations should be taken into account:

– The retinal photograph should be the non-mydriatic type, since the management of mydriatic is too complex and slow

– The retinal photograph should be taken by photographing at least 2 retinal fields of 45° (a single field has been rejected by several authors due to its insufficient validity,[11,12,14,16,20,21] and dilating with tropicamide, as it significantly improves sensitivity and the percentage of assessable photographs

– If the family doctor is going to read the photographs in the health centre, training must be improved to avoid the high number of false positives found

– The person who performs the retinal photographs should do the highest number possible, since the percentage of non-assessables significantly decreases with practice

With these recommendations, it would mean that only between 30% and 40 % of patients would have to be seen by the ophthalmologist in the first visit, and given the high percentage of opacities in the non-assessables, it is likely that in the following reviews the percentage of referrals would be even less on this problem being controlled.

# References

1. Lalaurie Dubernet F, Martín Hernández E. Consideraciones oftalmológicas sobre la evolución de la ceguera en España. Integración. 1999;29:12-6.
2. Early Treatment Diabetic Retinopathy Study Research Group. Early photocoagulation for diabetic retinopathy: ETDRS report number 9. Ophthalmology. 1991;98:766-85.
3. Harding SP, Broadbent DM, Neoh C, White MC, Vora J. Sensibility and specificity of photography and direct ophthalmoscopy in screening for sight threatening eye disease: the Liverpool Diabetic Eye Study. BMJ. 1995;311:1131-5.
4. Ryder REJ. Screening for diabetic retinopathy in the 21st century. Diabet Med. 1998;15:721-2.
5. Silva Ayçaguer LC. Muestreo para la investigación en ciencias de la salud. Madrid: Díaz de Santos; 1993.
6. Argimon Pallás JM, Jiménez Villa J. Métodos de investigación clínica y epidemiológica. Madrid: Harcourt; 2000.
7. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic colour fundus photographs. An extension of the modified Airlie House Classification. ETDRS report no. 10. Ophthalmology. 1991;98:786-806.
8. Aldington SJ, Kohner EM, Meuer S, Sjolie A-K, The EURODIAB IDDM Complications Study Group. Methodology for retinal photography and assessment of diabetic retinopathy: the EURODIAB IDDM Complications Study. Diabetologia. 1995;38:437-44.
9. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33:159-74.
10. Working Party of the British Diabetic Association. A British Diabetic Association Report. 1997.
11. Baeza Díaz M, Gil Guillén V, Orozco Beltrán D, Pedrera Carbonell V, Ribera Montes C, Pérez Pons LI, et al. Validez de la cámara no midriática en el cribado de la retinopatía diabética y análisis de indicadores de riesgo de la retinopatía. Arch Soc EspOftalmol. 2004;79:433-42.
12. Murgatroyd H, Ellingford A, Cox A, Binnie M, Ellis JD, MacEwen CJ, et al. Effect of mydriasis and different field strategies on digital image screening of diabetic eye disease. Br J Ophthalmol. 2004;88:920-4.
13. Harding SP, Broadbent DM, Neoh C, White MC, Vora J. Sensibility and specificity of photography and direct ophthalmoscopy in screening for sight threatening eye disease: the Liverpool Diabetic Eye Study. BMJ. 1995;311:1131-5.
14. Lawrence MG. The accuracy of digital-video retinal imaging to screen for diabetic retinopathy: an analysis of two digital-video retinal imaging systems using standard stereoscopic seven-field photography and dilated clinical examination as reference standards. Trans Am Ophthalmol Soc. 2004;102:321-40.
15. Scanlon PH, Malhotra R, Greenwood RH, Aldington SJ, Foy C, Flatman M, et al. Comparison of two reference standards in validating two field mydriatic digital photography as a method of screening for diabetic retinopathy. Br J Ophthalmol. 2003;87:1258-63.
16. Scanlon PH, Malhotra R, Thomas G, Foy C, Kirkpatrick JN, Lewis-Barned N, et al. The effectiveness of screening for diabetic retinopathy by digital imaging photography and technician ophthalmoscopy. Diabet Med. 2003;20:467-74.
17. Olson JA, Strachan FM, Hipwell JH, Goatman KA, McHardy KC, Forrester JV, et al. A comparative evaluation of digital imaging, retinal photography and optometrist examination in screening for diabetic retinopathy. Diabet Med. 2003;20:528-34.
18. Stellingwerf C, Hardus PL, Hooymans JM. Two-field photography can identify patients with vision-threatening diabetic retinopathy: a screening approach in the primary care setting. Diabetes Care. 2001;24:2086-90.
19. Perrier M, Boucher MC, Angioi K, Gresset JA, Olivier S. Comparison of two, three and four 45 degrees image fields obtained with the Topcon CRW6 non-mydriatic camera for screening for diabetic retinopathy. Can J Ophthalmol. 2003;38:569-74.
20. Moller F, Hansen M, Sjolie AK. Is one 60 degrees fundus photograph sufficient for screening of proliferative diabetic retinopathy? Diabetes Care. 2001;24:2083-5.
21. Herbert HM, Jordan K, Flanagan DW. Is screening with digital imaging using one retinal view adequate? Eye. 2003;17:497-500.