OBJECTIVE — Detecting and grading of diabetic retinopathy (DR) by means of digital retinal images sent via the Internet.

RESEARCH DESIGN AND METHODS — Four nonstereoscopic digital retinal images (45° field each) of 126 eye fundus images from 70 diabetic patients were obtained with a nonmydriatic camera at two peripheral units. The images were sent via the Internet using a web-based system to a reference center, where they were diagnosed and graded by one ophthalmologist. These results were compared with those obtained by two other ophthalmologists, one at each peripheral unit, after direct examination of the patients. A modified severity scale of Airline House was used for grading DR in all cases. Agreement between observers was assessed using unweighted $k$ for categorical data and the intraclass correlation coefficient (ICC) for continuous data.

RESULTS — Presence of DR was detected in 69 eyes (55%). All eyes with DR (69 of 69, 100%) were correctly identified ($k = 1$) by inspecting the digital images. In 118 eyes (118 of 126, 94%), 57 with no DR and 61 with DR, there was an agreement between the gradation made after the direct examination and the gradation made after the inspection of the images (ICC = 0.92). In eight eyes with DR (8 of 126, 6%), there was disagreement in the grading made with both techniques.

CONCLUSIONS — Inspection of digital retinal images sent via the Internet allowed diagnosis and grading of DR. The presence or absence of DR was correctly assessed by inspection of the images in all instances. We also found agreement, in most cases, between retinopathy gradation made from the images and the gradation made by direct examination of the eyes. These findings suggest that this technique is suitable for screening procedures.

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lists for patients with severe affectation. It would then be useful to undertake screening programs or develop techniques capable of filtering the affected cases and diverting urgent conditions.

Screening is a simple diagnostic procedure applied to a whole population at risk to detect lesions that should be further investigated and treated. It is not a complete clinical assessment but a method to identify patients at risk who will require further examination (14). Although there is consensus concerning the cost-effectiveness of screening (15–20), the standards by which screening programs should be assessed have not been defined in the European protocols. An alternative method to the traditional examinations would be to obtain retinal images in situ and send them to a specialist for examination. Nonmydriatic fundus cameras allow the acquisition of high-quality digital images with no need for medically induced mydriasis. It has been shown that fundus photographs are more reliable than ophthalmoscopy in the diagnosis of diabetic retinal lesions (21–24). Therefore, the use of these cameras might be considered for screening, diagnosis, and grading of DR (25–27). Telemedicine is an emerging application of telecommunication technology to provide health care services in regions where access to physicians may be difficult (28–31). Digital fundus photographs have the advantage that they can be obtained at minimal cost and inconvenience for the patient (26,32–34) and can be transmitted through the Internet to distant experts (35,36). Although these technologies may eventually allow retinopathy screening via telemedicine, there is no consensus in the methodology and validation of an appropriate system. The role of the ophthalmologist might be assessment and/or treatment of the patients after the screening made by other professionals.

The Fundusnet project was an innovative telemedicine project supported by the Spanish Agency Commission Interministerial de Ciencia y Tecnología from 1998 to 2000. The aim of the present study was to test a teleconsultation system, developed within the frame of the Fundusnet project, intended for detecting and grading DR.

**RESEARCH DESIGN AND METHODS** — A total of 140 eyes of 70 consecutive diabetic patients attending either an endocrinology unit or an ophthalmology unit from January to March 2000 were initially included in this study. Patient inclusion was made regardless of age, sex, ethnicity, socioeconomic status, or any known ocular disease.

Digital eye fundus images were obtained with a nonmydriatic camera from diabetic patients at peripheral units. The images were sent through the Internet for storage to a server based on the Active Server Pages technology to provide a secure environment. An ophthalmologist graded the stored digital retinal images at the reference center and made a diagnosis. These results were compared with those obtained by the ophthalmologists by direct examination of the patients at the peripheral units.

The ophthalmologist at the reference center inspected the downloaded digital images, evaluated them for the presence or absence of DR, and graded the retinopathy using a modified version of the Airlie House classification (37), as indicated below. Similarly, one ophthalmologist at each peripheral unit also evaluated the images for the presence or absence of DR and graded the retinopathy by direct examination of the eye fundus of the patients. Direct examination was performed under mydriasis, a slit lamp, and a 90-diopter lens. The ophthalmologists were not aware of the grading performed by the others.

Digital eye fundus images were obtained with a nonmydriatic funduscopic camera (model CR5-45NM; Canon, Amstelveen, the Netherlands). A video camera (model DXC950; Sony, Tokyo, Japan) attached to the funduscopic camera and a frame grab-
ber (model MV-300; Teac Deutschland, Wiesbaden-Erbenheim, Germany) were used to digitize the images. Various compression settings balanced resolution and file size using the Joint Photograph Experts Group (JPEG) compression method. Typically, the final mean file size of a single image after compression was ~140 KB, which resulted after performing a 1:3 compression ratio. Four images were taken of each eye, which covered the macula, the nasal retina and optic disc, and the superior and inferior temporal areas.

The images were then transferred to a conventional personal computer and sent via the Internet for storage in a server based on the Active Server Pages technology to provide a secure environment. The stored images were then downloaded by the ophthalmologist at the reference center and visualized on a 17-inch conventional computer monitor with a video board set at 24 bits per pixel. To improve image analysis, a sharpen filter was applied in some instances using commercial image processing software (Photoshop; Adobe, Seattle, WA). Contrast, brightness, and zoom facilities were also used for enhancement of the images whenever necessary.

According to a modified version of the Airlie House classification (37), eight grades of severity were established: non-DR (NDR), minimal nonproliferative DR (NPDR), moderate NPDR, severe NPDR, very severe NPDR, PDR without high-risk characteristics (HRCs), PDR with HRCs, and advanced PDR. Because the presence of retinal thickening with no hard exudates was difficult to detect in our nonstereoscopic digital images, grading of maculopathy was based on the presence of exudates in the macular region. The existence of hard exudates at <500 μm from the fovea was considered macular edema. No distinction was made between small hemorrhages and microaneurysms, because this difference does not modify the classification. Notes on other additional examinations that were recommended (fluorescein angiography, laser photocoagulation) to the patient were recorded for treatment purposes but were not considered in this study.

Comparisons were made between stages graded by both ophthalmologists at the peripheral by direct examination and those made by the ophthalmologist at the reference center by inspecting the digital images. Agreement between the existence or absence of DR was analyzed by using unweighted kappa (κ) for categorical data (38), where κ = 0 defines no correlation and κ = 1 defines total correlation. The interclass coefficient correlation (ICC) (38) was used to determine the level of agreement on the stage of DR.

### RESULTS

In seven eyes (7 of 140, 5%), no attempt was made to obtain any fundus image because of the existence of an opaque cataract. A total of 532 digital retinal images from 133 remaining eyes were analyzed in this study. A total of 7 of these 133 eyes (5%) were excluded because the quality of the images did not allow any grading or detection of retinopathy. The causes of poor image quality in these seven eyes were media opacities (vitreous hemorrhage in one, lens opacity in three) or small size of the pupil (three eyes). Therefore, the final data set of this study was 126 eyes from 70 diabetic patients. The results obtained in this study are summarized in Table 1.

After inspecting the images, diabetic lesions were not observed in 57 eyes (57 of 126, 45%) and DR was diagnosed in 69 eyes (69 of 126, 55%). Similar figures were also obtained after direct examination of the eye fundus. Therefore, there was an agreement of 100% (κ = 1) on the presence or absence of DR between both techniques (100% of sensitivity and specificity).

The Airlie House classification of the 126 eyes made after direct examination showed 57 eyes with NDR (45%), 28 with minimal NPDR (22%), 28 with moderate NPDR (22%), 7 with severe NPDR (6%), 5 with PDR without HRCs (4%), and 1 with PDR with HRCs (0.7%). After inspection of the digital images, 57 eyes were classified as NDR (45%), 29 as minimal NPDR (23%), 30 as moderate NPDR (24%), 9 as severe NPDR (7%), and 1 as PDR with HRCs (0.7%).

Agreement between the results obtained from retinal images and those from direct examination was found in 118 eyes (118 of 126, 94%), 57 with NDR and 61 with several degrees of DR. There was disagreement in the remaining eight eyes (8 of 126, 6%). The level of agreement between both techniques, as determined by the ICC, was 0.92 (95% CI 0.90–0.95). Disagreement in the grading of five eyes occurred because intraretinal neovessels were not seen in the digital images due to an important hemorrhagic component. Four of these five cases were classified as severe NPDR, and one case was classified...
CONCLUSIONS — In diseases in which diagnosis is based mainly on an image, as in DR, the contribution of new imaging technologies is essential. The possibility of using nonmydriatic cameras and sending digital images through the Internet allows interaction between the different health care professionals examining diabetic patients. Incorporation of these new technologies in the field of teleophthalmology presents a wide range of possibilities in a time when specialized examination is exceeded and when there is a demand for improving the quality of medical care in a diabetic population with a high probability of increasing in number during the next quarter of the century.

The main goals when screening for DR are the detection of the first signs of early retinopathy to evaluate the progression of retinopathy and, above all, to detect severe treatment-requiring lesions. With early identification, prompt incorporation into the health care system, adequate education of the patient, regular lifelong evaluation, appropriate referral, and timely treatment, the vast majority of severe visual loss can be prevented. We have developed and tested a teleophthalmological system that fulfills these requirements.

The JPEG file type is widely used for transferring images on the Internet because they have a small size and, therefore, can be transferred rapidly from one computer to another and do not take up much storage space (36). However, one problem with JPEG files is finding the highest compression of the image that preserves adequate definition of the lesions. We used a compression ratio of 1:3, which produced files of ~140 KB. This compression ratio allowed enough definition without significant impairing of the transmission of the image through the network. It has been shown that when the original retinal image size of 1.5 MB is reduced to 29 KB (compression ratio 1:52), using JPEG compression, there was no serious degradation in image quality and that this compression method is an excellent alternative to reducing the image file size (39).

Our study shows that the use of digital retinal images transmitted through the Internet may be highly effective for screening of DR. We found that the study of four retinal fields was enough to discard or confirm the presence of diabetic lesions in all eyes studied. The validation we made demonstrates that the detection of DR using nonmydriatic digital color retinal images taken with a 45° funduscope camera is in substantial agreement with direct examination of the eye fundus. For continuous data, one measure of reliability agreement is the ICC, as described by Bartko (38). A κ or ICC of ≥0.81 was defined as excellent agreement (40). Our analysis showed that there was excellent agreement (ICC = 0.92) between the clinical level of DR assessed from the undilated digital image and direct examination of the eye.

The assignment of a clinical level of DR can be an integration of the presence and location of different lesions and the relative severity of these lesions. Based on the known risks for progression from each level of DR, a referral frequency with respect to repeat digital retinal images, ophthalmic evaluation, or both can be recommended. In our study, we found that 57 eyes (57 of 126, 45%) did not show any retinal lesion, and therefore, these patients would be advised to repeat photography in 1 year, thus reducing the waiting list for a specialized examination. Teleconsultation could reduce referral to ophthalmology specialists, which is important in countries with public health systems covering a large number of people.

Approximately 50% of the eyes examined had DR lesions (69 of 126, 55%). In those eyes, instead of making a detailed account of retinal lesions, we made a classification (Airlie House classification) by stages (37). This has the advantage that it indicates whether a patient should be referred for specialized ophthalmic evaluation. This technique does not replace the need for comprehensive eye examinations but detects patients who require prompt referral to specialty ophthalmology services. To classify the retinopathy, we made no distinction between microaneurysms and small hemorrhages, because they did not imply differences in the stage. In our study, eight eyes (8 of 126, 6%) were infraclassified in the digital images. The reason was that it was difficult to differentiate among new vessels, large intraretinal hemorrhages, and intraretinal microvascular abnormalities in those DR forms with high hemorrhagic components.

There were no difficulties in reaching an agreement between image analysis and direct examination up to the severe NPDR stage. However, the proliferative forms, specially made with intraretinal new vessels and high hemorrhagic components, presented some difficulties for classification. This problem can be addressed by using more sophisticated equipment that will gradually obtain digital images of higher quality. However, because part of our patient sample was taken from a general patient pool of an endocrinology clinic that included only a few patients with PDR, we cannot conclude that the technique is not valid for visualizing intraretinal new vessels. In all cases in which disagreement was observed, the analysis of the digital images underestimated the retinopathy when compared with the gradation made by direct examination. We believe this may be explained by the fact that high-grade DR has image features that may be lost when inspection of the digital images is made. In some instances, manipulation of the image with a sharpen filter (in our case, the filter included in the Adobe Photoshop program) allowed us as well as other authors (41) to improve the diagnosis.

We were able to perform effective detection of DR and derive only the serious cases with a wide margin of confidence, avoiding specialized examinations for the less severe forms. A challenge for this system, however, was associated with media opacities or the small pupil size found in some eyes of patients with long-term diabetes or significant retinal disease. In seven eyes in our sample, we did not even attempt to obtain images, and in another seven cases, although images were obtained, they did not allow detection or grading of DR because of their poor quality caused by the problems mentioned above.

Due to the initial difficulty in distinguishing retinal thickening without hard exudates in our nonstereoscopic digital images, we considered that all eyes with hard exudates <500 μm from the fovea had macular edema. However, because
patients with macular edema have important reduction of visual acuity, a combination of eye fundus image and visual acuity assessment would help improve the accuracy of the technique. Moreover, use of the Amsler test would improve detection of macular edema in the context of telemedical screening. It is also possible that, in the near future, stereoscopic images may be available to solve this problem. A recent report shows that it is feasible to obtain such images with a non-mydriatic funduscopy system similar to the one we have used (42).

In summary, we demonstrated that sending digital retinal images via the Internet is a suitable method for detecting and grading DR in a nonselected diabetic population. However, it has some limitations for diagnosis of macular edema with no hard exudates and for diagnosis of vascular lesions in hemorrhagic forms of DR. In these cases, a study of longer series would be needed to evaluate the degree of specificity of the method.

Our results show good agreement between nonmydriatic digital retinal images and dilated direct examinations and suggest that the digital technique we have used may be an effective telemedicine tool for remote grading of DR. It is also useful for suggesting when the next retinal evaluation should be made and for determining the need for prompt referral to an ophthalmologist. The use of this system, however, should not be regarded as a paradigm that would replace the need for comprehensive eye examinations.

The use of teleophthalmology among health professionals may represent an effective alternative for treating diabetic patients at low cost, with high possibilities for expansion and adaptability (43). Moreover, hospital diabetes specialists, ophthalmologists, and primary care doctors could readily share the digital retinal images of their patients, which will certainly improve the treatment of the diabetic patient.

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