Potential Efficiency Benefits of Nonmydriatic Ultrawide Field Retinal Imaging in an Ocular Telehealth Diabetic Retinopathy Program

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OBJECTIVE

To compare efficiency of nonmydriatic ultrawide field retinal imaging (UWFI) and nonmydriatic fundus photography (NMFP) in a diabetic retinopathy (DR) ocular telehealth program.

RESEARCH DESIGN AND METHODS

Patients in this retrospective, comparative cohort study underwent NMFP and UWFI between 1 November 2011 and 1 November 2012. Images were evaluated for DR and diabetic macular edema (DME) by certified graders using a standard protocol at a centralized reading center. Identification of DR, image evaluation time, and rate of ungradable eyes were compared.

RESULTS

NMFP and UWFI were performed in 1,633 and 2,170 consecutive patients, respectively. No statistically significant differences were found between groups regarding age, diabetes duration, sex, ethnicity, or insulin use. The ungradable rate per patient for DR (2.9 vs. 9.9%, $P < 0.0001$) and DME (3.8 vs. 8.8%, $P < 0.0001$) was lower with UWFI than with NMFP. With UWFI, the median image evaluation time per patient was reduced from 12.8 to 9.2 min ($P < 0.0001$). The identification of patients with DR (38.4 vs. 33.8%) and vision-threatening DR (14.5 vs. 11.9%) was increased with UWFI versus NMFP. In a consecutive subgroup of 502 eyes of 301 patients with DR, the distribution of peripheral retinal lesions outside Early Treatment Diabetic Retinopathy Study fields suggested a more severe DR level in 9.0% (45 eyes).

CONCLUSIONS

In a standardized DR ocular telehealth program, nonmydriatic UWFI reduced the ungradable rate by 71% (to <3%) and reduced image evaluation time by 28%. DR was identified 17% more frequently after UWFI, and DR peripheral lesions suggested a more severe DR level in 9%. These data suggest that UWFI may improve efficiency of ocular telehealth programs evaluating DR and DME.

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The American Telemedicine Association has published evidence-based recommendations for ocular telehealth programs for diabetic retinopathy (DR) (1). Such programs rely on the acquisition of retinal images to determine the presence and severity level of DR and diabetic macular edema (DME) (2). Retinal imaging devices are key components of any ocular telehealth program, and the current gold standard to evaluate DR is mydriatic stereoscopic Early Treatment Diabetic Retinopathy Study (ETDRS) protocol seven-standard 30° field fundus photography (1). Recently, ultrawide field retinal imaging (UWFI) scanning laser ophthalmoscopes have been shown to compare favorably with ETDRS photography (3,4). Even without pupillary dilation, UWFI allows for the acquisition of more than double the total retinal surface area captured with dilated ETDRS seven-field photography. The image acquisition time with UWFI has been shown to be less than one-half that of ETDRS photography, even when the time for dilation is excluded (3).

Given the potential advantages of UWFI, we compared the efficiency of nonmydriatic UWFI and nonmydriatic fundus photography (NMFP) in an established, validated ocular telehealth program for DR. Measures of image evaluation time, proportion of ungradable eyes, DR identification rates, and DR severity were evaluated.

RESEARCH DESIGN AND METHODS

The Joslin Vision Network (JVN) is an ocular telehealth program for DR that has been in continuous clinical operation since 1998 at the Joslin Diabetes Center (5,6). The JVN follows a strict protocol for acquiring nonmydriatic retinal images and grading and reporting the level of DR. Early JVN programs were developed and deployed through a cooperative agreement with the U.S. Department of Defense and U.S. Department of Veterans Affairs. The JVN has served as a pilot program for several federally funded programs for ocular telemedicine for DR, including the Indian Health Service, U.S. Department of Defense, and U.S. Department of Veterans Affairs.

We reviewed the electronic records of all patients receiving JVN retinal imaging at the Joslin Diabetes Center in Boston, Massachusetts from 1 November 2011 to 1 November 2012. From 1 November 2011 to 31 March 2012, all patients underwent imaging with low light–adapted digital NMFP. Stereoscopic pairs of three 45° and two 30° retinal fields were acquired according to a prescribed protocol, which has been previously validated to compare favorably with mydriatic ETDRS seven-standard fields (7,8). From 1 April 2012 to 1 November 2012, all patients underwent UWFI. UWFI images were acquired with a previously validated image acquisition protocol (3) of stereoscopic pairs of 100° and 200° retinal fields for each eye by Optos P200MA and Optos P200C imagers (Optos, Fife, U.K.) (Fig. 1). Both NMFP and UWFI were acquired by corresponding JVN protocol-certified imagers. JVN imagers are trained to identify ungradable images at the time of imaging, and images are retaken up to three times if image quality is poor. All UWFI images were graded according to a standard validated protocol by certified and licensed eye care providers in a centralized reading center under retina specialist supervision.

The configuration of the reading stations was optimized for the particular imaging modality being used at that time. All NMFP images were evaluated on previously described four-monitor reading stations comprising two 20-in liquid crystal display (LCD) monitors (one to display the NMFP image thumbnails and one to display the image being evaluated), one 17-in LCD monitor to display patient records, and one 20-in 3-dimensional–capable cathode ray tube monitor for stereoscopic viewing of the images (7,8). All UWFI images were evaluated with dual-monitor reading stations comprising a 27-in color-calibrated high-definition LCD monitor (model VG278H; ASUS, Taipei, Taiwan) with Quadro 600 video cards (NVIDIA, Santa Clara, CA) and a 20-in monitor to display patient records.

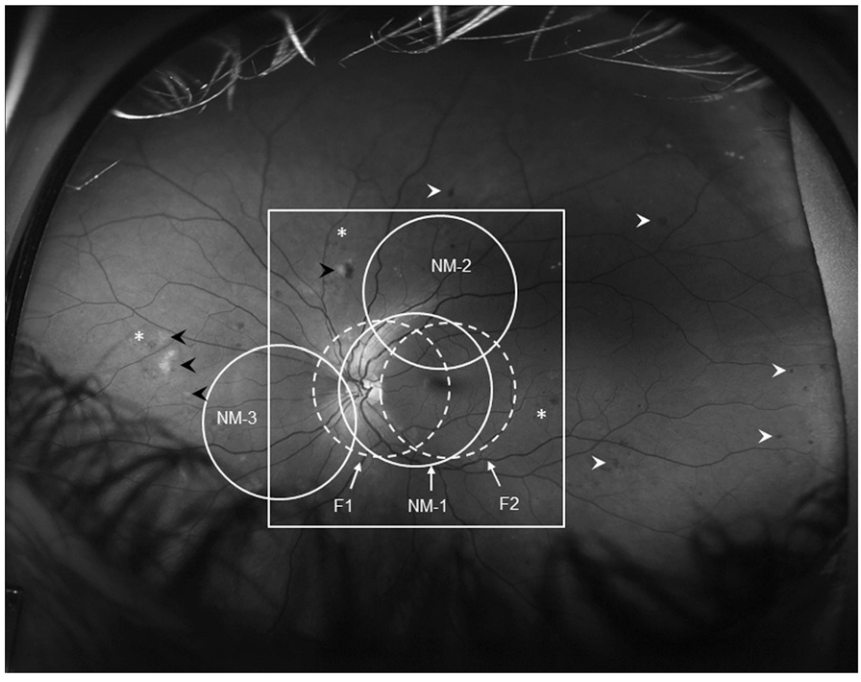

Figure 1—JVN NMFP (F1, 30° field centered on the optic disc; F2, 30° field centered on the macula; NM-1, 45° field centered between the optic disc and the macula; NM-2, 45° field superotemporal; NM-3, 45° field nasal) compared with JVN UWFI (rectangle, approximate area covered by 100° UWFI image; background image, 200° UWFI image). Highlighted areas show selected pathology evident peripheral to the JVN fields. Black arrowheads show selected areas of cotton wool spots. White arrowheads show selected areas of hemorrhages and/or microaneurysms. Asterisks show selected areas of intraretinal microvascular abnormalities.

Because there is only an indirect correlation between the three 45° fields in NMFP and the 200° and 100° fields in UWFI with the ETDRS seven-standard 30° fields, specific protocols were prospectively devised to extrapolate information from the 45°, 200°, and 100° fields. These detailed protocols for evaluating UWFI and NMFP images have been previously described and show substantial agreement with grading of dilated ETDRS seven-standard field photography (3,7,8). Both protocols are based on the ETDRS classification and evaluate the extent and severity of individual retinal lesions compared with ETDRS standard photographs to determine the severity of DR and DME. All images were acquired through undilated pupils. An eye was considered ungradable if there was inadequate photographic quality or if media opacity made it impossible to determine whether DR lesions were present in the images of that eye. If one or more disc area of retina was visible in an ETDRS-defined photographic field and that area was free of the characteristic, it was graded as no evidence rather than as ungradable. If the characteristic was present in the unobscured part of the field, it was estimated for the entire field. In the absence of definable lesions in the macula, no macular edema was entered, even if one image of the stereoscopic pair prevented stereoscopic reading of the macular area. The JVN reading center provides ongoing quality assurance by reviewing ~10% of all patient encounters to ensure standardized reading quality across time and different readers. Image evaluation time was calculated for each patient by reviewing the electronically recorded time that images were accessed for reading until the time when the images were saved as read.

The study design was consistent with the tenets of the Declaration of Helsinki, and the Committee on Human Studies of the Joslin Diabetes Center approved the retrospective review of the data. The conduct of the study complied with the Health Insurance Portability and Accountability Act.

Statistical Analysis

Nonparametric analyses (Wilcoxon rank sum) were used to compare distributions of continuous variables between groups. The χ^2 test was used to compare frequencies of categorical variables. When DR severity was evaluated per patient rather than per eye, the more severe level of DR and DME present in either eye was used as the severity present in the patient. If one eye was ungradable, the level of DR and DME present in the gradable eye was considered the level of DR and DME present in the patient. All analyses were performed with SAS version 9.2 (SAS Institute Inc., Cary, NC) statistical software.

RESULTS

During the study period, 7,606 eyes of 3,803 consecutive patients were evaluated. Overall, 3,266 eyes of 1,633 consecutive patients were imaged with NMFP and 4,340 eyes of 2,170 consecutive patients were imaged with UWFI immediately thereafter. The characteristics of both groups are shown in Table 1. There were no statistically significant differences between groups in age, sex, diabetes duration, ethnicity, or insulin use.

DR Severity and Peripheral Lesions

We have previously demonstrated that both imaging modalities have substantial agreement with both ETDRS protocol photography and retinal specialist dilated fundus examination (3,7,8). By NMFP, 33.8% of the patients had DR and 11.9% had potentially vision-threatening DR (defined as moderate nonproliferative DR or worse or any level of DME). By UWFI, the percentage of patients identified with DR and vision-threatening DR was 38.4 and 14.5%, respectively (Table 1). The distribution of DR severity in all eyes is shown in Table 2.

Given the greater retinal area imaged with UWFI, we evaluated a subgroup of 1,516 (36.9%) consecutive eyes imaged from 14 August to 1 November 2012 to determine the extent of peripheral retinal changes outside the ETDRS field areas (Fig. 1). This subgroup comprised 502 eyes of 301 patients with DR. In this subgroup, 71 eyes (14.1%) had hemorrhages and/or microaneurysms located outside the area covered by the ETDRS imaging protocol. Although less common, venous beading (two eyes), intraretinal microvascular abnormalities (six eyes), and new vessels elsewhere (three eyes) were also observed outside ETDRS fields. These peripheral findings might have resulted in assigning a more severe level of DR in 9.0% of eyes. Retinal tears were identified by UWFI and confirmed by clinical examination in two eyes (0.4%), of which neither was evident by NMFP.

Image Evaluation Time

The median time required to evaluate retinal images with the NMFP protocol was 12.8 min per patient. In contrast, the UWFI had a median evaluation time of 9.2 min per patient, which represents a 28% reduction of image evaluation time ($P < 0.0001$).

Ungradable Rate

The ungradable rate for DR and DME per patient by NMFP was 9.9 and 8.8%, respectively. These rates are generally consistent with our previous experience using this method of image acquisition (9–11). The ungradable rate for DR and

Table 1—Demographic characteristics of the patients undergoing NMFP and UWFI

	NMFP (n = 1,633)	UWFI (n = 2,170)	P value
Age (years)	53.6 ± 16.5	54.5 ± 16.4	0.15
Diabetes duration (years)	13 ± 10.6	13.2 ± 11.3	0.72
Female sex	708 (43.4)	941 (43.4)	1.00
White ethnicity	920 (81.1)	1,166 (80.5)	0.71
Insulin use	605 (62.8)	1,364 (63.2)	0.82
Retinopathy present	501 (33.8)	806 (38.4)	0.0053
Vision-threatening DR	176 (11.9)	305 (14.5)	0.0257
Patient ungradable for DR	161 (9.9)	63 (2.9)	<0.0001

Data are mean ± SD or n (%). Patients with unspecified or undeclared ethnicity were excluded in the calculations for ethnicity. Vision-threatening DR is defined as moderate nonproliferative DR or worse, proliferative DR, or any level of DME.

Table 2—Distribution of DR severity per eye in NMFP and UWFI

	NMFP (n = 3,266)	UWFI (n = 4,340)	P value
Ungradable eyes for DR	406 (12.4)	236 (5.4)	<0.0001
Ungradable eyes for DME	375 (11.5)	309 (7.1)	<0.0001
Gradable eyes	2,860 (87.6)	4,104 (94.6)	
No DR	2,058 (72.0)	2,773 (67.6)	
Very mild NPDR	288 (10.1)	409 (10.0)	
Mild NPDR	239 (8.4)	420 (10.2)	
Moderate NPDR	147 (5.1)	282 (6.9)	
Severe NPDR	24 (0.8)	48 (1.2)	
Very severe NPDR	5 (0.8)	1 (<0.01)	
PDR	92 (3.2)	162 (3.9)	
PDR with HRC	7 (0.2)	9 (0.2)	
DME present	176 (5.3)	278 (6.4)	<0.0001
DR present	802 (24.6)	1,331 (30.7)	<0.0001
Vision-threatening DR	301 (9.2)	520 (11.9)	<0.0001

Data are n (%). Vision-threatening DR is defined as moderate NPDR or worse, PDR, or any level of DME. HRC, high-risk characteristic; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

DME per patient with UWFI was 2.9 and 3.9%, respectively. With UWFI, there is a reduction in the ungradable rate per patient for DR of 71% ($P < 0.0001$) and for DME of 56% ($P < 0.0001$). Increasing age was associated with a substantial increase in ungradable rates for both DR and DME for both modalities (Table 3). Patient ungradable rates for DR with NMFP were 2.6% in patients less than 50 years of age, 10.5% in patients 50–70 years of age, and 24.6% in patients greater than 70 years of age. In contrast, when using UWFI for DR, the ungradable rates were 0.9, 2.3, and 9.0%, respectively. Results were similar for DME. In all cases, rates were lower for UWFI than for NMFP. The ungradable rate per eye for DR and DME is shown in Table 2.

CONCLUSIONS

In ocular telehealth programs for DR, the imaging system is a critical component that directly affects not only the ability to identify pathology, but also the efficiency and effectiveness of the telehealth program itself. Thus, technological changes to the imaging system can exert considerable influence, particularly in large-scale programs. Data from this comparative cohort study suggest that the adoption of UWFI may potentially improve the efficiency of DR ocular telehealth programs by reducing ungradable rates and image evaluation times. Combined with the identification of retinal lesions that would otherwise not have been observed by standard imaging, the use of UWFI with appropriate reading center protocols might have the synergistic benefits of increased disease detection, reduced ungradable rates, and shorter image evaluation times.

On the basis of prior reports in systematic population-based DR telemedicine programs, the ungradable rate with NMFP is ~20%, with a strong association for increasing ungradable images with increasing age and diabetes duration. This rate is reduced to ~4% with mydriasis (12). In community-based programs, the reported rate of ungradable images is 13% in patients aged <50 years, 39% in patients aged 50–70 years, and 54% in patients aged >70 years (13). In the current report, the NMFP ungradable rate ranged from 2.6 to 24.6% over this age range (Table 3). The ungradable rate for nonmydriatic UWFI was significantly lower, ranging from <1 to 9%. Compared with NMFP, nonmydriatic UWFI resulted in a reduction of the ungradable rate for DR by 71% overall, with a 63–78% reduction across age-groups. This improvement likely is partly due to the improved ability to image through small pupils and media opacities. Additionally, stereoscopic pairs were acquired. The additional image not only provides stereoscopic information, but also helps to exclude imaging artifacts and permits more complete evaluation when a field is partially obscured. Furthermore, nearly three times more retinal area is visible on UWFI without the need for gaze redirection or multiple images to capture the retinal periphery. The lower ungradable rate and the increased area of the retina imaged with UWFI may account for the 17 and 23% increase in the identification of DR and vision-threatening DR, respectively. In addition, peripheral lesions are identified that may suggest a more severe level of DR in 9% of eyes. This observation confirms an earlier report identifying peripheral lesions severe enough to potentially increase the severity level of DR in ~10% of eyes (14).

A potential limitation of the DR severity analyses is the comparison of imaging modalities used in two cohorts of patients at different times. However, this issue is minimized by evaluation of a large number of consecutive patients who underwent imaging over a relatively short period (one immediately after the other) within a single established DR telehealth program. There were no significant differences observed in the demographic characteristics between the two cohorts. Previous publications have shown consistent agreement between UWFI and dilated ETDRS photography (κ 0.77–0.79) (3,4). Substantial to near-perfect agreement has been reported with clinical examination, and agreement with the presence or absence of DR is as high as 0.95 (3,4).

Table 3—Effect of age on patient ungradable rates for DR

	NMFP			UWFI			P value	
Age-group	n	DR (%)	DME (%)	n	DR (%)	DME (%)	DR	DME
<50 years	615	2.6	2.8	748	0.9	1.2	0.02	0.04
50–70 years	742	10.5	8.8	1,028	2.3	3.2	<0.0001	<0.0001
>70 years	248	24.6	22.6	357	9.0	12.0	<0.0001	0.0006

The κ values for agreement with NMFP have been shown to have a substantial agreement of 0.81 for ETDRS photography, 0.71 for clinical examination, and 0.90 for the presence or absence of DR (8). These data suggest that both DR detection and determination of DR severity with UWFI and NMFP closely correlate with clinical examination and mydriatic ETDRS photography. Furthermore, the observation of an increased rate of DR detection with UWFI is consistent with other published studies (14).

UWFI also resulted in considerably shorter image evaluation time than NMFP (28% reduction). This finding might be attributable to improved image quality and the need to manipulate and evaluate fewer retinal images. Only four images per eye are evaluated with the UWFI protocol compared with 10 images per eye with NMFP. Additionally, 27-in high-definition monitors were used to display and evaluate the UWFI images compared with 20-in monitors for NMFP. This larger monitor size may have resulted in a lesser need to manipulate the images because a larger magnified image could be displayed.

In large-scale programs, these efficiency savings could be considerable. The JVN program evaluates >4,000 individuals per year. In this case alone, UWFI might save ~240 hours per year in evaluation time while preventing ~560 eyes from being ungradable for DR and identifying ~720 eyes with potentially more severe retinopathy than would otherwise have been recognized. Some programs dilate pupils to obtain adequate grading quality (12). In these situations, the UWFI approach might obviate the need for dilation while maintaining a comparable ungradable rate. Such an approach would be particularly beneficial in populations where the risk of angle closure is high or where access to specialized eye care is limited.

The cost-effectiveness of UWFI was not evaluated in this study and remains an important consideration because of the substantial cost of current UWFI devices, which can exceed $100,000. However, given the potential benefits of a substantially lower ungradable rate, decreased image acquisition time, ease of use, and increased disease detection, the higher capital outlay for UWFI devices may be offset, especially in large-volume telemedicine programs. Furthermore, costs are likely to decrease over time with further technological innovations and market competition.

Another important consideration with any imaging device is the ease of image acquisition. All JVN imagers have preferred using UWFI for telemedicine compared with the prior nonmydriatic standard field cameras. Image acquisition with the Optos 200MA and Optos 200C imagers are substantially different from traditional nonmydriatic retinal cameras. The Optos does not require manual focusing, is not affected as much by pupil constriction after repeated images, and obtains usable images through smaller pupils.

In summary, this study demonstrates for the first time in our knowledge that in a large-scale, well-established telemedicine program using standardized image acquisition and evaluation protocols, the implementation of UWFI reduces the ungradable rate by >71% for DR and 56% for DME to <3 and <4%, respectively. Additionally, compared with NMFP, image evaluation time was reduced by 28%. Furthermore, UWFI identified additional peripheral retinal lesions that may suggest a more severe level of DR in 9% of eyes. Generalizing these results to other ocular telemedicine programs needs further evaluation, especially given the rigorous standardized image acquisition and evaluation protocols and ongoing medical oversight and quality assurance used in the JVN environment. However, if replicated in other programs, UWFI might substantially enhance current DR telemedicine programs.

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Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. P.S.S. and J.D.C. researched data and wrote the manuscript. D.T., A.O., K.T., B.P., M.S., and A.M.T. researched data and reviewed and edited the manuscript. J.K.S. researched data, reviewed and edited the manuscript, and contributed to the discussion. L.M.A. and L.P.A. reviewed and edited the manuscript and contributed to the discussion. P.S.S. and J.D.C. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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