Eye Disease in Patients with Diabetes Screened with Telemedicine

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The protocol of this study is registered as "The Comparative Effectiveness of Telemedicine to Detect Diabetic Retinopathy" with ClinicalTrials.gov having clinical trial registration number NCT01364129.

Abstract

Background: *Telemedicine with nonmydriatic cameras can detect not only diabetic retinopathy but also other eye disease.* ***Objective:*** *To determine the prevalence of eye diseases detected by telemedicine in a population with a high prevalence of minority and American Indian/Alaskan Native (AI/AN) ethnicities.* ***Subjects and Methods:*** *We recruited diabetic patients 18 years and older and used telemedicine with nonmydriatic cameras to detect eye disease. Two trained readers graded the images for diabetic retinopathy, age-related macular degeneration (ARMD), glaucomatous features, macular edema, and other eye disease using a standard protocol. We included both eyes for analysis and excluded images that were too poor to grade.* ***Results:*** *We included 820 eyes from 424 patients with 72.3% nonwhite ethnicity and 50.3% AI/AN heritage. While 283/424 (66.7%) patients had normal eye images, 120/424 (28.3%) had one disease identified; 15/424 (3.5%) had two diseases; and 6/424 (1.4%) had three diseases in one or both eyes. After diabetic retinopathy (104/424, 24.5%), the most common eye diseases were glaucomatous features (44/424, 10.4%) and dry ARMD (24/424, 5.7%). Seventeen percent (72/424, 17.0%) showed eye disease other than diabetic retinopathy.* ***Conclusions:*** *Telemedicine with nonmydriatic cameras detected diabetic retinopathy, as well as other visually significant eye disease. This suggests that a diabetic retinopathy screening program needs to detect and report other eye disease, including glaucoma and macular disease.*

Keywords: *e-health, Ophthalmology, telehealth, telemedicine*

Introduction

Researchers estimate that 29.1 million U.S. citizens suffer from diabetes.[1] Among diabetic patients older than 40 years, 28.5% have diabetic retinopathy.[1] Diabetic retinopathy is the leading cause of blindness in the United States in the age group of 20 to 74.[2,3] However, less than 50% of those with diabetes receive annual eye examinations.[4]

Telemedicine screening using a nonmydriatic camera has emerged as a promising new technique for diabetic retinopathy because it has high diagnostic precision without requiring a face-to-face examination with an eye care provider.[5,6] It has also shown to increase the proportion of diabetic eye examinations compared to current surveillance techniques with eye care providers.[7] Other than diabetic retinopathy, nonmydriatic cameras can detect eye disease of the optic disc, macula, and peripheral retina.[8–11]

This report is a part of a multicenter randomized clinical trial comparing the effectiveness of telemedicine using nonmydriatic cameras to traditional care with eye care providers. We hypothesized that different eye diseases, including diabetic retinopathy, may be detectable and common, especially given that diabetes is a potential risk factor for other eye diseases such as glaucoma[12] and vascular occlusions.[13] Clinicians, researchers, and health systems may use this data to determine the burden of referral from diabetic retinopathy and other visually significant eye disease when using a diabetic retinopathy screening program with telemedicine and nonmydriatic cameras.

Subjects and Methods

The Institutional Review Boards of Legacy Health (Portland, OR), Oregon Health and Science University (Portland), and the Northwest Portland Area Indian Health Board (Portland) reviewed and approved the study protocol. All participants gave informed consent, and the study followed the tenets of the Declaration of Helsinki.

STUDY POPULATION

We enrolled diabetic patients who were 18 years or older, scheduled with primary care providers from Yellowhawk Tribal Health Center (Pendleton, OR) and Hunter Health Clinic (Wichita, KS), and had difficulty acquiring annual diabetic

retinopathy screening examinations. We also included patients who reported a recent eye examination. We excluded patients who were unable to transfer to a chair to perform nonmydriatic imaging or had cognitive impairment preventing informed consent.

We randomized participants to either the Telemedicine or Traditional Surveillance Group. However, after 2 years of the trial, we offered telemedicine to all participants. We describe our telemedicine program in detail in previous articles.[14,15] Briefly, photographers used a digital nonmydriatic fundus camera (model NM-1000; NIDEK, Fremont, CA). We captured 6 undilated, 1.5-megapixel, 45° fundus photographs of each eye, including a stereo-pair centered on the macula, a stereo-pair of photographs centered on the optic disc, a single image centered on the superior temporal retina, and a single image centered on the inferior temporal retina. The clinic staff uploaded images and patient data to an encrypted, compressed secure system, invented by Devers Eye Institute. The system utilized a Health Insurance Portability and Accountability Act–adherent database. Once clinic staff uploaded the images and patient information, the system sent an e-mail notification to the investigators.

Two trained Devers Eye Institute providers used a Screen-Vu stereoscope (PS Manufacturing, Portland, OR) to provide stereoscopic views of the optic discs and macula and graded the quality of the whole set of images (acceptable, poor but gradable, or too poor to grade). The "poor but gradable" category included a set where one or more images contained shadows or blurry images, but readers still could grade the other images for diseases of the retina, macula, and optic disc. If the readers could not fully assess the images for presence or absence of disease, the readers entered a "too poor to grade" category. *Table 1* describes the definitions of diabetic eye disease and other eye disease. We used a vertical cup-to-disc ratio of 0.67 to be the ≥99.5th percentile based on previously reported analysis of the U.S. population[17] and defined glaucoma if the vertical cup-to-disc ratio was greater or equal to 0.7.

The investigators used an electronic form to enter their findings into the system, and the system sent an evaluation report automatically to the clinics through e-mail or fax. The process was repeated for every visit, accruing multiple images per visit for the patients. However, in this study, we report the results of the first visit from both eyes of a single participant. We excluded images too poor to grade from the analysis.

DATA ANALYSIS

We used Microsoft Excel® (version 2010, Bellevue, Washington) to determine the proportion of eyes with diabetic retinopathy, age-related macular degeneration (ARMD), glaucomatous features, and macular edema. The prevalence of eye disease was the proportion of participants with eye disease as defined in *Table 1* in at least one eye. We used Student's *t* test to compare ages of participants with and without disease. We calculated Pearson product-moment correlation coefficient with Microsoft Excel® (version 2010) when comparing different studies.

Results

We evaluated 646 diabetic patients, with 567 (87.8%) enrolled and 79 (12.2%) not included. Of those not included, 78 refused participation, and 1 person was not eligible (not a health clinic participant). The Telemedicine Group consisted of 296 subjects. In addition, 164 of 271 in the Traditional Surveillance Group opted for a telemedicine examination once it was offered to them after 2 years. Out of total of 919 eyes from 460 patients, we included 820 eyes from 424 patients for analysis and excluded 99 (10.7%) eyes due to poor quality images.

Table 2 describes the demographic and medical history. When primary, secondary, and tertiary race/ethnicity data were combined, 50.3% reported American Indian/Alaskan Native (AI/AN) heritage, and 72.3% reported a nonwhite race/ethnicity. Participants averaged a hemoglobin A1c of 8.3% and had diabetes for 9.5 years.

Table 1. Eye Disease Definitions

Diabetic retinopathy	Definition and subcategories of mild, moderate, and severe nonproliferative diabetic retinopathy and proliferative diabetic retinopathy.[16]
Macular edema	Defined as having retinal thickening within 500 microns of the fovea, exudates associated with retina thickening within 500 microns of the fovea, or retinal thickening of one disc diameter in size within one disc diameter of the fovea.[16]
Glaucomatous features	Defined as having rim thinning, nerve fiber defect, or excavation.[17]
Glaucoma	Defined as having cup-to-disc ratio ≥99.5th percentile for the normal population (see the text for details).[17]
ARMD	Defined as soft drusen >125 microns or drusen with pigmentary changes, not caused by any other disorder.[18]

ARMD, age-related macular degeneration.

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Table 2. Demographics and Medical History (*N* = 567 Patients)

Age (years)	51.1 (11.8)
Gender (% female)	51.7
Primary ethnicity (%)	
White	52.9
AA	18
AI/AN	16.8
Hispanic/Latino	10.9
Asian/other	1.2
No response	0.2
Secondary ethnicity (%)	
White	6.2
AI/AN	32.6
AA	0.5
Hispanic/Latino	1.8
Asian/other	0.2
No secondary ethnicity	58.6
No response	0.2
Medical History	
Diastolic blood pressure (mm Hg)	76.9 (12.2)
Systolic blood pressure (mm Hg)	127.8 (19.8)
Hemoglobin A1c	8.3% (2.4)
Diabetes (years)	9.5 (8.1)

Data are presented in mean (standard deviation) unless otherwise specified.
AA, African American; AI/AN, American Indian/Alaskan Native.

Table 3 describes the prevalence and proportion of eye disease. The most prevalent eye disease was diabetic retinopathy (104/424, 24.5%), followed by glaucomatous features (44/424, 10.4%), ARMD (24/424, 5.7%), glaucoma (12/424, 2.8%), and other ocular disease (10/424, 2.4%). Other eye disease (observed in 2 or fewer eyes) included epiretinal membranes, vascular occlusions (branchial retinal artery occlusion and branchial retinal vein occlusion), and choroidal/retinal lesions such as nevi. When diabetic retinopathy was excluded, 72 patients out of 424 (17.0% ± 3.5%) showed other eye disease. Although 283/424 (66.7%) eyes had normal eye images, 120/424 (28.3%) had one disease identified, 15/424 (3.5%) had two diseases, and 6/424 (1.4%) had three diseases in one or both eyes.

Table 4 shows a higher age in those with glaucoma ($p = 0.02$) and ARMD ($p = 0.001$) compared to those without these diseases. We found no statistical difference ($p > 0.05$) in age with diabetic retinopathy or glaucomatous features.

Table 3. Prevalence and Proportion of Eye Disease in Participants with Diabetes Screened with Telemedicine

DISEASE	PREVALENCE (95% CI) *N* = 424 PERSONS	PROPORTION (95% CI) *N* = 820 EYES
Diabetic retinopathy		
Total	24.5% (20.4, 28.6%)	17.4% (14.8, 20.0%)
Mild nonproliferative	18.4% (14.7, 22.1%)	13.9% (11.5, 16.3%)
Moderate nonproliferative	4.0% (2.1, 5.9%)	3.2% (2.0, 4.4%)
Severe nonproliferative	0.0%	0.0%
Proliferative	2.1% (0.8, 3.5%)	1.6% (0.7, 2.4%)
Macular edema	0.7% (0, 1.5%)	0.6% (0.1, 1.1%)
Glaucomatous features	10.4% (7.5, 13.3%)	6.8% (5.1, 8.6%)
Glaucoma	2.8% (1.3, 4.4%)	2.4% (1.4, 3.5%)
ARMD	5.7% (3.5, 7.9%)	3.8% (2.5, 5.1%)
Other eye disease[a]	2.4% (0.9, 3.8%)	1.2% (0.5, 2.0%)

The prevalence of eye disease was the proportion of participants with eye disease as defined in *Table 1* in at least one eye. Proportion was calculated as number of the eyes with the particular disease divided by the total number of the eyes analyzed.

[a]Others category included nevus, epiretinal membrane, chorioretinal lesion, branch retinal arterial occlusion, branch retinal vein occlusion, choroidal tear, and retinoschisis. All other diseases were found in two or less eyes.

Discussion

We were interested in the prevalence of other eye disease when using telemedicine with nonmydriatic cameras to detect diabetic retinopathy. Our study found that one in four eyes

Table 4. Association of Age with Common Eye Diseases in Participants with Diabetes Screened with Telemedicine

	MEAN AGE (SD) WITH DISEASE	MEAN AGE (SD) WITHOUT DISEASE	P
Diabetic retinopathy	51.2 (11.9)	51.6 (11.4)	0.3
Glaucomatous features	53.5 (10.4)	51.1 (11.6)	0.1
Glaucoma	57.2 (10.2)	51 (11.3)	0.02
ARMD	57 (9.7)	51 (11.5)	0.001

Eye diseases are defined in *Table 1*.

Table 5. Studies Reporting Other Ocular Disease as Part of a Diabetic Retinopathy Screening Study Using Telemedicine

	CURRENT STUDY		OWSLEY ET AL.[8]	CAVALLERANO ET AL.[9]		MASSIN ET AL.[10]	JIVRAJ ET AL.[11]
Primary Ethnicity	53% White 18% AA 17% AI/AN		62% AA 15% Hispanic 12% White	Race not reported		French	Northwest Cameroon
Average age	51.1		54.4	63.2		59.9	54.2
	Per eye	Per person	Per person	Per eye	Per person	Per eye	Per eye unless specified
Diabetic retinopathy							
Total diabetic retinopathy	17.4% (143/820)	24.5% (104/424)	21.7% (NR[a])	26.8% (327/1219)	30.5% (207/679)	18.0% (91/506)	22.7% (197/868 persons)
Mild nonproliferative	13.9% (114/820)	18.4% (78/424)	Different definition used	18.8% (229/1219)	20.8% (141/679)	10.2% (52/506)	NR
Moderate nonproliferative	3.2% (26/820)	4.0% (17/424)		4.2% (51/1219)	5.5% (37/679)	5.3% (27/506)	NR
Severe nonproliferative	0.00%			2.7% (33/1219)	2.7% (18/679)	0%	NR
Proliferative	1.6% (13/820)	2.1% (9/424)		1.1% (14/1219)	1.6% (11/679)	2.4% (12/506)	0.2% (2/868 persons)
Cataract		NR	30.7% (581/1894)	30.7% (749/2437)	58.2% (395/679)	NR	29.6% (150/506)
Hypertensive retinopathy		NR	16.7% (316/1894)	1.3% (32/2437)	3.0% (20/679)	0.1% (2/1819)	NR
Cotton-wool spots		NR	11.1% (211/1894)	NR	NR	NR	NR
Glaucoma suspect	6.8% (56/820)	10.4% (44/424)	10.4% (197/1894)	9.6% (233/2437)	22.4% (152/679)	0.2% (3/1819)	3.6% (18/506)
ARMD (or macular drusen/RPE changes)	3.8% (31/820)	2.8% (12/424)	9.2% (174/1894)	5.6% (136/2437)	3.8% (26/679)	0.2% (3/1819)	2.2% (11/506)
Pterygium		NR	4.8% (90/1894)	0.5% (14/2437)	1.8% (12/679)	NR	1.2% (6/506)
Nevus	0.4% (3/820)	0.7% (3/424)	0.6% (11/1894)	NR (reported along with other lesions)	NR (reported along with other lesions)	NR	NR
Vascular occlusion	0.2% (2/820)	0.5% (2/424)	≤0.26% (≤5/1894)	0.3% (7/2437)	0.9% (6/679)	NR	1.6% (8/506)
Epiretinal membrane	0.2% (2/820)	0.5% (2/424)	≤0.26% (≤5/1894)	1.4% (35/2437)	4.7% (32/679)	NR	NR
Chorioretinal scar/atrophy	0.1% (1/820)	0.2% (1/420)	≤0.26% (≤5/1894)	0.6% (14/2437)	2.1% (14/679)	NR	NR
Retinal detachment		NR	NR	0.04% (1/2437)	0.2% (1/679)	NR	0.6% (3/506)

NR, not reported; RPE, retinal pigment epithelium.

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had at least one eye disease, and 17% of patients had disease other than diabetic retinopathy. Despite this high proportion of eye disease, we also determined that a large proportion did not need a subsequent visit with an eye care provider. Overall, this suggests that a diabetic retinopathy screening program has potential to improve patient care beyond diabetic retinopathy, but it also needs to detect and report other eye disease, including glaucoma and macular disease.

EYE DISEASE BURDEN

Table 5 shows similar results with our current study to previously published telemedicine studies of diabetic patients with some differences. The differences may be due to age, location, socioeconomic background, and/or ethnicity. Overall, our study findings agree with the other studies that diabetic retinopathy telemedicine program will detect other visually significant eye disease.

BURDEN OF REFERRAL

Our study demonstrates that a large percentage of eyes did not need further follow-up with an eye care provider because they did not have moderate non-proliferative diabetic retinopathy and worse, and most (66.7%) had a completely normal telemedicine examination. However, the proportion of other eye disease suggests that telemedicine programs will need to have systems in place to report and refer participants for glaucoma, retina, and other ocular disease. Our protocol encouraged all participants to see an eye care provider annually regardless of their telemedicine results in addition to informing the patients and the physicians of the detected diseases (if there was any disease detected).

STUDY LIMITATIONS

Our study demonstrates the proportion of eye diseases detected by telemedicine in this unique population. However, nonmydriatic imaging is unable to detect all eye diseases and may miss corneal disease, ocular hypertension, and mild uveitis. Similarly, a telemedicine program would not be able to diagnose retinal and optic disc disease with significant media opacities. About 10% of images were excluded in our study because of image quality and these participants were referred to a local eye care provider. Future studies could include longer follow-up data and further analysis of the benefits of telemedicine to follow patients with other eye disease such as glaucoma and macular degeneration.

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Disclosure Statement

No competing financial interests exist.

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