Nonmydriatic Digital Retinal Images for Determining Diabetic Retinopathy†

Jutalai Tanterdtham MD*, Apichart Singalavanija MD*,
Chakrapong Namatra MD*, Adisak Trinavarat MD*,
Nuttawut Rodanant MD*, Parapun Bamroongsuk MD*,
Somanus Thoongsuwan MD*, Wanna Euasobhon MD*

† *This paper was presented as Poster in Academic meeting of the Royal College of Ophthalmologist of Thailand on 27-28 July 2006*
* *Department of Ophthalmology, Faculty of Medicine, Siriraj Hospital, Mahidol University*

Objective: *To evaluate the efficacy of nonmydriatic digital retinal images for determining diabetic retinopathy.*
Material and Method: *Single field 45-degree digital retinal images of 225 eyes from 142 diabetic patients were obtained with a nonmydriatic camera. The images were diagnosed and graded by a general ophthalmologist. These results were compared with clinical diagnosis obtained by retinal specialists, after examination by using biomicroscope with plus lens and indirect ophthalmoscope of the patients. International clinical diabetic retinopathy disease severity scale was used for grading diabetic retinopathy in all cases.*
Results: *Presence of diabetic retinopathy was detected in 70 eyes (31.1%). The sensitivity and specificity for determining diabetic retinopathy was 68.57% (95%CI 57.00-78.20) and 92.25% (95%CI 87.00-95.50), respectively. The positive predictive value and negative predictive value was 80.00% (95%CI 68.20-88.20) and 86.67% (95%CI 80.60-91.00). Overall accuracy was 84.89%.*
Conclusion: *Single field 45-degree nonmydriatic digital retinal images were limited by fair sensitivity for determining diabetic retinopathy although overall accuracy from the present study was relatively high. Upcountry, this tool might facilitate increased access of diabetic patients for eye evaluation but cannot replace standard eye examination.*

Keywords: *Diabetic retinopathy screening, Digital retinal images, Nonmydriatic retinal images*

J Med Assoc Thai 2007; 90 (3): 508-12
Full text. e-Journal: *http://www.medassocthai.org/journal*

Diabetes mellitus is a major public health disease[1,2]. Early detection and treatment of diabetic retinopathy through screening is a cost-effective strategy for improving health care in diabetic patients. Current clinical guideline suggest on annual dilated eye examination. Because access to an ophthalmologist may be limited by geography or others, many diabetic patients do not undergo yearly examination.

A number of different teleophthalmology has been developed to overcome the difficulty for screening the patients who cannot access an ophthalmologist. Testing strategies include camera type. Early Treatment Diabetic Retinopathy Study (ETDRS) seven standard field 35-mm stereoscopic color fundus photographs (ETDRS photos) using the modified Airlie House classification provide an established and documented sensitivity for detecting and assessing severity of diabetic retinopathy[3]. However, this test is time consuming and pupil dilation is needed. The use of nonmydriatic digital retinal fundus camera can shorten the time for examination and give more comfort to patients. Nonmydriatic Joslin Vision Network image is validated agreement with dilated ETDRS photographs[4]. Many studies[5,6] have shown that single field nonmydriatic digital retinal image is a potentially acceptable tool for screening diabetic retinopathy but some studies[7] gave inadequate results. The aim of

Correspondence to : Tanterdtham J, Department of Ophthalmology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

the present study was to evaluate the diagnostic performance of nonmydriatic retinal images for determining diabetic retinopathy.

Material and Method

The present study is a prospective cross-sectional study. Two hundred and twenty five eyes of diabetic patients attending an ophthalmological unit, Siriraj Hospital between September 2005 and March 2006 were initially recruited in the present study. The patient enrollment was made from all types of diabetic patients, all spectrum of diabetic retinopathy regardless of any known ocular disease but did not have a history of laser or surgical treatment for diabetic retinopathy prior to present study. All patients were required to give informed consent. The authors excluded low quality digital retinal images. This was determined by two retinal specialists. The protocol was approved by the Ethical Committee on Researches Involving Human Subjects, Siriraj Hospital.

All patients obtained single fundus photography by nonmydriatic 45-degree digital fundus camera including optic disc and macular area (Kowa® VX-10, Kowa, Japan, 2.1 MegaPixel). After digital retinal image was captured, 1% tropicamide and 10% phenylephrine eye drops were instilled to the patients for clinical examination using slit lamp biomicroscope with high plus lens and indirect ophthalmoscope by retinal specialists. The gold standard of the present study was clinical diagnosis from retinal specialists who have been working in tertiary care centers and experienced in retinal subspecialty for over 10 years. The pictures were interpreted by a general ophthalmologist. The intra- observer reliability of the picture interpreted (kappa) by the general ophthalmologist was 0.85. The diagnosis from the general ophthalmologist was done without the knowledge of the diagnosis by the retinal specialists. The diabetic retinopathy level interpreted from both clinical and picture examinations were classified according to the guideline of International clinical diabetic retinopathy disease severity scale (Table 1)[8].

Demographic data was expressed as mean $\pm$ SD for age, the categorical data as percent. Statistical analysis was performed using SPSS v 11.5.

Results

The demographic characteristics of the patients are shown in Table 2. Among 225 eyes from 142 patients, 92 (65%) were female and 50 (35%) were male, age between 30-85 years (mean $\pm$ SD 57.97 $\pm$ 11.35 year). The majority of these patients had uncorrected visual acuity (VA) in the range of 6/6-6/18. Presence of diabetic retinopathy (DR) was detected in 70 eyes (31.10%). The other 59 eyes were excluded due to poor quality image.

Compared to the clinical diagnosis from the retinal specialists, the sensitivity and specificity for screening any retinopathy using single nonmydriatic 45 degree digital fundus picture interpreted by the general ophthalmologist were 68.57% (95%CI, 57.00-78.20) and 92.25% (95%CI, 87.00-95.50), respectively. The positive predictive value and negative predictive value were 80.00% (95%CI, 68.20-88.20) and 86.67% (95%CI, 80.60-91.00). Overall accuracy was 84.89%.

These data had high accuracy for no diabetic retinopathy and proliferative diabetic retinopathy (PDR) cases, but substantial accuracy for nonproliferative diabetic retinopathy (NPDR) cases. The data showed that over diagnosis from the image was 10.22% (23/225)

Table 1. International clinical diabetic retinopathy disease severity scale

Proposed disease severity level	Findings observable upon dilated ophthalmoscopy
No apparent retinopathy	No abnormality
Mild non-proliferative diabetic retinopathy	Microaneurysms only
Moderate non-proliferative diabetic retinopathy	More than just microaneurysms but less than severe non proliferative diabetic retinopathy
Severe non-proliferative diabetic retinopathy	Any of the following: - more than 20 intraretinal hemorrhages in each 4 quadrants - definite venous beading in 2 quadrants - prominent intraretinal microaneurysms in 1 quadrant
Proliferative diabetic retinopathy	Other or more of the following - neovascularization - vitreous / preretinal hemorrhage

Table 2. Demographic data

Variables	Results
Age	30-85 year
(Mean ± SD)	57.97 ± 11.35 year
Gender	n = 142 patients
Female	92 (64.78 %)
Male	50 (35.22 %)
VA	n = 225 eyes
6/6-6/18	179 (79.56 %)
6/24-6/60	43 (19.11 %)
5/60-1/60	None
<1/60	3 (1.33 %)
Prevalence of disease (Gold standard)	
No DR	155 (68.90 %)
Mild to moderate NPDR	58 (25.80 %)
Severe NPDR	7 (3.10 %)
PDR	5 (2.20%)

and under diagnosis was 11.11% (25/225) as shown in Table 5.

Discussion

Nonmydriatic digital retinal fundus camera was developed in 1980. The advantages of digital retinal image are patients' comfort and less time for examination. The patients can see their images immediately, the intensity of flash is less than that used to expose film and the electronic format of the image facilitates storage and transmission potentially for telemedicine. The disadvantage of digital retinal image is the image resolution is lower than that of film[9].

The present study was done to evaluate diagnostic performance of single field, nonmydriatic digital retinal images for determining diabetic retinopathy. The authors reduced bias by using the double-blinded technique and excluded known proliferative diabetic retinopathy cases that underwent laser or surgical treatment prior to the present study. A recent study revealed that retinal specialists might be the most reliable personnel to interpret single-field digital fundus images for diabetic retinopathy screening[10,11], however, the authors chose a general ophthalmologist for interpreting the picture diagnosis because of future application upcountry.

The sensitivity and specificity for determining diabetic retinopathy of the present study were 68.57% (95%CI, 57.00-78.20) and 92.25% (95%CI, 87.00-95.50). The positive predictive value and negative predictive value were 80.00% (95%CI, 68.20-88.20) and 86.67% (95%CI, 80.60-91.00). The authors found that the present study had more sensitivity than a previous study[7], but less sensitivity than several recent studies[6, 10]. The specificity from the present study was similar to previous studies[6,7,10]. The difference between sensitivity and specificity from other studies was probably due to difference between picture interpretators and gold standard. Additional training may be required for improvement in picture diagnosis. The results showed a high positive predictive value and a negative predictive value. As Siriraj Hospital is a tertiary hospital, the prevalence of the diabetic retinopathy is higher than in provincial hospitals. If the authors use the nonmydriatic fundus camera for determining diabetic retinopathy in provincial hospital, the positive predictive value will be lower.

The present study demonstrated the high accuracy for no DR and PDR cases from picture diagnosis, but in NPDR cases, the authors might not grade the stage from the pictures (Table 3). The potential factors influencing mislead diagnosis from the pictures was interesting. The authors found that drusen has a major effect for misleading. It can make both over diagnosis and under diagnosis because of its similarity to exudate. The others such as small microaneurysm, which was barely visible in the picture and peripheral lesion beyond 45°, cannot be detected from the picture also gave under diagnosis (Table 5).

Fifty-nine eyes from 142 patients were excluded from the present study because of low quality

Table 3. Differences between picture diagnosis and clinical diagnosis for grading diabetic retinopathy

Grading of diabetic retinopathy	n = 225	Correct diagnosis	Under diagnosis	Over diagnosis
No DR	155	143	0	12
Mild to moderate NPDR	58	25	22	11
Severe NPDR	7	4	3	0
PDR	5	5	0	0
Total	225	177	25	23

images (Table 4). This may be due to small size of pupils, opaque media (such as cataract) and poor fixation of the patients. The authors were interested in these groups and would like to clarify bad candidate for screening by this tool. The presented data suggested (but not concluded because of the limited number of cases) some patients with visual acuity below 6/60 with good clarity of ocular media could be investigated by this type of photography. However, in the practical aspect, the authors think that patients with low visual acuity might not be appropriate for photography because they can not focus at the fixation point. Therefore, the authors should have an ophthalmologist carefully examine the cause of visual loss. Instead of visual acuity, cooperation and associated ocular finding, especially from a significant cataract, should be considered before sending patients to photography.

As the images captured by nonmydriatic fundus camera may not have as good quality as that obtained when the pupil is dilated, this factor should be considered from a cost-effective aspect. Nevertheless, in hospitals or areas with no ophthalmologist available or not enough ophthalmologists, screening by this method may be helpful in detection of diabetic retinopathy.

Table 4. Number of poor digital retinal image quality in each group

Factor	n = 59 eyes (Percentage)
VA	
6/6-6/18	46 (77.97 %)
6/24-6/60	7 (11.87 %)
5/60-1/60	3 (5.08 %)
<1/60	3 (5.08 %)
Associated ocular finding	
Cornea opacity	2 (3.40 %)
Lens opacity	42 (71.20 %)
Vitreous opacity	1 (1.70 %)
Undetermined cause	14 (23.70 %)

Table 5. Potential errors from picture diagnosis

Overdiagnosis	- drusen
	- flamed shape hemorrhage
Underdiagnosis	- drusen
	- microaneurysm
	- peripheral lesion

The limitation of the present study is the limited number of cases in the subgroup for grading diabetic retinopathy, the resolution of the retinal image and the authors did not interpret the macular edema from the presented data. A future study may be set up for evaluating efficacy of this method in a multi-center trial and furthermore subgroup analysis was recommended.

Conclusion

Single field, 45-degree nonmydriatic digital retinal images had a fair sensitivity for determining diabetic retinopathy although overall accuracy from the present study was relatively high. Upcountry, this tool might facilitate the increased access of diabetic patients into eye evaluation but cannot replace standard eye examination.

Acknowledgement

The authors wish to thank Mr. Sutipol Udompunturak, statistician of the Clinical Epidemiology Unit, office of Research Institute, Siriraj Hospital for the statistical analysis.

References

1. Vinicor F. Is diabetes a public-health disorder? Diabetes Care 1994; 17(Suppl 1): 22-7.
2. Anderson LA, Bruner LA, Satterfield D. Diabetes control programs: new directions. Diabetes Educ 1995; 21: 432-8.
3. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs - an extension of the modified Airlie House classification. ETDRS report number 10. Ophthalmology 1991; 98: 786-806.
4. Bursell SE, Cavallerano JD, Cavallerano AA, Clermont AC, Birkmire-Peters D, Aiello LP, et al. Stereo nonmydriatic digital-video color retinal imaging compared with Early Treatment Diabetic Retinopathy Study seven standard field 35-mm stereo color photos for determining level of diabetic retinopathy. Ophthalmology 2001; 108: 572-85.
5. Lin DY, Blumenkranz MS, Brothers RJ, Grosvenor DM. The sensitivity and specificity of single-field nonmydriatic monochromatic digital fundus photography with remote image interpretation for diabetic retinopathy screening: a comparison with ophthalmoscopy and standardized mydriatic color photography. Am J Ophthalmol 2002; 134: 204-13.

6. Hansen AB, Hartvig NV, Jensen MS, Borch-Johnsen K, Lund-Andersen H, Larsen M. Diabetic retinopathy screening using digital non-mydriatic fundus photography and automated image analysis. Acta Ophthalmol Scand 2004; 82: 666-72.
7. Kuo HK, Hsieh HH, Liu RT. Screening for diabetic retinopathy by one-field, non-mydriatic, 45 degrees digital photography is inadequate. Ophthalmologica 2005; 219: 292-6.
8. American Diabetes Association: clinical practice recommendations 2002. Diabetic retinopathy. Diabetes Care 2002; 25(Suppl 1): S90-3.
9. Bursell SE. Diabetic retinopathy screening. In: Ciulla TA, Regillo CD, Haris A, editors. Retina and optic nerve imaging. Philadelphia: Lippincott Williams and Wilkins; 2003: 325-34.
10. Ruamviboonsuk P, Wongcumchang N, Surawongsin P, Panyawatananukul E, Tiensuwan M. Screening for diabetic retinopathy in rural area using single-field, digital fundus images. J Med Assoc Thai 2005; 88: 176-80.
11. Ruamviboonsuk P, Teerasuwanajak K, Tiensuwan M, Yuttitham K. Interobserver agreement in the interpretation of single-field digital fundus images for diabetic retinopathy screening. Ophthalmology 2006; 113: 826-32.

การตรวจจอประสาทตาผู้ป่วยเบาหวานด้วยกล้องถ่ายภาพโดยไม่ขยายม่านตา

จุฑาไล ตันฑเทอดธรรม, อภิชาติ สิงคาลวณิช, จักรพงศ์ นะมาตร์, อดิศักดิ์ ตรีนวรัตน์, ณัฐวุฒิ รอดอนันต์, โสมนัส ถุงสุวรรณ, วรรณา เอื้อโสภณ

วัตถุประสงค์*: เพื่อประเมินความไวและความจำเพาะในการตรวจจอประสาทตาผู้ป่วยเบาหวานด้วยกล้องถ่ายภาพและไม่ขยายรูม่านตา*

วัสดุและวิธีการ*: ศึกษาในผู้ป่วยเบาหวานที่ไม่เคยได้รับการรักษาด้วยเลเซอร์หรือการผ่าตัดในส่วนหลังของลูกตามาก่อน ถ่ายภาพจอประสาทตาโดยไม่ขยายม่านตา ด้วยกล้องถ่ายภาพ 45 องศา ถ่ายภาพให้เห็นขั้วประสาทตาและบริเวณแมคคูลา หลังจากนั้นจะขยายม่านตาผู้ป่วยแล้วตรวจโดยจักษุแพทย์ การตรวจใช้ biomicroscope และ non contact lens*

ผลการศึกษา*: ผู้ป่วยที่รับการตรวจและถ่ายภาพทั้งหมด 142 คน, 225 ตา การตรวจโดยจักษุแพทย์พบว่ามีเบาหวานที่จอประสาทตา 70 ตา (31.1%) ค่า sensitivity และ specificity ในการตรวจพบเบาหวานที่จอประสาทตาด้วยกล้องถ่ายภาพเท่ากับ 68.57% และ 92.25% ตามลำดับ ค่าความแม่นยำโดยรวม เท่ากับ 84.89%*

สรุป*: การตรวจหาเบาหวานที่จอประสาทตาโดยการใช้กล้องถ่ายภาพและไม่ขยายม่านตาได้ผลดีพอสมควรในที่ที่ยังไม่มีจักษุแพทย์หรือจักษุแพทย์มีจำนวนน้อย ไม่สามารถตรวจผู้ป่วยจำนวนมากได้ อาจใช้วิธีนี้ในการตรวจคัดกรองผู้ป่วย*