Non- Mydriatic Fundus Photograph Diabetic Retinopathy Screening in Primary Care Unit Setting by Paramedic Personnel

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ABSTRACT

Objective: To study the accuracy and agreement of non-mydriatic fundus photographic screening of diabetic retinopathy (DR) by well-trained paramedic personnel compared to retinal specialists and to obtain the prevalence of DR stages in primary care unit (PCU).

Methods: The non-mydriatic fundus photographs of diabetic patients taken at PCU were retrospectively reviewed and graded into three groups; no DR, non-proliferative DR (NPDR), proliferative DR (PDR) by two independent well-trained nurses compared to retinal specialists between November, 2015 to March, 2016. The results were statistically analyzed to determine the level of agreement between the nurses and the retinal specialists. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of each nurse were also calculated.

Results: Fundus photographs of 475 patients were obtained. The patients included 129 (27.2%) males and 346 (72.8%) females with the age of 59.94 ± 8.62 years. The agreements between two readers and the retinal specialists were moderate (κ =0.46 and 0.54). The sensitivity and specificity of the first reader were 71.69% and 87.91% and the second reader were 75.50% and 90.8%, respectively. The PPV and NPV were 42.69% and 98.11% for the first reader and 50.60% and 96.70% for the second. The overall accuracy of the first nurse was 86.1% while the second was 96.0%. The prevalence of any stages of DR was 11.1%, NPDR 10.5% and PDR 0.6%.

Conclusion: The single field non-mydriatic fundus photography read by trained paramedic personnel is one of the effective preliminary screening modalities. However, the continuous evaluation of the capabilities of the readers should be performed so that the patients with any stages of DR would be appropriately referred to ophthalmologists. This strategy would lead to the significant improvement of the DR screening in the country with high burden of diabetic patients.

Keywords: Diabetic retinopathy screening; fundus camera; single-filed fundus photographs; paramedic personnel (Siriraj Med J 2017;69: 122-127)

INTRODUCTION

Diabetic retinopathy is the leading cause of visual impairment and blindness in the developing world including Thailand. The incidence had largely increased when compared to the last decade from 1.86% in 1990 to 2.6% in 2010 of the total number of visually impaired population from various causes in South-east Asia.[1] Diabetic populations of both type I and type II are also on the rise. The World Health Organization (WHO) reported an increase in global prevalence of diabetic population from 4.7% in 1980 to 8.5% in 2014.[2] Although, most of the visual deficit is avoidable and treatable, many diabetic patients could not access the appropriate health care providers for diabetic eye screening.[3,4] Since the

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Received 18 November 2016 Revised 18 January 2017 Accepted 25 January 2017
doi:10.14456/smj.2017.25

nature of diabetic retinopathy is slow and progressive changing of retinal capillaries, vision of most diabetic retinopathy patients is not affected until the macula is involved which could be too late for effective treatments. An effective screening protocol is mandatory to adequately and effectively screen the diabetic population for diabetic retinopathy.

The burden of annual ocular examination by ophthalmologists to screen for diabetic retinopathy is largely increasing. According to the current diabetic retinopathy screening in Siriraj Hospital, a tertiary referral center of Thailand, patients have to appoint the screening period directly with responsible nurses. The nurses then schedule the patients on appropriate time slots for dilated eye examination depending on different baseline characteristics of each patient. The actual examination consumes time of the physicians, nurses, and the patients themselves and cost some expenses to hospital and eventually to the country. In some cases, the multiple steps of appointment and screening examination cause the patients to lose compliance for appropriate follow-up examination.

The primary care unit (PCU) of Siriraj Hospital is a small clinic built for the primary care of patients in responsible areas around Siriraj hospital. In the setting of this PCU, we propose and evaluate a different screening protocol to make the screening processes more convenient for the patients and to reduce burdens for ophthalmologists. This protocol involved non-dilated fundus photographs taken from the nearby PCU centers and interpretation of the images by trained PCU nurses.

MATERIALS AND METHODS

This retrospective study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. (Si 459/2015)

As a part of the PCU health screening program, type II diabetic patients living in the responsible areas of each PCU node were contacted and scheduled for diabetic retinopathy screening.

The single-field fundus photographs were taken without pharmacologic pupil dilatation with *Kowa nonmyd7* fundus camera and its own software (Kowa company, Nagoya, Aichi, Japan; Nikon camera; Windows 7 PC 32/64bit.) The obtained images are wide-angled at 45-degree, single-field, centered on macula including optic nerve head, and 16 megapixel in resolution. If one of the reader nurses could not see the images clearly, the multiple locations of fundus pictures more temporally and nasally would also be captured. A black sheet cover over the heads of patients and the camera was used to avoid pupil constriction and to improve the quality of the fundus photographs.

The two reader nurses were trained with our own modules before they read the fundus photographs. The photographs were interpreted independently and they were blinded to each other's results. The data were recorded as follows: no diabetic retinopathy (no DR), nonproliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) or uninterpretable due to poor image quality. The more advanced stage of DR between two eyes was chosen to be the correct diagnosis of the patients. Clinically significant diabetic macular edema (CSME) was also recorded. The fundus photographs were then sent to retinal specialist, SP, to re-interpret them. The results from the two independent readers were analyzed against those from the retina specialists.

We retrospectively reviewed and analyzed all the data. The protocol effectiveness was calculated by the percentage of actual patients coming for the screening out of the total number of the diabetic patients contacted. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the reading by the nurses were calculated using the interpretation by the retinal specialists as a reference.

RESULTS

A total of 553 diabetic patients were recruited. Seventy-eight patients were excluded due to poor image quality, leaving 475 patients left in the study, of which 129 (27.2%) were males and 346 (72.8%) were females. The age of patients was 59.94 ± 8.62 years.

Among the 78 excluded patients, the reasons for poor image quality were opaque media and small pupil size. The fundus photographs taken in these situations lacked clarity to show the underlying detail of the background or incomplete study area at the rim of the photographs.

There were 422 (88.8%) patients with no DR, 50 (10.5%) patients with NPDR and 3 (0.6%) with PDR as interpreted by the retinal specialists. The results from the first showed no DR, NPDR and PDR at 315 (66.3%), 64 (13.5%) and 3 (0.6%) patients, respectively. There were 93 (19.6%) patients uninterpretable for the first reader. The results from second reader showed no DR in 345 (72.6%), NPDR in 70 (14.7%), PDR in 1 (0.2%) and uninterpertable in 59 (12.4%) patients.

TABLE 1. Stage of diabetic retinopathy (DR) screening

Stage of DR	Number	Percentage
No DR	315	66.3%
Non proliferative DR	64	13.5%
Proliferative DR	3	0.6%
Uninterpretable by two readers	93	19.6%
Total	475	100%

The sensitivity and specificity of diabetic retinopathy screening were 71.70% and 87.91% for the first reader, respectively and those for the second reader were 75.5% and 90.8%, respectively. Positive predictive values were 42.7% for the first reader and 50.6% for the second reader. Negative predictive values were 96.11% and 96.7% for the first and second readers, respectively.

The agreement of interpretation between the retinal specialists and the reader nurses were moderate with the Kappa (κ) of 0.46 and 0.55 for the first and second readers respectively.

TABLE 2. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy between two readers.

Readers	Sensitivity	Specificity	PPV	NPV	Accuracy
First	71.7%	87.9%	42.7%	96.1%	86.1%
Second	75.5%	90.8%	50.60%	96.7%	89.0%

Then, we analyzed into detail of which stages were most commonly misdiagnosed. Within no DR group, there were 29 (6.1%) photos from the first reader and 31 (6.5%) photos from the second misinterpreted as NPDR. Within NPDR group, there were 3 (0.6%) and 1 (0.2%) misinterpreted as PDR and there were 6 (1.3%) and 8 (1.7%) photos incorrectly graded as no DR. Within PDR group, with the total number of 3 patients, the first reader staged as no DR in 1 case and NPDR in 2 cases while the second reader interpreted all 3 cases as NPDR.

TABLE 3. The stage of DR by readers compared to the correct diagnosis.

	Diagnosis			
First reader	No DR	NPDR	PDR	Total
No DR	308 (64.8%)	6 (1.3%)	1 (0.2%)	315 (66.3%)
NPDR	29 (6.1%)	33 (6.9%)	2 (0.4%)	64 (13.5%)
PDR	0	3 (0.6%)	0	3 (0.6%)
Uninterpretable	85 (17.9%)	8 (1.7%)	0	93 (19.6%)
Total	422 (88.8%)	50 (10.5%)	3 (0.6%)	475 (100%)

	Diagnosis			
Second reader	No DR	NPDR	PDR	Total
No DR	337 (70.9%)	8 (1.7%)	0	345 (72.6%)
NPDR	31 (6.5%)	36 (7.6%)	3 (0.6%)	70 (14.7%)
PDR	0	1 (0.2%)	0	1 (0.2%)
Uninterpretable	54 (11.4%)	5 (1.1%)	0	59 (12.4%)
Total	422 (88.8%)	50 (10.5%)	3 (0.6%)	475 (100%)

Diabetic macular edema by the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria of clinical significant macular edema (CSME) was found in 8 patients (1.7%). The first reader nurse had the sensitivity and specificity to interpret this condition in 37.5% and 97.0%, respectively. While the second reader nurse had the sensitivity and specificity of 62.5% and 96.4%. The agreement (k) for both readers was 0.22 and 0.32.

The coexisting diseases we found in the fundus photographs were enlarged cup to disc ratio of optic nerve head (n=43, 7.2%), non-neovascular age-related macular degeneration (n=23, 4.8%), epiretinal membrane (n=22, 4.6%), and other macular diseases (n=18, 3.8%).

DISCUSSION

Diabetic retinopathy is the most commonly found microvasculopathy complication of diabetic patients. The patients need to be screened and monitored periodically for the complications. The prompt intervention after DR detection significantly improves the quality of vision of the patients. A common pitfall for most Thai diabetic patients who never come for an ocular examination is that they do not realize any decline in visual acuity due to the imperfect correlation of deterioration of visual acuity and severity of diabetic retinopathy. Thus, they truly need to be examined at least annually as described in literatures.[6-8] The most widely used method of screening diabetic retinopathy is dilated-eye examination by an ophthalmologist which consumes time and expenses of the patients themselves and the hospital. Eventually, this could lead to a poor compliance of the adherence to the screening process. This brought us the idea of active and simple screening protocol based on the established PCU system described above. This strategy could lead to a better screening compliance especially for the elderly and immobilized. Therefore, with this protocol we would like to know that not only if the screening protocol is effective but also if the efficacy of the medical personnel who performed the process are sufficient in order to employ this as a sustained screening protocol for the primary care setting.

The results of diabetic retinopathy stages in our urban populations are NPDR 10.5% and PDR 0.6%. In urban area situations, these prevalences are dramatically reduced when compared to the previous report in Thailand in 2006 where the prevalence of overall DR was 31.4%; NPDR 22% and PDR 9.4%.[9] We believed that this improved result was caused by the strict screening protocol we had implemented into Thailand ocular screening, which unfortunately produced a huge workload to the ophthalmology clinic. The protocol of screening, in which the mobile unit was sent out to screen patients in this study reduces the burden of the outpatient unit of Siriraj Hospital with around 475 diabetic patients per year. This could lead to the improvement of outpatient services and waiting time for the crowded ophthalmology clinic as a whole. The patients whose ocular screening showed no diabetic retinopathy would not have to come to an ophthalmology clinic at the hospital.

The accuracy of fundus photographic interpretations varied among each group of DR stages. It was highest with 78.1% and 80.6% of accuracy for no DR group, with a decrease of the percentage for NPDR and PDR groups. The sensitivity in detecting DR from single color fundus photographs were 71.7% and 75.5% from both independent reader nurses, respectively. While the specificity were 87.9% and 90.8%, respectively. Vujosevic, et al., reported the sensitivity and specificity of 71% and 96%, respectively in detecting DR from non mydriatic single field digital color fundus photographs.[10] The sensitivity and specificity in that study were calculated from the reading of two retinal specialists compared to the gold standard of Early Treatment Diabetic Retinopathy Study 7 standard 35-mm stereoscopic color fundus photographs. Thus, when compared to our study in terms of detecting the DR, the reader nurses effectively interpreted the fundus photographs and this screening method could reasonably be performed by other paramedical personnel instead of ophthalmologists, reducing the unnecessary ophthalmologist visits.

The inter-observer agreement between independent reader nurses and a retinal specialist were moderate at the κ level of 0.46 and 0.55, respectively. This showed that the screening test of fundus photographs interpretation was moderately useful in some aspects, especially for using as a primarily screening protocol for diabetic retinopathy. Anyway, we agree that the inter-observer agreement should be higher and the continuous learning of fundus photograph interpretation from retinal specialists would play a helpful role. We did not find the agreement of the referral decision-making between three participants but Lin DY et.al., reported that the agreement between the single-field non-mydriatic monochromatic digital photographs and 7–standard field photographs was excellent (κ =0.97) for utilizing it as a referral tool.[11]

We also took the percentage of missed diagnosis of PDR as a serious complication from this protocol. We found 0.6% of misdiagnosis of PDR from both trained readers. This result was a serious false negative interpretation that we do not want to overlook. Thus, we

emphasized the reader nurses for a more strict screening ability to detect the abnormalities from the photographs and trained them periodically with a retina specialist as a continuous medical evaluation.

Our results reflect some limitations of the paramedic reading personnel with limited clinical experiences in ophthalmology. This result leads us to set a better protocol of screening, a more strict fundus photographs interpretations screening criteria and a channel with which they could directly refer all positive fundus photographs for DR or any other found abnormalities to an ophthalmologist or a retinal specialist. This screening protocol could reduce the rate of delayed treatment that we found in the past as we could schedule patients timely according to the severity of diabetic retinopathy found on the screening fundus photo.

In diagnosis of CSME, the reader nurses were not effectively making the diagnosis which varied in sensitivities and specificities and low in agreements. However, this condition was not solely diagnosed by fundus photographs interpretation or even stereoscopic slit-lamp examinations.[12] Nowadays, we would investigate them with optical coherence tomography (OCT) to determine the macular thickness and other parameters such as cystoid changes, hyperreflective materials and subretinal fluid to make the diagnosis more accurately. These low statistical values bring us to improve the protocol for poor visual acuity patients who can be sent for dilated ocular examination to find out the underlying pathology that would be missed by fundus photographs such as center-involved diabetic macular edema.

The non-mydriatic fundus camera is one of the screening machines used for diabetic screening in hospitals under the universal coverage paradigm of the Ministry of Health of Thailand. The screening protocol used in our study could easily be implemented for most public hospitals nationwide. However, important limitations of this protocol should be kept in mind, so the patients would not lose benefit from the false negative errors which could be the misinterpretation by poor quality images or lack of practice of the interpretation by the readers. Patients with uninterpretable images should be referred to the ophthalmology outpatient clinic directly for the accurate eye examinations. For one-eyed patients, we prefer to send them to have an eye examination with an ophthalmologist directly.

We also screened for other coincident retinal and optic nerve diseases such as enlarged cup to disc ratio of optic nerve head, age related-macular degeneration, polypoidal choroidal vasculopathy and epiretinal membrane. The reader nurses have the effective ability to report the suspicious photographs with abnormal findings, which would be confirmed by a retinal specialist. However, some of these coexisting diseases are not diagnosed with only looking at the fundus photographs and they need some special ocular examinations as well as more advanced ocular investigations. With fundus photograph documentation, the patients would not only benefit from diabetic retinopathy screening, but also screening of other silent coincident ophthalmologic conditions.

CONCLUSION

The single field non-dilated fundus photograph technique with interpretation by trained nurse readers could be one of the effective preliminary screening modalities for most countries with increasing burden of diabetic patients and ophthalmology services. The poor access to a public hospital for an annual eye examination for diabetic microvascular complications could lead the patients to some morbidities. This strategy was acceptable in accuracy, sensitivity, specificity, PPV and NPV. However, the continuous evaluation of the capabilities of the readers should be performed, so that the patients with any stages of DR would be appropriately referred to ophthalmologists. Lower threshold for referral to ophthalmologist should be considered in any unclear cases.

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