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Clinical biomicroscopy versus fluorescein angiography: Effectiveness and sensitivity in detecting diabetic retinopathy

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PURPOSE. *To compare diagnostic effectiveness and sensitivity of the two methods of screening for diabetic retinopathy.*
METHODS. *Prospective analytic study comparing diabetic retinopathy grading obtained from clinical slit lamp biomicroscopy and fundus fluorescein angiography (FFA). A total of 189 consecutive patients were examined in the ophthalmology department at Jordan University Hospital.*
RESULTS. *A total of 376 eyes were reviewed by consultant ophthalmologist for diabetic retinopathy grading on FFA. The sensitivity of ophthalmoscopy in diagnosing diabetic retinopathy grading was 91.2%, with a specificity of 97.9%. The degree of agreement kappa was 0.87.*
CONCLUSIONS. *Slit-lamp biomicroscopy is highly sensitive for screening diabetic retinopathy grading in diabetic patients and ophthalmologists do not need to confirm a suspected clinical diagnosis of proliferative diabetic retinopathy using FFA as ophthalmoscopy proved to be comparable to angiography. (Eur J Ophthalmol 2007; 17: 84-8)*

KEY WORDS. *Diabetes, Diabetic retinopathy, Fundus fluorescein angiography, Screening, Sensitivity and specificity, Slit-lamp biomicroscopy*

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INTRODUCTION

Diabetic retinopathy is a highly specific microvascular complication of diabetes and a leading cause of blindness in people of working age (1-3). After 20 years from the onset of diabetes, over 90% of patients with Type 1 and more than 60% of patients with Type 2 will have diabetic retinopathy (4, 5). Because of the sight-threatening potential of the disease and the availability of methods to slow down the rate of progression of the disease, screening is a high priority to every diabetic patient. It not only prevents blindness but is also cost-effective.

The initial sign of diabetic retinopathy is considered to be microaneurysm, determined by ophthalmoscopy. Early vascular changes can be elucidated by fluorescein angiography, which embraces dye leakage, dilatation of capillaries, filling defects, and microaneurysms (6). To evaluate how often an early vascular change seen in a fluorescein angiogram is missed by slit-lamp biomicroscopy, and whether ophthalmologists should confirm a suspected clinical diagnosis of proliferative diabetic retinopathy using fundus fluorescein angiography (FFA), this prospective study was performed.

PATIENTS AND METHODS

Ophthalmologic examination was performed for 189 diabetic patients from a consecutive series of patients attending the Diabetes Clinic at Ophthalmology Department, Jordan University Hospital in Amman. Two patients were one-eyed; therefore, 376 eyes were examined.

Examination involved best-corrected visual acuity, an-

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terior segment examination, and slit-lamp biomicroscopy during mydriasis. Then, patients were sent for FFA during mydriasis as well. Later, angiograms were interpreted by an experienced ophthalmologist without knowledge of the patients' diabetic or ophthalmic history.

MATERIALS

Clinical biomicroscopy

Indirect funduscopy was carried out by an experienced consultant ophthalmologist using slit-lamp biomicroscopy with 78 D lens for the posterior pole and a superfield lens for the periphery. Diabetic retinopathy stage was classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria as no diabetic retinopathy (no DR), mild nonproliferative DR (NPDR), moderate NPDR, severe NPDR, proliferative DR (PDR) with new vessels at the disc (NVD), PDR with new vessels elsewhere in the retina (NVE), or advanced PDR with vitreous hemorrhage, fibrous tissue, or recent retinal detachment.

TABLE I - DESCRIPTIVE STATISTICS OF THE STUDY GROUP (189 Patients)

	Minimum	Maximum	Mean	SD
Duration, yr	2.0	30.0	11.566	5.180
Age, yr	10.0	81.0	54.910	12.524

Fluorescein angiography

FA was carried out by an experienced technician using the OCULab system and digital camera (Kodak Megaplus 1.4i). After mydriasis, nine 20-degree field non-stereoscopic images were captured within a week of clinical biomicroscopy performed for the same eye. The filling phase of FFA was recorded followed by later phases (2–3 minutes and 7–9 minutes).
Angiographs were graded by the same ophthalmologist without previous knowledge of patients' clinical diabetic retinopathy staging. Retinopathy grading was also based on ETDRS system.

Statistics

Statistics were carried out using the SPSS program on the IBM computer.
Kappa (k) was used to measure the degree of agreement between ophthalmoscopy and FFA grading (7). A kappa statistic of zero indicates agreement equal

TABLE II - COMPARISON OF RETINOPATHY AS DETERMINED BY OPHTHALMOSCOPY AND FUNDUS FLUORESCEIN ANGIOGRAPHY (FFA)

			Ophthalmoscopy			Total
			No DR	NPDR	PDR	
FFA	No DR	Count	121	1		122
		%	99.2%	0.8%		100.0%
	NPDR	Count	12	200	4	216
		%	5.6%	92.6%	1.9%	100.0%
	PDR	Count		10	28	38
		%		26.3%	73.7%	100.0%
Total		Count	133	211	32	376
		%	35.4%	56.1%	8.5%	100.0%

Chi-square=543.15; df=4 (p=0.000). Measure of agreement: kappa 0.870; asymp. std error 0.024; approximate t 20.976; approximate significance 0.000. DR = Diabetic retinopathy; NPDR = Nonproliferative DR; PDR = Proliferative DR

to that expected by chance, whereas a value of unity indicates complete agreement. p Value was considered statistically significant when <0.05.
Chi-square (c^2) was calculated to study statistical significance of cataract as a factor affecting agreement between methods.
One-way analysis of variance (ANOVA) statistical test was used to measure the significant relation between duration of diabetes and agreement between both methods of screening, ophthalmoscopy and FFA.
British Diabetic Association (BDA) screening criteria were considered to prove sensitivity and specificity of screening methods. According to BDA, sensitivity should be >80%, specificity >95%, and <5% technical failure (8).

RESULTS

After undergoing ophthalmic examination, all 376 eyes attended FFA, giving a compliance rate of 100%. Therefore, all cases remained for statistical analysis.
Table I shows study descriptive results. Male:female ratio was 1:1 with a mean age of 54.91±12.52 SD years and duration of disease of 11.57±5.18 SD years. Only 31 cases (8.2%) were Type 1 DM.
Table II compares the retinopathy grading by ophthalmoscopy with FFA grading. The overall agreement between the methods was 87.0%. The kappa statistics for the data in the Table = 0.870 (standard error [SE] 0.024), indicating a statistically significant agreement between both screening methods over that expected by chance (c^2=543.150; *df*=4; p=0.000).
The agreements between methods for the eyes with different diabetic retinopathy grading are 99.2%, 92.6%, and 73.7% for no DR, NPDR, and PDR, respectively.

TABLE III - COMPARISON OF RETINOPATHY BY OPHTHALMOSCOPY AND PROLIFERATIVE DIABETIC RETINOPATHY (PDR) GRADING BY FUNDUS FLUORESCEIN ANGIOGRAPHY (FFA)

		Ophthalmoscopy		
		Mild NPDR	Moderate NPDR	Severe NPDR
FFA	NVD	0	1	1
	NVE	0	1	6
	Advanced	0	1	0

NPDR = Nonproliferative DR; NVD = New vessels at the disc; NVE = New vessels elsewhere in the retina

Of the 38 eyes in which PDR was found by FFA, less retinopathy was detected in 10 (26.3%) eyes. The angiographs of the eyes in which there was disagreement were reviewed to establish the reasons for the discrepancies. Two were found to be NVD, seven were NVE, and only one was fibrous proliferans missed by the ophthalmologist (Tab. III).
Angiographs diagnosed 200 eyes with NPDR. Agreement with ophthalmoscopy is 92.5%. Only 3 cases (1.5%) were graded as PDR (namely, 2 NVD and 1 NVE) by the ophthalmologist. These had severe NPDR on FFA. Another 12 (6.0%) eyes in the mild NPDR stage were misdiagnosed on ophthalmoscopy as no DR (Tab. II).
On the other hand, ophthalmoscopy agreed in 349 (92.8%) eyes and disagreed with FFA in 27 (7.2%) eyes, missing 22 diagnoses but overcalling 5 cases (Tab. II). Of the later, one case was mild NPDR on ophthalmoscopy. The remaining four cases were of intraretinal microvascular abnormalities (IRMA), which was called PDR by ophthalmologists.
As for the undercalled cases, 12 had microaneurysms detected on FFA but missed clinically. Seven were new vessels missed clinically as IRMAs. The remaining 3 cases were diagnosed as moderate NPDR on FFA but graded as NVD, NVE, and advanced PDR each for one of the 3 cases.
Disagreement between ophthalmoscopy and FFA is associated with disease duration only in NPDR cases for both undergrading as well as overgrading on slit-lamp biomicroscopy (p=0.001 and p=0.03, respectively) but not for PDR cases (p=0.964).
There was no significant correlation between decreased visual acuity due to cataract and missing some diabetic retinopathy changes on ophthalmoscopy in comparison to fluorescein angiography.
Cataract relation to disagreement between ophthalmoscopy and FFA was not statistically significant in PDR cases (p=0.365) as well as NPDR (p=0.572) cases.
Considering FFA as the gold standard for diabetic retinopathy screening and grading, sensitivity and specificity of ophthalmoscopy is found to be 91.2% and 97.9%, respectively (odds ratio=5.03).

DISCUSSION

There are several methods of screening including direct ophthalmoscopy, slit-lamp biomicroscopy, reti-

nal photography, and FFA. Until the early 1980s, several reports noted that photography was equivalent to angiography in detecting retinopathy while ophthalmoscopy was not as effective as either of the two methods (9). Others reported angiography to be more sensitive (10). In the late 1980s, and after seven-field stereoscopic photography and FFA had been regarded as the gold standard, the ETDRS report no. 5 supported the reliability of both clinical and photographic methods to assess retinopathy (11, 12).

In 1992, the review article by Singer et al listed the sensitivity/specificity of different techniques, showing that FFA was the gold standard (13). Until the late 1990s, the degree of peripheral diabetic retinal changes based on grading of fundus photographs was comparable to that based on angiograms (14).

FFA is expensive, time-consuming, and readily available. Therefore, we studied the sensitivity and specificity of slit-lamp biomicroscopy in grading diabetic retinopathy, which was found to be comparable to FFA.

Sensitivity of 91.2% and specificity of 97.9% are comparable to other studies; Buxton et al found a sensitivity of 67.0% and specificity of 96.0% for hospital physician group (15). Therefore, management of diabetic retinopathy can be based on the results of the ophthalmologists' examination.

In our study, there was a statistically significant association between duration of diabetes and both overgrading as well as undergrading diabetic retinopathy by slit-lamp examination only in cases of NPDR. We noticed a shorter duration of diabetes in patients when biomicroscopy undercalls retinopathy compared to FFA grading and longer duration when it overcalls. This confirms an observer bias which was noticed in previous studies (13). As examiners had known about disease duration from history taking, they may have expected the grading before detecting retinopathy for diabetic patients biomicroscopically.

Cataract was expected to affect agreement between biomicroscopy and FFA grading but in our study it did not show any statistically significant correlation. It may have equal effect on both methods of retinopathy grading.

CONCLUSIONS

Slit-lamp biomicroscopy is highly sensitive for screening diabetic retinopathy grading in diabetic patients and ophthalmologists do not need to confirm a suspected clinical diagnosis of PDR using FFA as ophthalmoscopy proved to be comparable to angiography.

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