Al-Azhar Med. J. *Vol. 49(3), July, 2020, 1017-1026*
DOI : 10.12816/amj.2020.91625
https://amj.journals.ekb.eg/article_91625.html

FLOURESCEIN FUNDUS ANGIOGRAPHY VERSUS OPTICAL COHERENCE TOMOGRAPHY IN DIABETIC MACULAR EDEMA

By

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ABSTRACT

Background: Diabetic maculopathy is the leading cause of visual loss in diabetic patients. The pathogenesis is not fully understood and a satisfactory therapy is currently not available. The most common tools to diagnose diabetic retinopathy and diabetic macular edema are flourscien fundus angiography (FA) and optical coherene tomography (OCT).

Objective: To compare between the assessment of diabetic macular edema by Fluorescein fundus angiography and by Optical coherence tomography in the same patients.

Patients and Methods: Forty eyes were included in the study with non-proliferative diabetic retinopathy with maculopathy those met the inclusion criteria. Patients were fully evaluated including history, examination and investigations. Investigations used Optical Coherence Tomography and Flouresien Fundus Angiography. Study setting at Memorial Institute of Ophthalmic Research (MIOR) and Al-Azhar University Hospitals from March 2019 to October 2019.

Results: The distribution of FA patterns showed diffuse leakage at macula as the most common pattern seen in 60% of eyes followed by focal leakage at macula seen in 27.5% of eyes, and combined (focal and diffuse leakage at macula) was seen in 12.5% of eyes. Eyes with focal leakage were more likely to have CME, whereas eyes with diffuse leakage were more likely to have serous foveal detachment and combined pattern on OCT show cystoid macular edema with serous foveal detachment.

Conclusion: FA is known to be a sensitive method for qualitative assessment of fluid leakage in diabetic macular edema; however, actual macular thickening assessed by OCT is better correlated with the loss of visual acuity. Furthermore, FA is an invasive procedure with side effects ranging from nausea to its rare complication of anaphylaxis and death. OCT is noninvasive, comfortable, safe, fast and can be repeated as often as required and offers an alternative to FA in the follow up of changes in retinal thickness after laser photocoagulation and intra-vitreal steroid injection. However, FA is still essential for the assessment of the foveal perfusion state, which cannot be demonstrated by the OCT.

Keywords: Diabetic Macular edema, Optical Coherence Tomography and Flouresien Fundus Angiography.

INTRODUCTION

Diabetic retinopathy is the leading cause of blindness among working –age adults, approximately 35% of diabetic patients will have some form of DR, and 5 to 10 % of these individuals will suffer from vision loss due to diabetic macular edema *(Antonetti et al., 2012)*. Duration of diabetes is a major risk factor associated with the development of diabetic retinopathy, also glycemic control is the key modifiable risk factor associated with development of diabetic retinopathy *(Nicholas et al., 2016)*. Once retinopathy is present, duration of diabetes appears to be a less important factor than glycemic

controlee in forecasting progression from earlier to later stages of retinopathy *(Kilpatrick et al., 2012)*.

Diabetic maculopathy (foveal edema, exudates or ischemia) is the most common cause of visual impairment in diabetic patients, particularly type 2. Diffuse retinal oedema is caused by extensive capillary leakage, and localized oedema by focal leakage from micro-aneurysms and dilated capillary segments. The fluid is initially located between the outer plexiform and inner nuclear layers; later it may also involve the inner plexiform and nerve fiber layers, until eventually, the entire thickness of the retina becomes edematous. With central accumulation of fluid the fovea assumes a cystoid appearance – cystoid macular edema (CMO) that is readily detectable on optical coherence tomography (OCT) and assumes a central flower petal pattern on FA *(Kanski, 2016)*.

Examination with OCT or slit-lamp bio microscopy using a contact lens is the appropriate means to evaluate eyes for the presence or absence of macular thickening. Leakage shown on the angiogram may occur in the absence of macular retinal thickening and is thus not considered macular edema *(American Academy, 2014)*. OCT is used rather than stereoscopic photo graphs or clinical examination to evaluate and follow up macular edema status because it allows an objective, accurate assessment of the amount and location of retinal thickness *(Elman et al., 2012* and *Brown et al., 2013)*. OCT may be used to predict visual acuity in patients with DME. The correlation between photoreceptor layer status following resolution of DME by intravitreal injection and final visual acuity has been shown *(Shin et al., 2012* and *Yohannan et al., 2013)*.

OCT cannot detect no perfusion which may explain the vision loss in some cases. Fluorescein angiography is still an important method to evaluate macular no perfusion. It provides important information about retinal perfusion, blood retinal barrier integrity and macular ischemia, so, it should be performed if treatment of DME is being considered. It shows localization of focal or diffuse leakage areas and can be use complementary to OCT for guiding laser photocoagulation, OCT is an accurate devise for the early diagnosis, analysis and monitoring of retinopathy, with high repeatability and resolution, it allow not only the qualitative diagnosis of DME, but also the objective and quantitative assessment of edema, probably, OCT is the most important diagnostic and prognostic tool in the management of DME *(Lee et al., 2013)*.

Fluorescein angiography (FA) is useful for selected patients with diabetic retinopathy, particularly in the presence of macular edema to identify treatable lesions for laser photocoagulation Typically, FA is not necessary in the absence of macular edema or to identify PDR. Recently, wide- field FA has been used to identify peripheral capillary no perfusion for selective photocoagulation. The benefits of this approach compared to convention photocoagulation remain to be determined *(Oliver et al., 2010)*.

The present work aimed to compare between the assessment of diabetic macular edema by Fluorescein fundus

angiography and by Optical coherence tomography in the same patients.

PATIENTS AND METHODS

Forty eyes were included in the study with non-proliferative diabetic retinopathy with maculopathy those met the inclusion criteria. Patients were fully evaluated including (history, examination and investigations). History includes personal data (name, age, gender, residency, telephone number and occupation).

Inclusion criteria:

- Patients with diabetes type 2.
- Non-proliferative diabetic retinopathy with maculopathy.
- Best corrected visual acuity is 6/36 or less.

Exclusion criteria:

- Patients with media opacity, eg Cataract.
- Patients with retinal disease other than diabetic retinopathy, eg macular degeneration.
- Patients with co-existing pathology eg Uveitis, papillitis, papilledema.
- Patients with previous Intra-ocular surgery.

Examination include visual acuity assessment; unaided and best corrected with spectacles, cycloplegic refraction using Topcon (8800) Auto- refract meter, Anterior segment evaluation using; Haag-striet slit –lamp and Fundus examination using Haag- Stiet- Slit lamp bio microscopy with Volks non-contact lens power +78.

Investigations:

- Optical coherence tomography OPKO OCT SLO device.
- Flourescien fundus angiography **Topcon TRC 50EX fundus camera.**

Study setting:

Memorial Institute of Ophthalmic Research (MIOR) and Al Azhar University Hospitals from March 2019 to October 2019.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric and. Also qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test. The comparison between more than two group was done by Using One Way ANOVA test or Mann Whrtney U Tesf. The confidence interval was set to 95% and the margin of error accepted was set to 5%. value was considered significant < 0.05:

RESULTS

Regarding gender of the patient, (67.5%) of patient were females, while (32.5%) were males. In addition, we noted that the right eye was (52.5%) of the sample size and the left eye was (47.5%) of the sample size **(Table 1)**.

Table (1): Descriptive data regarding Demographic data

		No. = 40
Age	Mean±SD	56.70 ± 6.97
	Range	46 – 72
Gender	Female	27 (67.5%)
	Male	13 (32.5%)
Laterality	RT eye	21 (52.5%)
	LT eye	19 (47.5%)
Duration of DM	Mean±SD	8.90 ± 3.36
	Range	4 – 15

The mean age of all patiens was (56.70 ± 6.97) years.

The following tables show the comparative study between Fluorescein angiography and Optical coherent tomography in diagnosing and detecting type of Diabetic macular edema. The distribution of FA patterns showed diffuse leakage at macula as the most common pattern seen in 60% of eyes followed by focal leakage at macula seen in 27.5% of eyes and combined (focal and diffuse leakage at macula) was seen in 12.5% of eyes **(Table 2)**.

Table (1): Descriptive data regarding OCT & FFA

		No.	**%**
OCT	Diffuse	24	60.0%
	CME	11	27.5%
	Diffuse &CME	5	12.5%
FFA	Diffuse	24	60.0%
	Focal	11	27.5%
	Diffuse &Focal	5	12.5%

There was a statistically significant difference found between OCT groups regarding FFA (P-value< 0.01) **(Table 3)**.

Table (2): Relation between OCT and FFA

FFA	**OCT**						**P-value**
	Diffuse NO:24		**CME NO:11**		**Diffuse& CME NO:5**		
	No.	**%**	**No.**	**%**	**No.**	**%**	
Diffuse	24	100.0%	0	0.0%	0	0.0%	0.001
Focal	0	0.0%	11	100.0%	0	0.0%	
Diffuse& Focal	0	0.0%	0	0.0%	5	100.0%	

*: Chi-square test

There was no statistically significant difference between FFA groups regarding degree of NPDR **(Table 4)**.

Table (3): Relation between FFA and Degree of NPDR

Degree of NPDR	FFA						P-value
	Diffuse		Focal		Diffuse &Focal		
	No.	%	No.	%	No.	%	
Mild	1	4.2%	2	18.2%	0	0.0%	0.615
Moderate	8	33.3%	3	27.3%	2	40.0%	
Severe	15	62.5%	6	54.5%	3	60.0%	

*: Chi-square test

There was a statistically significant difference between OCT groups regarding Macular thickness. The Mean±SD of diffuse type (298.79 ± 90.57), the Mean±SD of CME (348.45 ± 84.19), the Mean±SD of combined type (430.20 ± 189.71) **(Table 5)**.

Table (4): Relation between OCT and Macular thickness

Macular thickness	OCT			P-value
	Diffuse	CME	Diffuse &CME	
Mean±SD	298.79 ± 90.57	348.45 ± 84.19	430.20 ± 189.71	0.039
Range	109 – 591	212 – 456	218 – 700	

•: One Way ANOVA test

There was no statistically significant difference between Degree of NPDR regarding duration of DM **(Table 6)**.

Table (5): Relation between Degree of NPDR and Duration of DM

Duration of DM	Degree of NPDR			P-value
	Mild	Moderate	Severe	
	No. = 3	No. = 13	No. = 24	
Mean±SD	10.00 ± 0.00	7.54 ± 3.53	9.50 ± 3.34	0.204
Range	10 – 10	4 – 15	5 – 15	

•: One Way ANOVA test

DISCUSSION

The distribution of FA patterns showed diffuse leakage at macula as the most common pattern seen in 60% of eyes followed by focal leakage at macula seen in 27.5% of eyes and combined (focal and diffuse leakage at macula) was seen in 12.5% of eyes.

Eyes with focal leakage were more likely to have CME whereas eyes with diffuse leakage were more likely to have serous foveal detachment and combined pattern on OCT show cystoid macular edema with serous foveal detachment, some cases are not detected by slit-lamp examination or FA, this is a striking feature, demonstrating the importance of OCT in early detection of diabetic changes

In this study patients were classified according to the degree of NPDR to mild

(4.2%), moderate (33.3%) and severe (62.5).

In this study there was highly statically significant difference found between OCT groups regarding FFA, also there was statistically significant difference found between OCT groups regarding to macular thickness.

Danis et al. (2010) conducted a study on 323 eyes and 203 fellow non-study eyes were analyzed. They concluded that fluorescein leakage is associated with visual acuity and some OCT and color photographic variables. They did not identify any unique FA variables that had a stronger association with visual acuity than OCT measures of retinal thickness. These data may be useful to investigators planning future DME clinical trials.

Shoughy and Kozak (2016) concluded that FA and OCT are complementary investigation. OCT provides detailed imaging of anatomical retinal layers and helps perform quantitative assessment during follow up. FA is used to evaluate retinal vascular perfusion and the integrity of the inner blood retinal barrier.

Malika and Sudha (2017) conducted a study on 69 eyes to evaluate diabetic macular edema with spectral domain optical coherence tomography and fundus fluorescein angiography. They concluded that there is minimal agreement between FFA and OCT in the evaluation of DME.

Sheth et al. (2017) they concluded that both FFA and OCT are indispensable tools for diagnosis and management of diabetic macular oedema. Measurement of central foveal thickness, traction, ERM was possible with OCT but large number of patients showed macular ischemia on FFA which was not possible to diagnose with OCT. So, both FFA and OCT are necessary for management of Diabetic macular edema.

Rathi et al. (2017) conducted a study on 32 eyes to study if any correlation exists between FA and OCT patterns in CSME. They concluded that there is a significant correlation between OCT and fluorescein angiography findings for clinically significant macular oedema. Furthermore, they have concluded that the foveal thickness correlates with BCVA. They found diffuse leakage in 59.37%, focal leakage in 31.25% and combined leakage in 12.5%.

Govindan (2018) who concluded that combination of OCT and FA in sreening protocol along with routine evaluation can prevent vision loss in diabetic retinopathy.

Optical coherence tomograghy offers additional structural and quantitative information in characterization of DME, and because of its noninvasiveness it has been surpassing the use of invasive FA. the topographic location and morphologic patterns of edema on the OCT retinal thickness map have served as useful predictors of treatment response in diffuse DME *(Vemala et al., 2011)*. Both FA and OTC are complementary in diagnosing the type and extend of DME *(Byeon et al., 2012)*.

CONCLUSION

FA is known to be a sensitive method for qualitative assessment of fluid leakage in diabetic macular edema; however, actual macular thickening assessed by OCT is better correlated with the loss of visual acuity. Furthermore, FA is an invasive procedure with side effects

ranging from nausea to its rare complication of anaphylaxis and death. OCT is noninvasive, comfortable, safe, fast and can be repeated as often as required and offers an alternative to FA in the follow up of changes in retinal thickness after laser photocoagulation and intra-vitreal steroid injection.

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تصوير قاع العين بصبغة الفلوروسين وبالأشعة المقطعية في حالات ارتشاح ماقولة العين بمرض السكر

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خلفية البحث: ارتشاحات ماقولة العين الحادثة بسبب السكر هي أحد الأسباب الرئيسية المؤدية إلى فقدان البصر لدى مرضى ارتفاع السكر في الدم، وكيفية حدوث هذه الارتشاحات ليست مفهومة تماما كما أنها ليس لها علاج فعال حتى الآن.

الهدف من البحث: المقارنة بين تقييم ارتشاحات الشبكية السكري بالتصوير المقطعي وبالتصوير باستخدام صبغة الفلورسين في نفس المرضى.

المرضي وطرق البحث: شملت الدراسه أربعين عيناً وتم تصوير كل عين بالتصوير المقطعي وباستخدام صبغة الفلورسين لتقييم ارتشاحات الشبكيه في مرضي السكر من النوع (2) ،وقوة النظر 36/6 أو أقل وان يكون إعتلال الشبكيه السكري غير التكاثري. و المرضي ليس لديهم أمراض اخري في العين مثل المياه البيضاء ولم يقوموا باجراء عمليات أخري في العين.

نتائج البحث: أظهرت النتائج أنه بتصوير قاع العين باستخدام صبغة الفلوروسين فان 60% من العيون يوجد بها ارتشاح منتشر بمركز الابصار، بينما 27.5% من العيون يوجد بها ارتشاح. مركزي بمركز الابصار، وأن 12.5% من العيون كان بها النوعين من الارتشاح وبتصوير قاع العين بالأشعه المقطعيه ظهر ان العيون التي تعاني من ارتشاح مركزي بمركز الابصار بها تورم بقعي بمركز الابصار بينما تلك العيون التي تعاني من ارتشاح منتشر بمركز الابصار بها انفصال بمركز الابصار من النوع المائي، وتلك العيون التي تعاني من كليهما بها تورم بقعي كيسي وأيضا بها انفصال من النوع المائي بمركز الابصار.

الاســـتنتاج: أظهــرت النتـــائج أن تصـــوير قـــاع العـــين بصـــبغة الفولوروســـين مهـــم جـــدا فـــي حالـــة ارتشـــاحات ماقولـــة العـــين الحادثـــة بســـبب مـــرض الســـكرى الا أن ألأشـــعة المقطعيـــة تقـــوم بحســـاب ســـمك الشـــبكية التـــي لا يمكـــن تحديـــده بتصـــوير قـــاع العـــين بصـــبغة الفولوروســـين، كمـــا أن تصـــوير قـــاع العـــين بصـــبغة الفلوروســـين لـــه أضـــرارا جانبيـــة تتـــدرج مـــن حـــدوث ميـــل للقـــئ إلـــي حساســـية شـــديدة قـــد تـــؤدي الـــي المـــوت، كمـــا أن تصـــوير قـــاع العـــين بالاشـــعة المقطعيـــة أمـــن ومـــريح وســـريع ،ويمكـــن تكـــراره إذا لـــزم الأمـــر، ويســـتخدم أيضـــاً لمتابعـــة المرضي.