Macular Thickness Measurement in Diabetic Patients without Diabetic Retinopathy Using Optical Coherence Tomography

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Abstract: Purpose: to evaluate retinal thickness (RT) measurements with optical coherence tomography (OCT) in diabetic patients without diabetic retinopathy (DR) as documented clinically and by fluorescein angiography (FA). Materials and Methods: 36 diabetic patients with no DR underwent full ophthalmic examination, FA and OCT. Macular thickness was measured by OCT and correlated to the gender and age of the patients. Results: 58.3% (21/36) of our studied patients have changes in the central fovea and fovea either in the form of thickening or thinning. Significant thinning was found in 33.3% of the fovea of studied patients (12/36). Significant thickening was encountered in the central fovea in 25% of the studied eyes (9/36). Central foveal and foveal values are greater in men than in women. Central foveal and foveal values are greater in patients > 55years compared with younger patients. Conclusion: The OCT is a reproducible diagnostic technique that can detect macular changes in diabetic patients without diabetic retinopathy changes as documented clinically and by FFA. [Sherif H. Emerah, Hany M. Labib, Mohamed Y. Farag and Hesham F. Kamel **Macular Thickness Measurement in Diabetic Patients without Diabetic Retinopathy Using Optical Coherence Tomography**] Journal of American Science 2011; 7(11): 223-227].(ISSN: 1545-1003). http://www.americanscience.org.

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1. Introduction

Diabetic retinopathy (DR) is one of the leading causes of blindness in the developed countries, especially in patients aged 20-60 years. Early detection of DR is important to prevent loss of vision in patients with diabetes mellitus (DM). DR classically presents with microaneurysms and small haemorrhages in an early stage of the disease, and is detected with slit-lamp biomicroscopy and fundus photography.

Fluorescein angiography (FA) is one of the most efficient methods to identify areas of vascular leakage in retinal studies. FA has been able to show early edema in 21% to 42% of diabetic adults who had results that were considered negative for retinopathy with other methods ***(Richer, 2007)***.

There was a significant correlation between the features of OCT and fluorescein angiography in clinically significant diabetic macular edema. The combined data from both OCT and fluorescein angiography may provide a clearer understanding of the anatomic and physiologic characteristics of clinically significant diabetic macular edema ***(Kang et al.,2004)***.

Optical coherence tomography (OCT) is a powerful tool that has been used to assess retinal structure since 1991. This instrument emits an 820 nm near infra red illumination to generate high resolution images of the retina ***(Browning et al., 2004)***.

The OCT is a diagnostic technique that provides cross sectional imaging of retinal structure and of other ocular tissues, with high accuracy and resolution. Thus, its capacity to reproduce details (10 µm) gets close to the optical microscopy, being compared to a biopsy *in vivo*. The OCT increases the ability of clinical diagnosis and imaging techniques in ancillary exams, for giving precise and reproducible results that corroborate diagnostic impressions and allow monitoring the progression of diseases, as well as the evolution of retinal responses in therapeutic interventions ***(Hannouche and Avila, 2009)***.

From a clinical perspective, it can be said that diagnosing macular edema clinically, probably would lead to an unnecessary intervention with focal photocoagulation, which leads to paracentral scotomas. OCT can reduce the risk of scotomas induced by laser in eyes to which clinical suspicion of edema exists, but objective verification does not. Therefore, the reduction of macular edema can be documented objectively, which makes the OCT, as said in various studies, the right technique to be chosen to follow macular edema ***(Sugimoto et al., 2005)***.

OCT presents limitations when considering its applicability. Opacities, such as corneal edemas and opacities, cataract with significant opacity, vitreous hemorrhage, among other changes of dioptric media, attenuate the incidence and reflection of light required to final imaging ***(Massin et al., 2002)***.

OCT demonstrates that the macular edema is a complex clinical entity with various morphologies,

and goes beyond the limitations of a simple clinical definition. In the early stages of edema, OCT is of main importance, because structural changes in the retina are still not evident with biomicroscopy or fluorescein angiogram ***(Ozdek et al., 2005)***.

In this study we use OCT to verify the presence of macular changes in diabetic patients with no diabetic changes as documented clinically and by FFA.

2. Patients and Methods:

The study includes thirty six patients. Subjects have type1 or type 2 diabetes with no history of renal failure requiring dialysis, no medical treatment of retinal disorder or any therapy that affect retinal edema.

A complete ophthalmologic exam was done, as well as the detection of clinically significant macular edema (CSME) through biomicroscopy. After pupil dilation with 0.5% phenylephrine hydrochloride and 0.1% tropicamide, patients were examined with slit-lamp biomicroscopy with a 90-diopter lens and stereoscopic fundus photographs 50° central posterior segment were taken.

Patients with diabetic retinal changes, macular edema or any other clinically relevant ocular disease were excluded. Patients were excluded if they had refractive errors of more than S +5, or S -8 dioptres, significant media opacities, glaucoma or uveitis.

The fluorescein angiography is performed using a digital retinal camera system (Topcon TRC-50EX; Topcon Medical Systems Inc.). One retinal colour, one early phase, one middle phase and one late phase frames were obtained from each eye. If the patient has normal FFA, we proceed for OCT, so all our patients have normal FFA **(Figure 1)**.

All subjects were examined with the Stratus OCT (Model 3000, Carl Zeiss Meditec, Dublin, CA, USA, software version 4.0.1). Both the fast macular thickness and regular macular thickness OCT scan protocols were performed on both eyes. Both scan protocols obtain six cross-sectional scan lines, 6 mm in length, at equally spaced angular orientations (30°) in a radial spoke pattern centred on the fovea. RT is defined by the software algorithm as the distance between the surface of the retina and the first highly reflective layer visible at the level of the outer retina and retinal pigment epithelium. An interpolated RT map is constructed from the six scan lines by the software. For analysis of the RT, the mean RT was calculated in four areas: the central fovea (the cross-section of the six radial scans), the fovea (central circle, with a diameter of 1 mm), the pericentral area (donut shaped ring with an inner diameter of 1 mm and an outer diameter of 3 mm) and the peripheral area (inner diameter of 3 mm and outer diameter of 6 mm **(Figure 2)**.

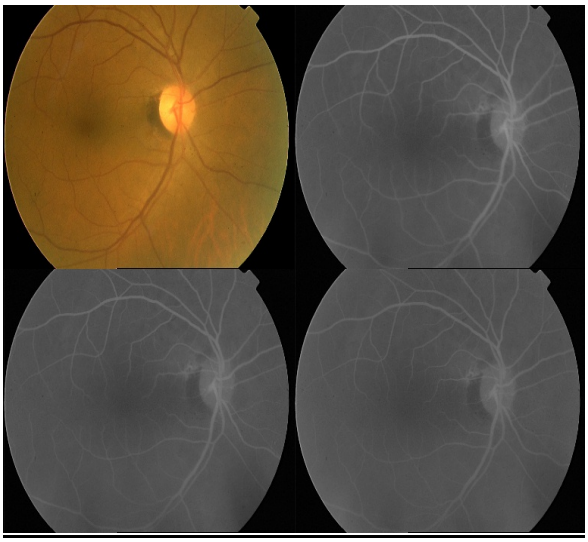

Fig.1 FFA of a diabetic patient shows no visible changes.

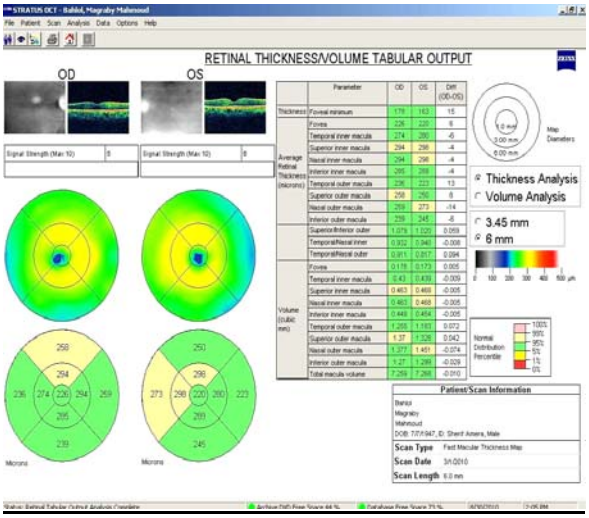

Fig.2 OCT of the same patient shows increased pericentral thickening.

Statistical methods

Data was revised for its completeness and consistency. Double data entry on SPSS program version 15 was done. Quantitative data was summarized by Mean, standard deviation while qualitative data was summarized by frequencies and percentages. Independent sample t test of significance was used in analysis of this study. A "P value" of less than 0.05 was considered statistically significant.

3. Results:

36 patients were included in this study. The

mean age of the patients was 56.6 (range 40-69), 21(58.3%) were males, and 15 (41.7%) were females.

The mean, standard deviation and range for the central fovea, fovea, 4 inner subfields and the 4 outer subfields are shown in **(Table 1).**

Table (1) Descriptive statistics of studied retinal values by OCT.

	Mean	SD	Range
Central fovea	176.1	42.6	121-270
Fovea	205.5	29.9	164-265
Temporal Inner (TI)	265.9	11.4	255-298
Superior Inner (SI)	278.0	10.1	261-298
Nasal Inner (NI)	268.0	10.7	254-294
Inferior Inner (II)	265.8	15.4	240-289
Temporal Outer (TO)	238.5	16.7	214-273
Superior Outer (SO)	238.0	11.3	222-258
Nasal Outer (NO)	239.4	18.1	217-268
Inferior Outer (IO)	240.5	10.4	218-258

58.3% (21/36) of our studied patients have changes in the central fovea and fovea either in the form of thickening or thinning. It shows: Significant thinning was found in 33.3% of the fovea of studied patients (12/36). Significant thickening was encountered in the central fovea in 25% of the studied eyes (9/36) **(Figure 3)**.

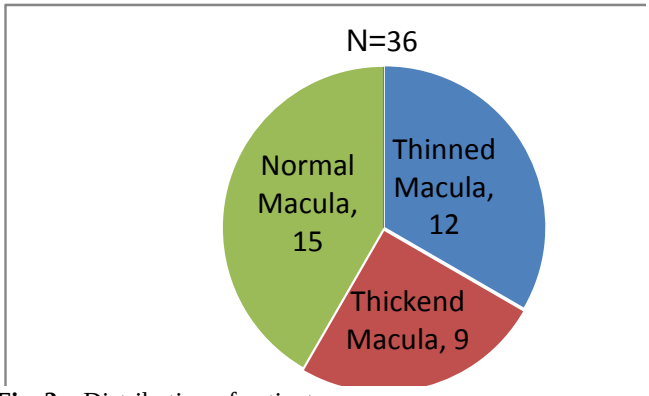

Fig. 3 Distribution of patients.

According to gender, the statistical analysis of data shows, a decrease in mean central foveal and foveal values among females (more thinning) compared to males; and the difference is highly significant statistically (P<0.01). There is a lower mean Temporal Inner quadrant (TI) value among females (more thinning) compared to males; and the difference is statistically significant (P<0.05) **(Table 2)**.

Table (2) studied OCT values comparison between males and females.

	Male(N=21) Mean ± SD	Female(N=15) Mean ± SD	t	P
Fovea minimum	198.5± 41.0	**144.8** ±18.4	3.8	**0.001****
Fovea	223.7± 25.3	**180.0**±11.4	5.0	**0.000****
TI	269.8± 13.4	**260.4**±4.0	2.1	**0.04***
SI	278.7± 12.4	277.2±5.9	0.3	0.7
NI	271.1±12.3	263.8±6.6	1.7	0.1
II	270.0±13.3	260.0±16.9	1.6	0.1
TO	239.7±18.5	236.8±14.7	0.4	0.6
SO	238.5±13.7	237.2±7.2	0.2	0.7
NO	235.2±14.6	245.2±21.6	1.3	0.1
IO	238.1±11.7	244.0±7.6	1.3	0.1

* P<0.05 Significant ** P<0.01 Highly significant

OCT values comparison related to age shows, a high mean central foveal and foveal values (Thickening) among older age group patients > 55years compared to younger patients and the difference is highly significant statistically (P<0.01). There are high mean values (Thickening) in Temporal Inner (TI) , Nasal Inner (NI) and Superior Outer (SO) quadrants among older age group patients compared to younger patients and the difference is statistically significant (P<0.05) **(Table 3)**.

Table (3) studied OCT values comparison related to age.

	<=55 years N=21 Mean±SD	> 55 years N=15 Mean±SD	t	P
Fovea minimum	150.4±18.9	**212.2**±40.6	5.0	**0.000****
Fovea	183.5± 12.3	**236.2**±16.8	8.8	**0.000****
TI	261.2± 5.5	**272.4**±14.4	2.6	**0.01***
SI	275.8±5.3	281.2±14.1	1.2	0.2
NI	263.1±5.8	**275.0**±12.5	2.7	**0.01***
II	262.1±14.5	271.0±15.8	1.4	0.1
TO	234.2±15.0	244.4±17.9	1.4	0.1
SO	233.7± 8.3	**244.0** ±12.6	2.4	**0.02***
NO	240.5±20.6	237.8±14.9	0.3	0.7
IO	241.7±7.7	239.0±13.7	0.6	0.5

* P<0.05 Significant ** P<0.01 Highly significant

4. Discussion

This clinical study *was conducted to* evaluate RT measurements with OCT in diabetic patients with minimal or no diabetic retinopathy. Our results show that 58.3% (21/36) of our studied patients have changes in the fovea and central fovea either in the form of thickening or thinning.

Biallosterski and co-workers demonstrated a significantly thinner pericentral RT at two different time points, in patients with DM type 1 and minimal DR compared to a healthy control group, supporting the hypothesis of neuroglial loss in the earliest stage of DR ***(Biallosterski et al., 2007)***.

A different study by Nilsson et al reported reduced retinal thickness in a subgroup of patients with DM with no or mild retinopathy and this observation supports the concept of low degree of neural damage ***(Nilsson et al., 2007)***.

The mean and superior quadrant peripapillary retinal nerve fibre layer thickness was slightly less in diabetic patients without abnormal vascular manifestations than in healthy subjects ***(Peng et al., 2009)***.

Reduced retinal nerve fiber layer thickness was found in the pericentral and peripheral regions and reduced thickness of ganglion cell/inner plexiform layer complex in the pericentral region of the in the mild diabetic retinopathy (MDR) group. Macular thickness was reduced in the pericentral and peripheral region of the macula in the MDR group.

The results support the view of neuro degeneration in diabetes in the early stage of retinopathy which seems to involve the ganglion cells and cells of the inner plexiform layers mostly ***(Cabrera DeBuc and Somfai, 2010)***.

Our results here show a decrease in the RT in the fovea in 33.3% of studied patients which is statistically significant. This could be attributed to neuroretinal degeneration that happens in the very early stages of diabetic retinopathy.

The macular thickness found in diabetic patients was always greater than that for control group. The OCT showed the existence of a correlation between macular thickness and retinopathy level. The patients with diabetic retinopathy and retinal thickening presented different degrees of oedema, and, as a result, variations of retinal thickness. According to gender; a significant result in the values of central foveal thickness was found. These values were greater for men than for women ***(Hannouche and Avila, 2009)***.

Mean retinal thickness was greater in diabetic patients (with and without DR) than in healthy subjects. Patients with DR had thicker retinas than patients without DR. Spectral-domain OCT seemed to be useful for the detection of early diabetic macular edema (DME) in patients with retinopathy and no clinical evidence of macular edema. Patients with early DME should have a closer follow-up ***(Koleva-Georgieva and Sivkova, 2010)***.

In our study we found increase in the RT in the central fovea in 25% of the studied eyes which is statistically significant. This could be explained by macular oedema which happens later during the process of the disease and could not be detected clinically or angiographically. We also found a significant difference in central foveal and foveal values between males and females being greater in males.

Two studies have suggested that patients with diabetes mellitus and no retinopathy have retinal thickness values that are similar to values from populations without diabetes and a normal retina ***(Massin et al., 2002), (Hee et al., 1998)***. However, these studies used an earlier model of OCT than is commonly available today.

Another study found no difference between patients with or without mild diabetic retinopathy and the control group for all OCT parameters investigated. This study suggests that MDR without macular edema in patients with T1D cannot be detected with OCT ***(Ciresi et al., 2010)***.

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