Relationship between mean macular thickness and visual acuity in diabetic patients

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Objective
The aim of the study was to correlate the relationship between optical coherence tomography (OCT) changes and visual acuity in patients with diabetic retinopathy (DR) compared with nondiabetic healthy persons.

Patients and methods
This study was done at Alforsan Eye Research Center, Assiut, Egypt. OCT was done at the center in the period from January 2018 to October 2018. This study was performed on 142 eyes of 71 adults who were divided into two groups. The first group was the diabetic group that included 102 eyes of 51 patients, whereas the second group was the nondiabetic group that included 40 eyes of 20 control.

Results
In this study, the mean macular thickness in normal individuals was (224.61 ± 8.8 μm). The authors found that the mean macular thickness of the diabetic patients included in this study was (327.9 ± 11.2 μm), which represents a statistically significant increase in thickness compared with the control ($P < 0.001$). Central macular thickness (CMT) measured by OCT was significantly correlated with best corrected visual acuity (r=−0.375 which represents a moderate significant negative correlation).

Conclusion
This study indicated that the CMT in OCT has a negative moderate correlation with visual acuity, which means that patients with decreased macular thickness have better visual acuity. The authors also reported a positive mild correlation between age in years and CMT, which means that increase in the age of patients was associated with an increase in CMT.

Keywords:
central corneal thickness, optical coherence tomography, visual acuity

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Introduction

Diabetes mellitus is one of the most common chronic diseases affecting all populations especially developed countries. Diabetic macular edema (DME), being a complication of diabetes, is an important cause of visual loss in developed countries.

DME has been reported at rates of 10% and occurs more frequently in type 2 diabetes mellitus than in type 1.

Macular edema can develop at any stage of diabetic retinopathy (DR), in the past; macular edema was diagnosed with slit-lamp view. Fundus fluorescein angiography provides guidance for the treatment of macular edema.

DME is a major cause of vision loss in patients with both insulin-dependent and non-insulin-dependent diabetes mellitus. Classically, patients have a gradual onset of blurred vision, and in more advanced cases, the macula becomes thickened and even cystic with profound visual loss [1].

Several therapeutic modalities have been reported including grid laser photocoagulation, vitrectomy, intravitreal injection of triamcinolone acetonide, anti-VEGF, (Vascular Endothelial Growth Factor) or combined treatment. Through these studies the authors have found that some eyes with DME have poor visual outcomes despite successful treatment and complete resolution of edema which suggests that macular thickness is only one of the several factors to affect best corrected visual acuity (BCVA) [2].

Aim

The aim of the study was to correlate the relationship between optical coherence tomography (OCT) changes and visual acuity in patients with DR compared with nondiabetic healthy persons.

Patients and methods

The study was approved and monitored by the Medical Ethics Committee, Assiut Faculty of Medicine.

The investigators explained the steps and value of the research to all eligible participants. Those who agreed to be included in the study signed a fully informed consent.

Patients

A prospective noninterventional study (case–control study) that included 142 eyes of adults:

(1) 102 eyes in the diabetic group (51 patients).
(2) 40 eyes in the nondiabetic group (20 controls).

A written consent was signed by all participants after discussing the procedure. The study was done at Alforsan Eye Research Center, Assiut, Egypt.

Inclusion criteria

(1) Diabetic patients having either nonproliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR).
(2) Nondiabetic healthy persons (controls).

Exclusion criteria

(1) Previous ocular surgery.
*Silicon-filled eyes.
(2) Patients with media opacities.
*Dense cataract, corneal opacities, and vitreous hemorrhage.
(3) Uncontrolled hypertension.
(4) History of intraocular inflammation such as anterior or posterior uveitis.

Duration of the study

From January 2018 to October 2018.

Methods

All patients were subjected to the following examinations:

(1) Ocular examination.
(2) BCVA, assessed by Snellen's chart.
(3) Central macular thickness (CMT) from ETDRS macular thickness map of optical coherence tomography (DRI OCT Triton; Topcon, Dublin, California, USA).

Ethical considerations

An informed consent was obtained and signed from the participants of the study. Confidentiality was maintained during the whole study. The steps and results of the investigations of the study were explained to them.

Statistical analysis

Data were verified, coded by the researcher, and analyzed using IBM-SPSS 21.0 (IBM-SPSS Inc., Chicago, Illinois, USA).

Results

Sociodemographic differences between DR cases and control

Age distribution of patients

We studied 142 eyes of adults, 102 eyes in the diabetic group (51 patients) with a mean age of 56.94 ± 9.8 (32–83) years and 40 eyes in the nondiabetic group (20 controls) with a mean age of 28.1 ± 7.8 (20–47) years (Table 1).

Regarding the participant's age (years), DR cases were significantly older (56.9 years) compared with controls (28.1 years). For DR cases, the age ranged from 32 to 83 years while for the control group it ranged from 20 to 47 years ($P < 0.001$).

Sex distribution of patients

The study included 142 eyes; of the cases, 49% ($n = 25$) were men and 51% ($n = 26$) were women. Likewise, 25% ($n = 5$) of the controls were men and 75% ($n = 15$) were women (Table 1).

Additionally, there was statistically insignificant distribution of the sexes between DR cases and controls ($P > 0.05$).

The effect of DM on visual acuity and macular thickness

The mean UCVA value was lower (0.23 ± 0.1) in the DR case in comparison with the control group (0.95 ± 0.05).

This association was statistically significant ($P < 0.001$). Likewise, DR cases reported lower mean BCVA

Table 1 Sociodemographic differences between diabetic retinopathy cases and control

Parameter	DR cases (*n*=51)	Control (*n*=20)	*P*
Age (years)			**<0.001***
Mean±SD	56.94±9.8	28.10±7.8	
Median (range)	56 (32-83)	26.5 (20-47)	
Sex [*n* (%)]			0.065**
Female	26 (51)	15 (75)	
Male	25 (49)	5 (25)	

DR, diabetic retinopathy. *t-test was used to compare the mean difference between groups. **χ^2-test was used to compare the proportion difference between groups.

values (0.38 ± 0.2) than the control group (0.95 ± 0.05). This association was also statistically significant (P < 0.001). Moreover, the mean CMT was statistically higher (327.9 ± 11.2 μm) in the DR group compared with the control group (224.61 ± 8.8 μm) (P < 0.001) (Table 2).

Independent effect of diabetes on visual acuity and macular thickness: multivariate logistic regression analysis

The multivariate regression analysis is used to detect the independent predictors of DR. The unadjusted model included age, sex, UCVA, BCVA, and CMT. In other words, with a 1-year increase in age there was 33% increase in the risk of getting DR and this was statistically significant (P < 0.001). Moreover, male respondents had 3.22 times increase in the risk of getting DR and this was statistically significant (P < 0.05). Also, with 1-μm increase in CMT, there was 5% increase in the probability of having DR, which was statistically significant (P < 0.05). However, with one-point increase in UCVA there was 97% decrease in the probability of having DR, which was statistically significant (P < 0.05). Likewise, with 1-point increase in BCVA there was 95% decrease in the probability of having DR, which was statistically significant (P < 0.05).

After adjusting for age and sex, the final adjusted logistic regression model contained CMT only. In other words, with 1 μm increase in CMT there was 2.5% increase in the probability of having DR, which was statistically significant (P < 0.05) (Table 3).

Table 2 Effect of diabetes on visual acuity and macular thickness

Parameters	DR cases (n=102)	Control (n=40)	P
UCVA			
Mean±SD	0.23±0.1	0.95±0.05	<0.001*
Median (range)	0.2 (0.05-1.0)	0.9 (0.9-1.0)	
BCVA			
Mean±SD	0.38±0.2	0.95±0.05	<0.001*
Median (range)	0.4 (0.05-1.0)	0.9 (0.9-1.0)	
CMT			
Mean±SD	327.91±11.2	224.61±8.8	<0.001*
Median (Range)	294 (167-765)	227 (207-243)	

BCVA, best corrected visual acuity; CMT, central macular thickness (μm); UCVA, uncorrected visual acuity. *t-test was used to compare the mean difference between groups.

DR staging of the studied DR cases

There were two main stages in NPDR and PDR.

NPDR represented 69% of cases (n = 70) which was subdivided into 4%, mild (n = 4); 63% moderate (n = 64); and 2%, severe (n = 2)).

PDR represented 31% of cases (n = 32) (Table 4).

The correlation between visual acuity parameter and central macular thickness and other disease correlates

There was statistically significant (P < 0.001) negative moderate correlation between BCVA and CMT (r=–0.375), that is, increase in CMT was associated with a decrease in BCVA (Table 5).

Unlike, there was statistically significant (P = 0.009) positive mild correlation between age in years and CMT (r = 0.232), that is, increase in the age of patient was associated with an increase in CMT. The correlation between CMT or BCVA and disease duration and age in years were statistically insignificant (P > 0.05) no or mild correlations (r<±02).

Relationship between BCVA and CMT and their correlates among the studied DR cases

There were statistically significant differences in mean CMT according to sex (P = 0.005); women had higher mean CMT (358.7 ± 19.5) compared with men (297.1 ± 9.3).

Multivariate linear regression analysis of significant factors affecting CMT

The final linear regression model contained four predictors: sex, type of DM, duration of DM, and BCVA.

In a nutshell, the intercept (CMT) values was 374.8 μm (152–597 μm) after adjusting for all correlates (P < 0.001). Moreover, male patients had lower CMT value by 72.5 μm (–115 to –30 μm) compared with women (P = 0.001). Also, patients with type 2 DM had higher CMT value by about 27 μm (8–68 μm) compared with those with type 1 DM (P = 0.002). Furthermore, patients with DM

Table 3 Independent effect of diabetes on visual acuity and macular thickness: multivariate logistic regression analysis

Factors	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	LRT P
Age (years)	1.327 (1.191--1.478)	<0.001	1.340 (1.141-2.574)	**0.001**
Sex (male)	3.222 (1.390-7.470)	=0.006	1.208 (0.299-9.411)	0.287
UCVA	0.030 (0.001-0.060)	<0.001		
BCVA	0.049 (0.002-0.099)	<0.001		
CMT	1.052 (1.028-1.077)	<0.001	1.024 (1.001-1.181)	**0.017**

BCVA, best corrected visual acuity; CI, confidence interval; CMT, central macular thickness; LRT, likelihood ratio test; OR, odds ratio; UCVA, uncorrected visual acuity.

disease duration greater than or equal to 15 years had higher CMT value by about 50.5 μm (8–93 μm) compared with those with DM disease duration less than 15 years (P = 0.012). Finally, with one-point increase in the BCVA there was about 186 μm (−243 to 138 μm) decrease in CMT value and this was statistically significant (P < 0.001) (Table 6).

Discussion

DME is a major cause of visual deterioration in DR. The concern in studying DME is directed toward early detection of vision-threatening changes before they become clinically detectable and hence we can avoid irreversible damage to retinal elements in this group of patients.

Our study was conducted on 142 eyes of 71 subjects classified into two groups: group A contained 102 eyes of 51 diabetic patients, having DR. Their mean age was 56.94 ± 9.8 years (range 32–83 years) and the mean duration of diabetes was 15.7 ± 6.3 years with a median of 15 years (7–33 years). The patients were 26 women and 25 men.

Group B contained 40 eyes of 20 normal individuals and used as a control group; their ages ranged from 20 to 47 years. Controls were 5 men and 15 women.

Table 4 Diabetic retinopathy staging of the studied cases

Variables	Category	Subcategory	*n*=102 [*n* (%)]
DR	NPDR (*n*=70)	Mild	4 (3.9)
		Moderate	64 (62.8)
		Severe	2 (1.9)
	PDR (*n*=32)		32 (31.4)

DR, diabetic retinopathy; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Table 5 Correlation between best corrected visual acuity, central macular thickness, age, and disease duration among cases (*n*=102)

	BCVA		CMT	
	*r**	*P***	*r*	*P*
BCVA	1		-0.375	**<0.001**
Age (years)	−0.049	0.321	0.232	**0.009**
Disease duration (years)	−0.112	0.129	0.147	0.068

BCVA, best corrected visual acuity; CMT, central macular thickness. *Pearson's correlation coefficient. **Based on normal approximation.

In our study, the mean macular thickness in normal individuals was (224.61 ± 8.8 μm); this value lies within the range reported by several authors. Hee and colleagues found that the mean macular thickness of normal individuals was 147 ± 17 μm. In the study conducted by Nasr and colleagues, the normal macular thickness was estimated to be 148 ± 5.3 μm. Otani and colleagues reported that the retinal thickness at the central macula was 133.4 ± 9.3 μm. Schaudig and colleagues estimated macular thickness of 152 ± 17 μm. Neubauer and colleagues found that the mean macular thickness of normal eyes measured was 153 um with OCT and the results of Goebel and Kretzchmar-Gross, 153 ± 15 μm, were consistent with the above values, and with our results.

In our study, we found that the mean macular thickness of the diabetic patients (group A) included in this study was (327.9 ± 11.2 μm), which represents statistically significant increase in thickness compared with the control (P < 0.001). Previous studies reported variable figures for macular thickness in cases of DME; these figures may vary according to the duration of macular edema which may influence both anatomic and functional results as mentioned by Yamamoto and colleagues.

In the study of Otani and colleagues, the mean macular thickness was 424.6 ± 18 μm in eyes with diffuse macular edema, and 527.6 ± 18 μm in eyes with cystoid macular edema. Yang and colleagues reported a mean macular thickness of 255.6 μm in eyes with CSME, and 174.6 μm in eyes without CSME.

In the study of Yamamoto and colleagues, the mean macular thickness was increased to 252.7 μm in patients with diffuse macular edema and to 537.1 μm in patients with cystoid macular edema.

In our study, macular thickening by OCT was also generally correlated with clinical diagnosis; however, there were many occasions in which OCT detected thickening in areas that clinically appeared normal. This observation goes in accordance with the study of Hee and colleagues. Also, Schaudig and colleagues demonstrated significant retinal swelling or cystoid macular edema with the use of OCT in more than half of the eyes of their study in the absence of

Table 6 Independent correlates of central macular thickness; multiple linear regression analyses

	Estimate	SE	*t*-statistics	*P*
Intercept	374.84 (152.3: 597.4)	34.4	13.94	<0.001
Sex (male)	−72.50 (−115.1: −29.9)	−21.5	−3.44	=0.001
Type 2 DM	26.99 (8.4: 68.3)	14.7	12.35	=0.002
DM duration (>15 years)	50.45 (7.8: 93.1)	21.5	2.35	=0.012
BCVA	−185.75 (−233.7: −137.8)	24.3	−7.7	<0.001

BCVA, best corrected visual acuity; CI, confidence interval; DM, diabetes mellitus; LRT, likelihood ratio test.

ophthalmoscopic evidence of CSME. Consequently, Yang and colleagues suggested that the ETDRS standard for defining CSME seems to be insufficient in really identifying macular edema. Alternatively, OCT may be more sensitive than a clinical fundus examination for early detection of intraretinal changes in DME. This is confirmed by Browning and colleagues, who suggested that the wider use of OCT may beneficially impact visual disability from DME.

In our study, CMT measured by OCT was significantly correlated with BCVA (r=–0.375 which represents moderate significant negative correlation, $P < 0.001$).

This observation agrees with previous studies conducted by several authors.

Otani and colleagues found negative correlation between macular thickness and BCVA (correlation coefficient: r=–0.61, $P < 0.01$), in eyes with diffuse macular edema, and a similar correlation in eyes with cystoid macular edema (correlation coefficient: r=–0.64, $P < 0.01$).

Yamamoto and colleagues also reported a significant correlation between BCVA and macular thickness (r=–0.76, $P < 0.001$). All these studies in addition to our findings confirm the earlier suggestion of Nussenblatt and colleagues, who reported that actual macular thickness is better correlated with visual loss in patients with DR.

The relationship of visual acuity and OCT-measured central retinal thickness before intervention is roughly linear. Other studies such as Bandello and colleagues; Otani and colleagues; Martidis and colleagues; Laursen and colleagues; Catier and colleagues; Ozdemir and colleagues; Massin and colleagues; Goebel and colleagues; and Hee and colleagues have found similar results; however, the strengths of correlation have varied widely [3–11].

The variance of ETDRS letters read at any given observed center point thickness is large, and there may be a tendency for a greater spread in letters read in thicker maculas. Most eyes with DME have center point thicknesses of less than 400μm (74%). In the study of Browning and colleagues, the standard deviation in letters read for any given center point value is 9.7 (~two ETDRS lines), illustrating how crude OCT center point thickness is as a surrogate index for visual acuity. For the very edematous eyes, the spread is even greater.

Conclusion

We found significant negative moderate correlation between BCVA and CMT, that is, increase in CMT was associated with a decrease in BCVA.

We concluded that the VA in DR is multifactorial and the CMT is only one of the many other factors; some of them have been proved, others are still under trial and many others have not discovered yet.

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Conflicts of interest

There are no conflicts of interest.

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