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Macular thickness measurement in clinically significant macular edema before and after meal

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Abstract

***Purpose*:** To evaluate the macular thickness changes in diabetic macular edema after meal.
***Methods*:** In this prospective case series, macular thicknesses of diabetic patients with clinically significant macular edema (CSME) were measured after 7 h of fasting and repeated 2 h after breakfast.
***Results*:** Thirty six eyes of 20 diabetic patients were evaluated. The mean central subfield thickness (CST) and maximum retinal thickness (MRT) significantly decreased after meal (mean change of -10.3 ± 14.3 μm and -13.1 ± 12.7 μm, respectively, both $P < 0.001$). A decrease in CST and MRT values was found in 23 (63.8%) and 28 (77.7%) eyes, respectively, and no eye had an increase in retinal thickness measurements. Significant correlation was found between CST and MRT change and fasting thickness measurements ($P = 0.001$ and $P = 0.01$, respectively) and intraretinal cystic spaces ($P = 0.001$ and $P = 0.03$, respectively). Mean MRT change was significantly higher in the presence of subretinal fluid ($P = 0.01$).
***Conclusion*:** Retinal thickness measurements may change after meal. So, fasting state of diabetic patient should be considered in measurement of macular thickness of patients with CSME.

Keywords: Diabetic Macular Edema; Retinal thickness; Fasting; Meal

Introduction

Optical coherence tomography (OCT) imaging is commonly used for qualitative and quantitative assessment of various vitreoretinal pathologies. It is also the preferred method for objective monitoring of disease progression and response to treatment in many large clinical trials.[1]

Despite the advantages of OCT compared to other imaging modalities, caution is still required in the interpretation of OCT images, as many factors may affect the repeatability of OCT measurements. Various types of artifacts including operator-induced acquisition errors, patient motion or eccentric fixation, and segmentation errors have been reported.[2–5] Also, media opacity, large refractive error and pupil size may affect OCT measurements.[6–8]

Few studies have reported diurnal variations in macular thickness in normal subjects and patients with macular diseases.[9–17] In diabetic macular edema (DME), significant diurnal changes have been reported in retinal thickness measurements.[12–15] These changes have been ascribed to the changes in blood pressure, retinal metabolism, and standing

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position.[12,13] In a literature search using the Pubmed database, we did not find any study specifically reporting the retinal thickness changes in eyes with diabetic macular edema, in relation to fasting and meal.

In this study we evaluated the macular thickness changes between the fasting state and after eating in patients with diabetic macular edema.

Methods

This study was a prospective case series. From July to August 2013, diabetic patients who met the inclusion criteria were studied. The study was approved by the Rassoul Hospital Eye Research Center Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Inclusion criteria were clinically significant macular edema (CSME) in fundus examination and a central subfield thickness (CST) of >250 μm (μm) in OCT examination. Diabetic eyes with opaque media preventing OCT imaging, history of intraocular surgery or macular or retinal photocoagulation within the recent 6 months, and those with choroidal neovascularization or Retinal vein occlusion or any other ocular pathology were excluded. Also excluded were subjects with spherical refraction of more than 6 diopters of myopia or 3 diopters of hyperopia.

For OCT imaging, a Topcon instrument (Topcon 3D-OCT 1000; Topcon Corp.) with a 6 × 6 mm 3D macular scan protocol was used. An expert examiner (FA) performed all OCT examinations. Patients were asked to fixate on an internal fixation target during the scanning process and if fixation was not central, the external fixation target was used to move the scanning area centrally over the macula. OCT scans were segmented automatically by the segmentation algorithms incorporated in the Topcon 3D OCT 1000 software, which demarcates the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE) and the retinal thickness map was generated. For each eye, the CST of the automatically-registered ETDRS grid over the topographic map was recorded. If the ETDRS grid was not properly placed over the fovea, the grid was manually moved to the correct position. The retinal thickness map was scanned by moving the computer curser in the macular area and the point with the highest retinal thickness was recorded as maximum retinal thickness (MRT). Scans with a quality factor <40 and blinking during the scanning process were excluded.

The OCT examination was performed at the 7-8 AM after 7 h of fasting and then repeated 2 h after breakfast. No change was made in the protocol of the patients' medications.

Data were analyzed using a SPSS software (version 15, SPSS Inc. Chicago, IL). To evaluate the differences in retinal thickness between fasting and after meal measurements, a paired t test was performed. A student t test was used to evaluate the difference in mean thickness changes in different subgroups. The correlation between the changes in thickness measurements and the age and fasting thickness measurements was evaluated by Pearson's correlation analysis. A $P < 0.05$ was considered significant. Changes >1 μm in CST and MRT were recorded, while changes >14.5 μm were recorded as clinically significant.[16]

Results

Thirty six eyes of 20 diabetic patients with a mean age of 59.8 ± 7.8 years were studied. Ten patients were men (50%). Subretinal fluid and epimacular membranes were found in 5 (13.8%) and 5 (13.8%) eyes, respectively. All eyes had intraretinal cystic changes, however, the cystic changes involved >50% of retinal thickness in 15 eyes (41.6%).

The mean CST statistically significantly decreased after meal (mean change of −10.3 ± 14.3 μm, $P < 0.001$, Table 1). Similarly, the change in mean MRT measurements was statistically significant (mean change of −13.1 ± 12.7 μm, $P < 0.001$). To remove the effect of including 2 eyes of the patients in the study, the analysis repeated with only right eyes of patients (in addition to the patients with only one eye included in the study). The analysis revealed the same results ($P < 0.001$ for both CST and MRT). A decrease in CST and MRT values was found in 23 (63.8%) and 28 (77.7%) eyes, respectively. No eye had an increase in retinal thickness measurements. Clinically significant changes were found in 10 eyes (27.7%) for CST and 12 eyes (33.3%) for MRT measurements.

Table 2 shows the effect of intraretinal cystic spaces, epimacular membrane and subretinal fluid on thickness changes. CST and MRT changes were not correlated with age ($P = 0.3$ and $P = 0.2$, respectively), however, significant correlation was found between CST change and fasting CST measurements ($P = 0.001$) and between MRT change and fasting MRT measurements ($P = 0.01$). Mean CST change was not significantly affected by the presence of the subretinal fluid and epimacular membrane ($P = 0.3$, and $P = 0.4$, respectively). Mean MRT change was significantly higher in the presence of subretinal fluid ($P = 0.01$), however, it was not statistically affected by epimacular membrane ($P = 0.6$). Mean CST and MRT changes were statistically significantly higher in eyes with intraretinal cystic spaces of >50% of the retinal thickness ($P = 0.001$ and $P = 0.03$, respectively).

Discussion

Previous studies reported the diurnal variation of retinal thickness in patients with macular edema using time-domain OCT instruments.[12–15] They showed a decrease in retinal thickness over time, however, did not report the timing of the OCT examinations in relation to the fasting status of the patients. In the largest study, 156 eyes of 96 DME patients were evaluated. The mean central macular thickness of 368 μm in the morning decreased by 13 μm in the evening and the

Table 1
Retinal thickness measurements before and after meal in diabetic eyes with clinically significant macular edema.

	Fasting	Two hours after meal	P value
Central subfield thickness (μm)	385.1 ± 145.1	375.5 ± 136.5	<0.001[a]
Maximum retinal thickness (μm)	518.1 ± 137.3	504.9 ± 122.7	<0.001[a]

[a] Paired t test.

Table 2
Mean retinal thickness changes in various morphologic subgroups of diabetic eyes.

	Present	Absent	P value
Intraretinal cysts of >50% of retinal thickness			
Central subfield thickness (μm)	22.9 ± 18.2	4.8 ± 7.6	0.001[a]
Maximum retinal thickness (μm)	19.8 ± 14.3	10.2 ± 11.0	0.03[a]
Subretinal fluid			
Central subfield thickness (μm)	15.6 ± 18.4	9.4 ± 13.7	0.3[a]
Maximum retinal thickness (μm)	26.6 ± 17.2	10.9 ± 10.3	0.01[a]
Epimacular membrane			
Central subfield thickness (μm)	12.8 ± 14.5	9.9 ± 14.5	0.4[a]
Maximum retinal thickness (μm)	18.0 ± 10.6	12.3 ± 13.0	0.6[a]

[a] Student t test.

change was significantly greater in retinas that were thicker at morning. The change in retinal thickness correlated weakly ($r = -0.13$) with change in blood glucose.[14] Kotsidis et al[12] evaluated 24-h variation in retinal thickness in 53 eyes with DME. The CST showed significant change over time and reached a minimum at 3 pm. Thickening changes were higher in more thickened retinas, however, blood pressure, blood glucose, and body temperature did not vary over time. Frank, et al[15] reported that retinal thickening in 10 eyes with DME varied according to time of day. Four of the 10 subjects had decreased thickening in one or both eyes and the eyes with greater initial retinal thickening tended to show a greater change over the day.

The pathophysiology of the diurnal variation in retinal thickness remained unknown. The proposed mechanisms include the effect of gravity and hydrostatic pressure on edema formation, nocturnal hypotension, and improved retinal perfusion and oxygenation associated with an improved retinal arterial perfusion pressure during waking hours.[12,13] Considering the lack of the data in the previous studies regarding the fasting condition of the patients during measurements, we evaluated the changes in the retinal thickness in relation to meal. Our results show that retinal thickness measurements significantly decrease after meal. The diurnal variation reported in the previous studies may be explained according to the fasting condition of the patient. Several studies have shown that retinal blood flow increases after acute elevation of blood glucose level in diabetic patients.[18–21] Arlotte et al[18] showed an increase in oscillatory potentials of electroretinography, which is a reflection of retinal circulation, within 90 min after a meal. Similarly, Holfort et al[19] reported dark adapted retinal function increased after acute hyperglycemia. These are in agreement with laser Doppler velocimetry studies in which significantly increased retinal blood flow was found at higher blood glucose levels in patients with diabetic retinopathy.[20,21] Also, Oomen et al[22] showed that hyperglycemia results in an increase in laser Doppler flow without changes in endothelial dysfunction. It may be concluded that increased retinal circulation after postprandial hyperglycemia results in absorption of the intracellular and extracellular fluid, and decreased retinal thickness.

Central subfield thickness measurement is used by large clinical trials to study the effect of treatment modalities on diabetic macular edema.[23] Our results show a clinically significant change of 27.7% after meal. The changes were more prominent in the presence of significant intraretinal cystic spaces and subretinal fluid. In patients with focal non-central CSME, CST is normal and the changes after treatment may be evaluated using the maximum point of retinal thickness. We found a high rate of clinically important change in MRT after meal.

Our study has some limitations. The sample size is small. We did not evaluate the changes in normal subjects. Also, we did not measure the blood sugar to see the correlation with the changes in retinal thickness. The blood glucose level at fasting and after breakfast would be of particular importance, which may be directly related to the macular thickness changes observed in this study. Despite these limitations, our study is the first that shows significant changes in retinal thickness measurements in diabetic macular edema after meal. The retinal thickness changes in relation to fasting state should be taken into account when evaluating the effect of a treatment modality in diabetic macular edema. Future studies with larger sample size and the blood sugar measurements are needed to further elucidate our results. Thickness measurements after 2 h awakening without having breakfast may explain the effect of gravity and upright position.

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