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ORIGINAL ARTICLE

# Correlation between optical coherence tomography-derived macular measurements and glycosylated haemoglobin, age, visual acuity and diabetes duration in patients with type 2 diabetes mellitus

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**Abstract** This study aims to correlate optical coherence tomography (OCT)-derived macular measurements and glycosylated haemoglobin (haemoglobin A1c, HbA1c), age, visual acuity and the duration of diabetes in patients with type 2 diabetes mellitus (DM). In this observational, cross-sectional study, measurements for central macular thickness (CMT), average macular thickness (AMT) and macular volume (MV) were obtained using OCT in 165 eyes of 165 patients with type 2 diabetes mellitus. The level of HbA1c, age, visual acuity and duration of diabetes were taken and compared to the macular measurements. The mean age of the patients was 61.26 years. The duration of DM and level of HbA1c was 12.95 years and 8.10 %, respectively. HbA1c showed a modest, positive correlation with AMT ($r$=0.304, $p$<0.05) and MV ($r$=0.349, $p$<0.05) but was poorly correlated with CMT ($r$=0.160, $p$<0.05). Age was inversely correlated with AMT ($r$=−0.227, $p$<0.05) and MV ($r$=−0.275, $p$<0.05). No correlation was found between the duration of DM and all macular measurements. Near visual acuity had a slightly higher correlation with macular thickness and volume compared to far visual acuity, although the correlation strength was weak. HbA1c, age and near visual acuity are moderately correlated with AMT and MV. Among these, MV had the strongest correlation with HbA1c. Our results suggest that HbA1c may be used as an early predictor of OCT-derived macular volume changes and thus plays an important role in the early identification and manifestation of diabetic macular oedema.

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## Introduction

Diabetic retinopathy, one of the most common complications of diabetes, continues to be a major public health concern with significant socioeconomic impact. Diabetic macular oedema (DMO), which is a manifestation of diabetic retinopathy, is the leading cause of visual loss in the diabetic population [1]. The changes in macular thickness and volume are often seen in DMO. Evolving trends of higher prevalence of diabetic patients in a younger age group necessitates the early diagnosis of DMO. Although slit lamp biomicroscopy and fundus photography remain as reliable screening methods, the advent of more objective methods to quantify macular measurement may contribute to the ease and accuracy of earlier diagnosis.

Optical coherence tomography (OCT) enables us to better study the structures of the macula. OCT also allows detection of minimal changes in macular thickness and volume which may not be identified by slit lamp biomicroscopy or fluorescein angiography [2–4]. Furthermore, these devices are dependent on the observer experience and most often do not offer a reproducible measurement. In previous studies, OCT measurements of macular thickness and volume have been demonstrated to be very reliable and precise [5–7]. Several studies have reported demographic and clinical characteristic factors that could affect the macular thickness and volume. However, only a few were conducted among type 2 diabetic patients in the Asian population. Furthermore, previous

studies have reported different degrees of correlation between OCT-measured macular thickness and volume and the level of haemoglobin A1c (HbA1c), age, visual acuity and the duration of diabetes mellitus (DM).

In this study, we assessed the relationship of macular thickness and volume to HbA1c, age, visual acuity and DM duration in patients with type 2 diabetes. We particularly intended to determine which of these factors best correlates with the changes in macular thickness and volume.

## Methods

### Patients

One hundred and sixty-five patients with type 2 diabetes mellitus (DM) who attended the ophthalmology clinic at the University of Malaya Medical Centre, Kuala Lumpur, Malaysia, between July 2009 and January 2010, were recruited in this observational, cross-sectional study. Ethics Committee approval was obtained and all participants gave their informed consent.

Patients with type 2 DM above 30 years of age were included in this study. Patients were excluded if they had (1) previous eye injury causing ocular derangement, retinal scarring or media opacity; (2) images with signal strengths weaker than 5 (on a scale from 0 to 10); (3) any cause of maculopathy other than diabetes; (4) patients who underwent intraocular surgery, laser therapy or intravitreal injection within 1 year of evaluation; and (5) patients with anaemia, haemoglobinopathies or uncontrolled hypertension (dBP> 90 mmHg, sBP>140 mmHg).

Only the right eye was examined in the study. In cases where the right eye did not fulfil the above mentioned criteria, the left eye was examined. The ophthalmological examinations included refraction and best corrected visual acuity, anterior segment examination, intraocular pressure measurement and fundus examination performed using the slit lamp and biomicroscope +78 D lens. Age and the duration of type 2 DM was recorded. The level of glycosylated haemoglobin (HbA1c) was measured, after which OCT was performed.

### Optical coherence tomography measurements

Optical coherence tomography (OCT) scanning was performed on all patients using the Cirrus HD OCT (Carl Zeiss Meditec, Dublin, CA, USA) version 3.0. Macular thickness and volume was obtained from the right eye of the patients after pupil dilatation using tropicamide 1 % and phenylephrine 2.5 %. Measurement of the central macular thickness (CMT) was taken between the internal limiting membrane (ILM) and the retinal pigmented epithelium (RPE) of the circle with a radius of 500 mm centred on the fovea. Average macular thickness (AMT) measurement was taken between the ILM and the RPE tissue layer over the entire 6×6 $mm^2$ scanned area centred on the fovea. Macular volume (MV) was measured between the ILM and RPE at a fixed diameter (6×6 $mm^2$) around the central foveal pit.

**Table 1** Demographics and clinical characteristics of patients in this study ($n$=165)

| Characteristics | Mean±SD |
|---|---|
| Age (years) | 61.26±9.24 |
| Gender (male/female) | 1:1.09 |
| Duration of DM (years) | 12.95±9.11 |
| HbA1c (%) | 8.10±1.63 |
| Central macular thickness (μm) | 262.16±34.09 |
| Average macular thickness (μm) | 278.8±22.14 |
| Macular volume ($mm^3$) | 9.96±0.79 |

*DM* diabetes mellitus; *HbA1c* haemoglobin A1c

### Statistical analysis

Pearson's correlation coefficient was used to evaluate the relationship between HbA1c, age, visual acuity and duration of DM. Statistical analyses were performed using the Statistical Package for the Social Sciences, Version 17.0 (SPSS Inc., Chicago, IL, USA). A $p$ value of <0.05 was considered to be statistically significant.

**Table 2** Correlation between central macular thickness, average macular thickness and macular volume with glycosylated haemoglobin (HbA1c), age, visual acuity and diabetes mellitus duration

| | Correlation coefficient ($r$) | $p$ value |
|---|---|---|
| CMT-HbA1c | 0.160 | < 0.05 |
| CMT-age | −0.012 | NS |
| CMT-DM duration | −0.041 | NS |
| CMT-near visual acuity | 0.214 | < 0.05 |
| CMT-far visual acuity | 0.140 | NS |
| AMT-HbA1c | 0.304 | < 0.05 |
| AMT-age | −0.227 | < 0.05 |
| AMT-DM duration | −0.020 | NS |
| AMT-near visual acuity | 0.274 | < 0.05 |
| AMT-far visual acuity | 0.192 | < 0.05 |
| MV-HbA1c | 0.349 | < 0.05 |
| MV-age | −0.275 | < 0.05 |
| MV-DM duration | −0.028 | NS |
| MV-near visual acuity | 0.242 | < 0.05 |
| MV-far visual acuity | 0.165 | < 0.05 |

*AMT* average macular thickness, *CMT* central macular thickness, *DM* diabetes mellitus, *HbA1c* haemoglobin A1c, *MV* macular volume

## Results

Demographics and clinical characteristics of 165 patients are shown in Table 1. The age of all patients was between 34 and 82 years, with the duration of DM ranging from 0.25 to 40 years. The value of HbA1c was in the range of 4.9 to 13.4 %. Of the 165 patients, 117 patients had no maculopathy, 48 had maculopathy without clinically significant macular oedema (CSME) and 20 had maculopathy with CSME. Further analysis showed statistically significant differences in the mean macular measurements between these three subgroups ($p<0.01$).

Using OCT, the central and average macular thickness as well as the macular volume for all patients were evaluated. HbA1c showed a moderately positive correlation with AMT and MV, but a weaker correlation with CMT (Table 2). There was a modest, statistically significant inverse correlation between age and AMT and MV, but not CMT. No significant correlation was found between the duration of diabetes and CMT, AMT or MV. Near visual acuity had a slightly stronger positive correlation with CMT, AMT and MV as compared to far visual acuity. Compared to age and visual acuity, HbA1c showed the strongest correlation to macular volume in patients with type 2 diabetes.

## Discussion

In the present study, we identified HbA1c, age and visual acuity as factors that significantly affected central and average macular thickness as well as macular volume in patients with type 2 diabetes. Our results showed that age was inversely correlated with AMT and MV. The thinning of the macular could possibly be due to neuronal degeneration in diabetic patients. Our finding was consistent with previous studies on the correlation between age and macular measurements in diabetic patients [7–10]. Sng and co-workers pointed out that macular thinning that occurs with age was non uniform as they found greater foveal thickness but reduced macular volume with increasing age [10]. This would likely explain the reason CMT was not significantly correlated with age in our study. It is also noteworthy that in most studies which assessed the relationship between age and macular measurements using OCT in subjects with healthy eyes, no significant correlation was found [11–13].

In this study, we demonstrated that HbA1c had a moderately positive correlation with AMT and MV. This was consistent with several studies [8, 9, 14, 15] and inconsistent with others [10, 16]. The variability seen in these studies could possibly be due to a few factors. Firstly, different studies could have assessed macular thickness using different OCT devices [17, 18]. Secondly, some studies included subjects with macular oedema while others only recruited diabetic patients with no or mild diabetic retinopathy [19–21]. Thirdly, some studies did not adjust for age and gender which are possible confounders for macular thickness measurement [13, 20, 22]. In this study, the correlation between HbA1c and MV was stronger than those between CMT or AMT and age or visual acuity. Thus, we proposed that HbA1c is a more significant predictor of the changes in macular volume.

To the best of our knowledge, no studies have characterized visual function into near or far visual acuity and correlated them with macular measurements in diabetic patients. In this study, we found that near visual acuity had a moderately positive correlation with macular thickness and volume while far visual acuity had a weak correlation. Near visual acuity is therefore a better predictor of the changes in macular thickness and volume, although further studies are required to corroborate our findings.

No correlation was observed between the duration of diabetes and macular thickness or volume. However, in a study by Asefzadeh et al. [23] on diabetics with no or mild non-proliferative diabetic retinopathy (NPDR), they found that the fovea was significantly thinner with longer duration of disease. This was thought to be due to the neurodegenerative changes associated with diabetic retina over time. The discrepancies between our results and the former study could be due to the difference in patient recruitment, with the absence or severity of diabetic macular oedema. Interestingly, a study by Chou et al. found a significant relationship between macular thickness and DM duration of less than 10 years, but no relationship was found in patients with more than 10 years of the disease. This result corresponds to our study where the mean DM duration in our patients was 12.95 years.

Recently, it has been proposed that accommodation-induced changes in retinal thickness in the macular area may be a confounding factor especially in young patients and this can be one of limitation factors that should be considered [24].

In conclusion, our results demonstrated that AMT and MV are moderately correlated with HbA1c, age and near visual acuity in patients with type 2 diabetes. Among these, HbA1c had the strongest correlation with MV. Therefore, HbA1c may be used as an early predictor of OCT-derived macular volume changes, thereby playing an important role in the early identification and manifestation of diabetic macular oedema.

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**Conflicts of interest** None

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