Scanning laser edema index: A reliable tool to correlate with diabetic retinopathy and systemic risk factors?

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ABSTRACT

To correlate Heidelberg Retina Tomograph (HRT) derived macular edema (DME) index with severity of diabetic retinopathy and systemic factors.

A total of 300 diabetic patients were recruited for the study for each of them a value for the macular edema index was obtained using the HRT II. Patients’ age, gender, duration and type of diabetes mellitus, latest HbA1c result and presence or absence of co-morbid factors (hypertension, ischemic heart disease, nephropathy) were recorded together with the stage of diabetic retinopathy. These were correlated with DME.

Out of 300 patients, HRT defined macula edema was seen in 68 patients (22.6%). There is a wider and higher range (95% percentile) of macula edema index in the severe non proliferative diabetic retinopathy (NPDR) group. Independent samples t test showed significant difference between the severe NPDR group and no DR group (p<0.001), mild NPDR group (p<0.05) and moderate NPDR group (p<0.05). A higher macula edema index was also found to have a low degree of correlation with more advanced stages of retinopathy (r=0.310; p<0.001). Also nephropathy showed a strong and significant correlation with DME. Hypertension had moderately significant correlation with DME. This study found no correlation between ischemic heart disease and DME.

HRT derived scanning laser edema index is a reliable objective tool to evaluate diabetic retinopathy and systemic risk factors.

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1. Introduction

Diabetic macula edema is the most common cause of visual loss in type 2 diabetes (Vitale, 1998). Up to 10 % of all patients with diabetes will develop diabetic macula edema (DME) during their lifetime (Fareed, 1997).

Slit lamp biomicroscopy, fluorescein angiography and stereo fundus photography are relatively insensitive to small changes in retinal thickness (Sanchez-Tocino, Alvarez-Vidal, Maldonado, et al., 2002). The recent Preliminary Study of Subclinical Diabetic Macular Oedema Study has shown that 55% of the DME detected by OCT was not detected by biomicroscopy examination (Bressler, Edwards, Antoszyk, et al., 2008; Brown, Solomon, Bressler, et al., 2004).

Current methods for in vivo assessment of DME include volumetric analysis with the Heidelberg Retina Tomograph (HRT) scanning laser (HRT, Heidelberg Engineering) (McDonald, Williams, Scott, Haller, & Maguire, 2007; Zambarakji, Evans, Arnoaku, & Vernon, 1998), optical coherence tomography (OCT) (McDonald et al., 2007) and The Retinal Thickness Analyzer (McDonald et al., 2007) (RTA, Talia Technology Ltd., Neve-Ilan, Israel). HRT II is a confocal laser scanning system designed for acquisition and analysis of 3D images of the posterior segment. Compared to OCT, the HRT II has less axial resolution; however, it has far superior spatial resolution and thereby avoids the under sampling in the periphery of the image that is inherent in the OCT macular maps (Kisilevsky, Hudson, et al., 2006). A recent also showed that the sensitivity of HRT-II is better than that of OCT, with a lower false-negative result (Tian et al., 2006).

HRT edema index is a quantitative analysis of the volume of the macula and based on a previous published study, a good spatial agreement has been demonstrated between areas of elevated edema index and clinically detected areas of retinal thickening in diabetic patients (Subrayan, Chuah, Peyman, Pei, & Iqbal, 2010). In this paper, we have described in detail of how we arrived at a value for the diabetic macular edema index. Theoretically, by utilising this value for scanning laser edema index we can make an objective diagnosis of DME and also correlate it with other related data like HbA1c and serum creatinine levels.

Hence, this study was conducted to correlate the value for scanning laser derived macular edema index using Heidelberg Retina Tomograph II (Macular Oedema Module) with the severity of diabetic retinopathy and its systemic associations.

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2. Methods and Materials

This was a hospital based, cross-sectional, double-masked, non-interventional diagnostic study. All consecutive diabetic patients who attended the ophthalmology clinic in University Malaya Medical Centre from 1st January 2010 until 31st June 2010 were recruited into the study. Out of these, patients with high refractive errors (>±12.00D sphere) were excluded as this high refractive error may affect the macula edema index of HRT machine. Also excluded were those patients who received previous treatment for diabetic retinopathy such as laser photocoagulation, intravitreal injections or underwent any form of intraocular surgery. After exclusion, a total of 300 diabetic patients were included in the final study. The Ethical Committee Board of University Malaya Medical Centre (UMMC) approved all aspects of this study. The tenets set out in the Declaration of Helsinki were strictly adhered and informed consent was obtained from all the patients who participated in the study.

The study patients had all their characteristics recorded which included the age, gender, duration of diabetes, type of diabetes, latest HbA1c results and presence or absence of co-morbid factors (hypertension, ischemic heart disease, nephropathy). Nephropathy was defined when urine protein was more than 300 mg/24 h in more than two samples (Silveiro, 2008).

Visual acuity was recorded for each patient using the LogMar chart. All the patients underwent a complete eye examination that included a dilated retinal examination and 7-field stereoscopic Diabetic Retinopathy Study retinal photographs (The Diabetic Retinopathy Study Research Group, 1981). The color fundus photographs were graded for DR severity in a masked fashion by two independent ophthalmologists at University of Malaya Eye Research Center in Kuala Lumpur. The modified Early Treatment of Diabetic Retinopathy Study Airlie House classification of DR was used to grade the retinopathy into the following categories: mild non-proliferative retinopathy (mild NPDR), moderate non-proliferative retinopathy (moderate NPDR), severe non-proliferative retinopathy (severe NPDR) and proliferative retinopathy (PDR) (Early Treatment of Diabetic Retinopathy Study Research Group, 1991; Early Treatment of Diabetic Retinopathy Study Research Group (ETDRS), 1991). In 194 patients, both eyes were measurable. The remaining 106 patients had only one eye included in the study due to the presence of cataract, vitreous haemorrhage and other exclusion criteria in the other eye. The status of diabetic retinopathy of a patient is defined by the eye with the more severe condition.

Next, the HRT image acquisition of the macula was performed by an experienced operator and 3 sets of images were obtained for each eye. The best image quality for each eye was chosen for data analysis. The macula edema index values were documented for each of the 9 sectors but only data from the innermost circle of 500 μm will be used for analysis in this study.

For the macula edema index, the cut-off point chosen for determination of DME by HRT was 1.835 with sensitivity of 86.8% and specificity of 94.6%. This value was based on a previous study we conducted to derive the value of the edema index for diabetic patients (Subrayan et al., 2010). In patients where both eyes were measurable, the eye with the worst value for the diabetic macular edema index was chosen. The raw agreement, chance corrected agreement (κ) and chance independent agreement (φ) between the HRT and fundus biomicroscopy were calculated. Multiple logistic regression analysis was carried out to search for associations between selected case characteristic (hypertension, ischemic heart disease, nephropathy) as well as severity of diabetic retinopathy and diabetic macula edema. All values were counted as significant when \( p < 0.05 \).

3. Result

The type of DM, the co-morbidity and other case characteristics of the 300 patients in the study are shown in Tables 1 and 2. Out of 300 patients, HRT defined macula edema was seen in 68 patients (22.6%) (Table 3). 57 patients presented with DME in one eye (either right or left) and 11 patients had DME in both eyes.

In terms of severity of DR, the severe NPDR group had the highest mean macula edema index value of 2.62 ± 0.21. Independent samples t test showed significant difference between the severe NPDR group and no DR group (\( p < 0.001 \)), mild NPDR group (\( p < 0.05 \)) and moderate NPDR group (\( p < 0.05 \)).

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![Graph showing how presence of macula edema varies between different stages of retinopathy](image)

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By using logistic regression analysis, the study results revealed that nephropathy had a strong and significant correlation with DME. Hypertension had moderately significant correlation with DME. This study found no correlation between ischemic heart disease and DME (Table 4).

There was also significant but moderately weak correlation between duration of diabetes (years) and macula edema index in patients with HRT defined macula edema (Pearson correlation coefficient = 0.293 (p < 0.05)) (Fig. 2).

4. Discussion

This is a cross-sectional, double-masked diagnostic study carried out on consecutive patients attending an ophthalmology clinic in a tertiary referral centre. By taking consecutive patients attending the clinic, it represents a true cohort of patients receiving care in this centre.

HRT is currently considered a biomedical imaging tool for high-resolution macular and optic disc evaluation. Previous studies showed objective value for HRT II index in evaluating the macula. (Subrayan et al., 2010) Finding any correlation between objective severity of macular edema and diabetic retinopathy may give a very important clue in assessing the retinopathy severity especially in early and subclinical stages.

Different studies have come up with different cut off values for the macular edema index using HRT II. They have recruited different numbers of patients and selected different values for sensitivity and specificity.

As mentioned before the cut off value selected for the macula edema index for the determination of DME by HRT in this project was 1.835. This was based on a study done in our centre which to date represents a true cohort of patients receiving care in this centre.

Analysis of HRT defined macula edema across different stages of retinopathy yielded some interesting result. HRT defined macula edema occurred most commonly in patients with severe NPDR. There is a wider and higher range (95% percentile) of macula edema index in the severe non proliferative diabetic retinopathy (NPDR) group.

In our study, there was significant positive correlation between HbA1C, duration of DM, hypertension and nephropathy with macula edema index (HRT). This result concurred with the findings reported by Asensio-Sánchez et al (Asensio-Sánchez & Gómez-Ramírez, 2008) in 2008 where 208 eyes with DME were reviewed. In that study, every 1% of increase in HbA1C level doubled the risk of developing DME; and nephropathy increased almost twice the risk of macula edema. Our study also showed that hypertension had a moderately high correlation with the development of DME. However, there was no correlation between ischemic heart disease and DME (Table 5).

In a recent study, Knudsen LL (Knudsen et al., 2007) was unable to establish in type 1 diabetics an association between DME and the systemic parameters of the study, but in type 2 diabetics a significant association was found with the duration of the diabetes, HbA1C, nephropathy and albuminuria. None of these studies used HRT macular index to correlate with the systemic factors.

The prevalence of macula edema increases with the severity of retinopathy in this study as in some others (ETDRS Research Group, 1991; Klein, Moss, Klein, Davis, & DeMets, 1989).

References


