

EVALUATION OF DIABETIC MACULAR OEDEMA WITH SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY AND FUNDUS FLUORESCIN ANGIOGRAPHY

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ABSTRACT

BACKGROUND

Macular oedema is an important cause of visual morbidity in Diabetic Retinopathy. It can be assessed by both Fundus Fluorescein Angiography (FFA) and Optical Coherence Tomography (OCT).

The aims of this study were to evaluate the agreement between morphological features on spectral domain Optical Coherence Tomography and Fluorescein Angiographic leakage patterns in Diabetic Macular Oedema, and to study the correlation between the best corrected visual acuity and central foveal thickness measured by Optical Coherence Tomography.

MATERIALS AND METHODS

This was an observational study. All patients with Diabetic Macular Oedema underwent complete ophthalmic examination and subjected to FFA and OCT. Presence or absence of macular oedema by FFA and OCT was noted and agreement between two modalities of imaging was assessed. Sensitivity of these modalities were also found out using appropriate statistical methods. Best Corrected Visual Acuity (BCVA) measured were converted to LogMAR scale and Central foveal thickness measured by OCT. Linear regression analysis was done with central foveal thickness and LogMAR visual acuity.

RESULTS

A total of 69 eyes of 39 patients were studied. OCT revealed Diabetic Macular Oedema in 97.5% of eyes. Fundus Fluorescein Angiography performed in these patients identified leakage in 95.6% of eyes. Sensitivity and specificity of FFA and OCT were calculated keeping one as the gold standard for sensitivity and specificity of the other. FFA and OCT had almost equal sensitivity (95.46 for OCT and 96.92 for FFA) for detection of DME. Specificity of OCT was found to be slightly higher (33.33%) compared to FFA (25%). Our results suggest that there is minimal agreement between these two imaging modalities in evaluating DME. Statistically, Kappa value was 0.248. Linear regression analysis showed that central foveal thickness had a significant correlation with visual acuity, with Pearson correlation coefficient $r=0.442$, $p=0$, significant at 1% level. $r^2=0.195$.

CONCLUSION

There is minimal agreement between FFA and OCT in the evaluation of DME. Central foveal thickness correlates to BCVA.

KEYWORDS

Diabetic Macular Oedema, Fluorescein Angiography, Optical Coherence Tomography.

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BACKGROUND

Macular oedema is responsible for a significant degree of visual loss in Diabetic patients. The ETDRS defined DME as retinal thickening or presence of hard exudates within 1 Disc diameter of the centre of the macula. To characterize the severity of macular oedema, and for treatment guidelines the term Clinically Significant Macular Oedema (CSME) is used. Macular edema is clinically significant, if one of the following conditions is present: 1. Retinal thickening at or

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within 500 μ of the centre of the macula 2. Hard exudates at or within 500 μ of the centre of the macula if associated with thickening of retina 3. A zone or zones of retinal thickening one disc area or larger, any part of which is within one disc diameter of the centre of the macula.¹

Apart from slit lamp biomicroscopy, Fluorescein angiography (FA) and Optical coherence tomography (OCT) are commonly used in conjunction with each other for the diagnosis of macular oedema. Macular thickening which is picked up by clinical examination does not reflect severity and extent of oedema source of fluid leakage and affected layer of retina. FA identifies the anatomical location and pattern of vascular leakage, and is a qualitative and functional study, whereas OCT allows a morphological assessment of macular oedema by producing two or three-dimensional images of the retinal tissue.² OCT can objectively measure retinal thickness and thus is an

indispensable instrument in the diagnosis and management of diabetic macular oedema.

AIM

To study the agreement between morphological features on spectral domain Optical Coherence Tomography and Fluorescein Angiographic leakage patterns in Diabetic Macular Oedema, and to study the correlation between the best corrected visual acuity and central foveal thickness measured by Optical Coherence Tomography.

MATERIALS AND METHODS

This was an observational study done between October 2010 and March 2011 in patients who attended the retina clinic of Govt. Medical College, Thrissur. Diabetic Macular Oedema was defined as the presence of retinal thickening or Hard Exudates within 1 Disc diameter of the centre of the macula when examined with slitlamp biomicroscope. 69 eyes of 39 patients were evaluated. The study group included both insulin dependent and non-insulin dependent proliferative diabetic retinopathy and non-proliferative diabetic retinopathy between the ages of 35-75 years.

None of these patients in our study had undergone previous focal laser or pan-retinal photocoagulation, or ocular surgery in the past six months. Other exclusion criteria were dense cataract, macular oedema owing to other ocular illness and advanced diabetic eye disease.

All these patients underwent visual acuity assessment by Snellen’s visual acuity chart, and dilated slit lamp biomicroscopic examination. Fundus photographs were taken and FFA and spectral domain OCT (OPKO OCT SLO machine) done on the same day, by the same examiner. In OCT, line scan images and retinal thickness mapping protocols were processed and analysed for presence and pattern of DME and central foveal thickness. With Fluorescein angiography, the presence or absence of dye leakage and patterns of dye leakage were noted.

Macular oedema was categorized into mild (with a thickness of 201-300µ), moderate (301-400µ) and severe (≥400µ) according to the central foveal thickness measurement values in OCT.

Best Corrected Visual Acuity (BCVA) values measured by Snellen’s chart were converted into LogMAR values. Linear regression analysis was then done with these central foveal thickness values and LogMAR visual acuity values.

Sensitivity of FFA and OCT in detecting Diabetic macular oedema were calculated using appropriate statistical method. The presence and absence of macular oedema by each test in each of the eyes was noted and agreement between the two modalities of imaging was assessed by calculating the Kappa value.

RESULTS

Of the 39 patients we analysed, there were 10 patients in the age group 36-45 years (26%), 12 (31%) in 46-55 years

age group, 15 (38%) in 56-65 years age group, 2 (5%) in 66-75 years age groups and 1 (4%) in 70-79 age group. Males predominated with M: F of 5.9:1. 84% had NPDR and 16% PDR. Mean diabetic age was 14.08 years.

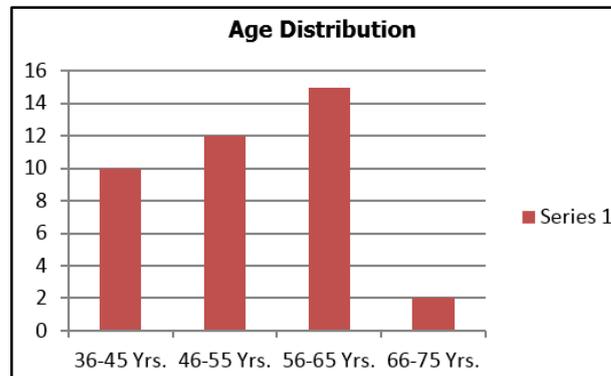


Chart 1. Age Distribution in Study Group

Biomicroscopically, all these patients had Diabetic macular oedema, 9% had DME associated with cystoid macular oedema (CME), and 1% had DME with vitreo-macular traction (VMT) and 1% Epiretinal membrane (ERM). No patients had Serous Macular Detachment with SubRetinal Fluid (SRF) clinically.

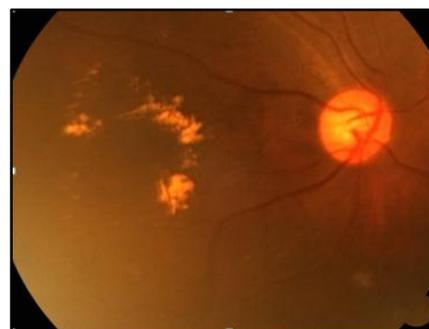


Figure 1. Fundus Picture of Diabetic Macular Oedema

OCT revealed Diabetic Macular Oedema in 97.5% of eyes. Various patterns were identified.

DME Patterns in OCT	Percentage Manifestation
Spongy oedema	18
Cystoid oedema	35
Mixed pattern (Cystoid and spongiform)	25
ERM	6
SRF	10
VMT	3
Hard Exudate Plaques	25

Table 1. Morphology of DME in SD OCT

Measurement of macular thickness revealed, 33% of eyes with mild macular oedema, 21% moderate oedema and 35% with severe diabetic macular oedema.

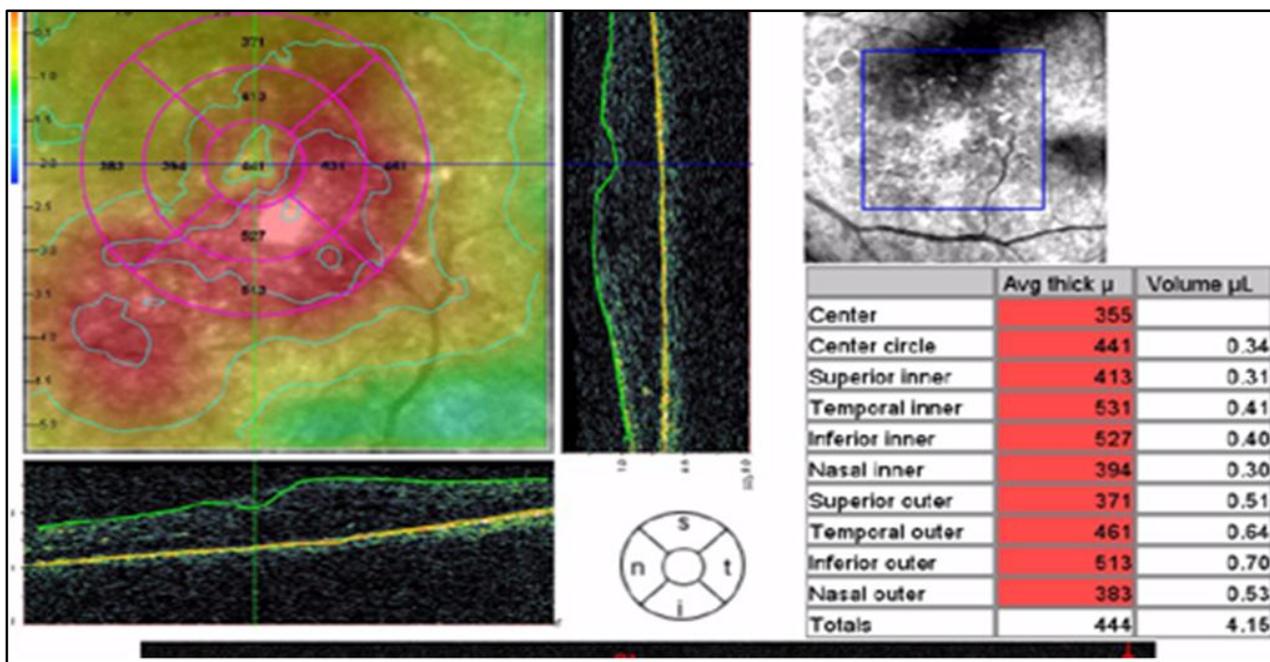


Figure 2. Macular Thickness Mapping

Fundus Fluorescein Angiography performed in these patients identified leakage in 95.6% of eyes. We classified leakage patterns on FA into either diffuse or cystoid based on analysis of late films. Diffuse leakage was defined as irregular widespread leakage in late films. Petalloid leakage pattern suggestive of Cystoid macular oedema was seen in 28% of our patients.

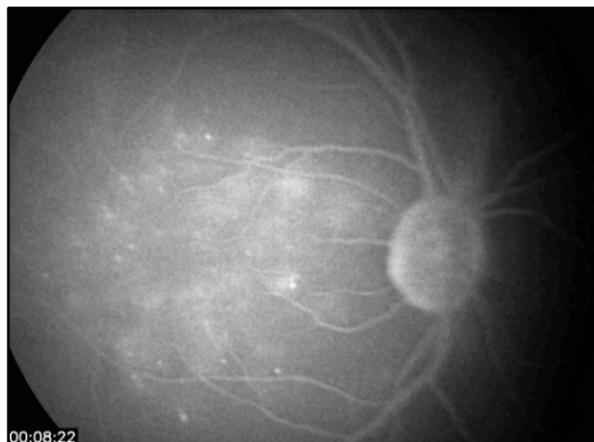


Figure 3. Cystoid Macular Oedema

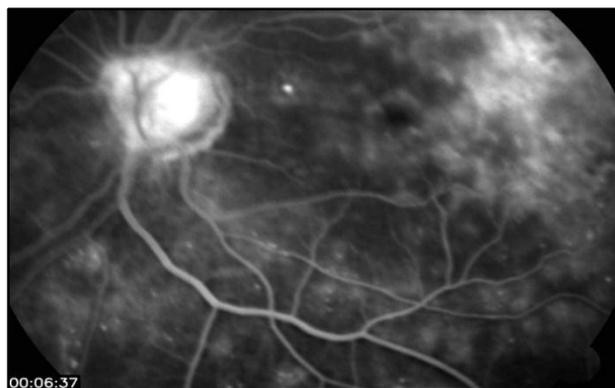


Figure 4. Diffuse Leakage

Sensitivity and specificity of FFA and OCT were calculated keeping one as the gold standard for sensitivity and specificity of the other. We found that FFA and OCT had almost equal sensitivity (95.46 for OCT and 96.92 for FFA) for detection of DME. Specificity of OCT was found to be slightly higher (33.33%) compared to FFA (25%).

There were two eyes which showed late leakage but OCT in them showed no macular oedema. There were 3 eyes which showed oedema as per OCT but without dye leakage in FFA. Our results suggest that there is minimal agreement between these two imaging modalities in evaluating DME. Statistically, Kappa value was 0.248.

Type of DME	Biomicroscopy	OCT	FFA
CME	9%	35%	28%
SRF	nil	10%	nil
VMT	1%	3%	nil
ERM	1%	6%	Nil

Table 2. Comparison of DME Characteristics Identified by Biomicroscopy, FFA and OCT

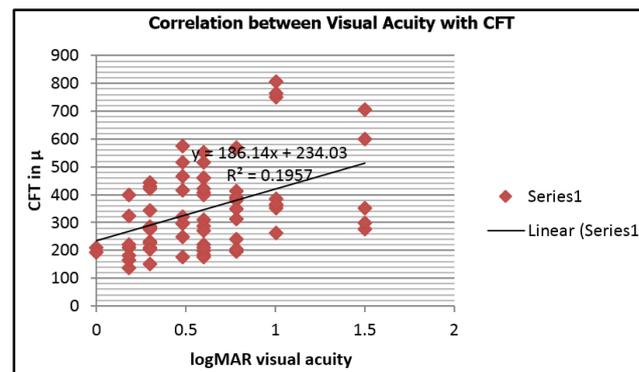


Figure 5. Correlation between Central Foveal Thickness and Best Corrected Visual Acuity

It was found that there is a near linear relationship between central foveal thickness values and LogMAR visual acuity in our study group. Linear regression analysis showed that central foveal thickness had a significant correlation with visual acuity, with Pearson correlation coefficient $r=0.442$, $p=0$, significant at 1% level. $r^2=0.195$. This means that changes in macular thickening at the central fovea can explain nearly 20% of variations in visual acuity reported on LogMAR scale.

DISCUSSION

Optical Coherence Tomography is a fast and non-invasive tool for examining the retina in cross sectional images that correlates reasonably with the retinal histology. Till recently slit lamp biomicroscopy and FFA were the tools for the diagnosis and management of DME. It is true that they are highly sensitive for the qualitative detection of DME. OCT enables us to detect and understand the accurate subclinical retinal changes associated with DME that may not be detectable even in FFA. Yang et al have suggested that OCT may be more sensitive than clinical examination in assessing DME and is a better tool for documenting changes in macular thickening.³ In his series, OCT identified spongy retinal thickness was seen in 58% of eyes. Otani et al found spongy retinal thickness in 88%, CME in 47%, SRF in 15% of eyes with CSME.² Kim et al found spongy retinal swelling in 97%, CME in 55%, SRF in 7%, VMT in 13% of eyes with DME.⁴ Ozdek et al had reported spongy swelling in 66%, CME in 16%, SRF in 10% of eyes with DME. In our series, cystoid macular was the common form of presentation.⁵ The present study revealed that 18% had macular thickening with spongy oedema, 35% with cystoid changes, 25% with mixed spongy and cystoids oedema, 6% ERM, 10% with serous retinal detachment, 3% with vitreo-macular traction and 25% with plaques of hard exudates.

In the present series, 35% of the eyes had CME on OCT, compared to 9% detected by biomicroscopy and 28% by FFA.

Present study shows a minimal agreement between FFA and OCT in the evaluation of DME. Lack of this much of agreement in our study could be due small sample size. Two of patients who had DME in OCT but did not show leakage in FFA, had macular ischemia which could be the reason for no leakage. Two of patients showing leakage in FFA did not have DME by OCT. These patients had minimal quantity of leakage which probably could not produce any structural changes at macula. Ozdek et al also found that 40% of CME detected on OCT were not detected by biomicroscopy and 63% were not detected even by FFA.⁵ But according to Igor Kozak et al, agreement between the two techniques was high—almost 95%.⁶

An observation similar to present study relating to FA/OCT discrepancy was reported previously by Eter and Spaide during a comparison of FA and OCT after photodynamic therapy. Even though macular cystoid changes were detected better by OCT than by FA, some of their patients had leakage by FFA that did not have any observable OCT abnormality attributable to fluid

accumulation. This might have been the result of the subtle diffusion of dye that does not produce or is not associated with retinal tissue changes, which could be detected by available OCT resolution. We might assume a similar mechanism in the present set of cases.⁷

Ling Yeung, et al studied the relationship between SD-OCT findings and FFA patterns in DME, they could find that the pathological changes on SD-OCT correlated well with FFA findings.⁸ But, they evaluated the findings by superimposing aligning the SLO images onto the FFA photos.

Manpreet Brar et al have found that eyes with DME and retinal vein occlusions have a significantly higher incidence of cyst formation on SD-OCT. Diffuse non-cystoid angiographic macular oedema may show micro cysts on SD-OCT, but diffuse oedema is more commonly associated with thickening or distortion of the retinal layers without cyst formation.⁹ Cystoid leakage on FA is always associated with cystic changes on SD-OCT. Present study also showed almost similar results.

Various modalities used for assessing macular thickness include slitlamp biomicroscopy, stereoscopic fundus photography and fundus fluorescein angiography. Interpretation by all these methods are subjective and semi-quantitative. Optical Coherence Tomography offers an objective method of high-resolution cross-sectional imaging of the retina utilising near infrared light to detect relative changes in reflection at optical interfaces. In several studies, measurements from OCT have been found accurate, precise, reproducible and repeatable.¹⁰

Hee MR and co-workers and Otani and coworkers in their study have shown that Optical coherence Tomography appears useful for objectively monitoring retinal thickness with high resolution in patients with macular oedema. It may eventually prove to be a sensitive diagnostic test for the early detection of macular thickening in patients with diabetic retinopathy.¹⁰

Hortensia Sánchez-Tocino, et al have shown that foveal thickening over 180 μm measured by OCT may be useful for the early detection of macular thickening and may be an indicator for a closer follow-up of the patient with diabetes.¹¹ OCT offers a way to make measurements of retinal thickness that are repeatable over different sessions as noted by Dara Koozekanani et al¹²

According to our study, there is significant correlation between central foveal thickness and best corrected visual acuity expressed on LogMAR scale. David J Browning in his study of correlation between OCT measured central foveal thickness and visual acuity before and after photocoagulation in diabetic macular oedema, has concluded that there a modest correlation between OCT-measured center point thickness and visual acuity, and modest correlation of changes in retinal thickening and visual acuity following focal laser treatment for DME.¹³

Chang-Sue-Yang et al also suggest a moderate correlation between BCVA and the foveal thickness measured using OCT.¹⁴

But there are a few studies, which suggest a weak correlation between central foveal thickness and BCVA. As per the studies by Nunes and coworkers, correlations between retinal thickening and BCVA in CSME are only present when the central 500- μ m-diameter circle is involved. However, even in this circumstance, a correlation was found in only 48.8% of the cases.¹⁵

CONCLUSION

Our study revealed that there is minimal agreement between FFA and OCT in the evaluation of DME. Both FFA and SD OCT are highly sensitive techniques in the detection of Diabetic macular oedema and have near total agreement with detection of cystoid macular oedema. Some of the diabetic structural changes in fovea such as serous foveal detachment, vitreo-macular traction detected by OCT may not be evident in slit lamp biomicroscopy or FFA. As BCVA correlates significantly with the central foveal thickness, measurement of central foveal thickness by OCT may be used as an easy guide in monitoring the response to treatment for DME.

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