Optical coherence tomography patterns of diabetic macular edema and their correlation with visual acuity

Omar M. Ali[a], Mohammad S. Saad[a], Hazem A.M. Hazem[a], Mariam N. Dawood[b]

[a]Department of Ophthalmology, Faculty of Medicine, Assiut University, Assiut
[b]El Ramad Hospital, Assiut City, Egypt

Correspondence to Mariam N. Dawood, MSc, El Ramad Hospital, Assiut City, Egypt.
Zip Code: 71111;
Tel: +20 128 886 8800;
e-mail: drmariam3030@gmail.com

Received 21 December 2019
Revised 22 December 2019
Accepted 22 January 2020
Published 20 November 2020

Journal of Current Medical Research and Practice
2020, 5:365–370

Aim
The aim was to identify and evaluate the patterns of diabetic macular edema (DME) currently known by optical coherence tomography (OCT) and correlation of these patterns with visual acuity.

Patients and methods
OCT scans were done for 60 eyes of 36 patients with diabetes. OCT is used to define the pattern of DME and measure the central macular thickness (CMT). Analysis of data was done to evaluate the relationship between retinal thickness and visual acuity and prevalence of each different morphological subtype and investigate the presence of relationship between different patterns and visual acuity.

Results
Our OCT-based classification was as follows: group 1 had diffuse macular edema without cysts (35%), group 2 had cystoid macular edema (CME) (26.67%), group 3 had CME with serous retinal detachment (SRD) (16.67%), group 4 had SRD with diffuse thickening (8.33%), and group 5 had tractional macular edema (13.33%). Eyes with sponge-like retinal swelling had the best-corrected visual acuity. Best-corrected visual acuity in eyes with CME and CME with SRD was significantly worse. Eyes with CME, CME with serous sensory detachment, and tractional had CMT significantly larger than eyes with diffuse retinal thickening. There was a reverse correlation between best-corrected visual acuity and CMT at the fovea in eyes with diffuse thickening alone, whereas the correlation was not significant in eyes associated with CME or serous sensory detachment.

Conclusions
Our study affirmed that OCT is very useful in routine assessment of DME and in detecting vitreoretinal traction and SRD undetectable on biomicroscopy.

Keywords:
diabetic macular edema, macular thickness, optical coherence tomography, visual acuity

J Curr Med Res Pract 5:365–370

2357-0121

Introduction

Diabetic macular edema (DME) is the greatest cause of loss of visual acuity in diabetes [1]. Studying the history of DME shows that 24% of eyes with DME will lose at least three lines of vision within 3 years [2]. DME may occur at any stage of diabetic retinopathy (DR), either mild, moderate, or severe nonproliferative DR, or at progressed stages of DR [3].

Collection of subretinal and intraretinal fluid in the inner and outer plexiform layers is owing to dysfunction of outer and inner retinal barriers. Vascular endothelial growth factor plays the main role in disrupting the function of the inner blood retinal barrier [4].

In recent times, optical coherence tomography (OCT) had greatly altered the diagnosis and follow-up of DME. Most patients can accept OCT, as it is noninvasive. It gives dependable and objective cross-sectional images of the retina and the vitreoretinal interface and permits quantitative measurements of the thickness of the retina [5,6].

According to OCT, four categories of DME were found:

(1) Diffuse DME (DRT): thickening of retina and light reflection weakening.
(2) Cystoid macular edema (CME): there is cystoid dark cavity.
(3) Serous sensory detachment DME [serous retinal detachment (SRD)].
(4) Vitreomacular interface abnormalities: there are incomplete or complete posterior vitreous detachment and ERM formation or vitreomacular traction or both [7].

Patients and methods

This is a prospective observational study. OCT scans were done for 60 eyes of 36 diabetic patients in Assiut Diagnostic Eye centers (El Nour, EL Forsan, Tiba) during a period of 10 months (from May 2016 to March 2017).

Inclusion criteria

Patients with diabetes mellitus with evidence of any stage DR clinically and with evidence of a macular edema involving center of the macula clinically or angiographically were included.

Exclusion criteria

The following were the exclusion criteria:

(1) Eyes with marked media opacities were excluded (cataract, intravitreal hemorrhage, and corneal opacity).
(2) Eyes with diseases that affect vision such as ischemic maculopathy, glaucoma, retinal detachment, and optic nerve diseases.
(3) Other causes of macular edema such as age-related macular degeneration, retinal venous occlusion, hereditary disorders, and inflammatory eye diseases.
(4) Pregnant women and patients with renal disease.

Methods of ocular examination

(1) History taking included the following:
(a) Name.
(b) Age.
(c) Sex.
(d) Type and diabetes duration.
(e) Treatment (insulin, oral hypoglycemic, or combined).
(f) Detailed visual complaints.
(g) Past ocular history (disease, surgery, laser photocoagulation, and intravitreal injection).
(h) Other associated systemic diseases.
(i) An informed consent was obtained for each patient.
(2) Ocular examination:

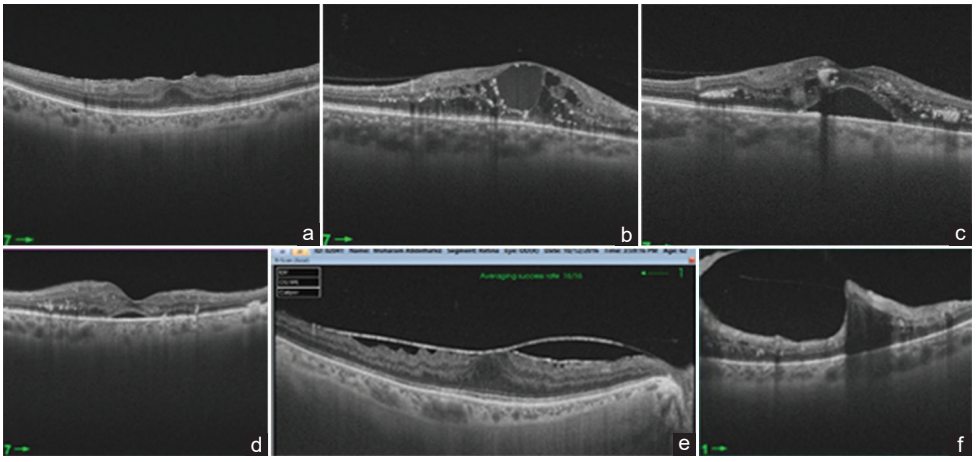
Detailed ophthalmic examination was performed as follows:

(1) Best-corrected visual acuity (BCVA), by Snellen's chart and converted to logMAR using visual acuity conversion tables.
(2) Examination by slit lamp.
(3) Examination of fundus and macula: by slit lamp with the +90 D lens.
(4) Color fundus photography.
(5) Fundus fluorescein angiography: to document DR stage and define the type of leakage (focal or diffuse), its site, size, and relation to the fovea, either center involved or not.
(6) OCT: OCT was done using the optical coherence tomography scanner (DRI OCT Triton, Swept source OCT) made in Japan.

OCT is used for the following:

(1) To define the pattern of DME either:
(a) Noncystoid sponge-like diffuse retinal thinking (DRT).
(b) DRT with CME.
(c) CME with SRD.
(d) DRT with SRD.
(e) Tractional macular edema: any previous pattern plus either posterior hyaloid traction or epiretinal membrane or both.
(2) To measure the central macular thickness (CMT).

Figure 1



Diabetic macular edema by optical coherence tomography. (a) Diffuse retinal thickening; (b) cystoid macular edema; (c) cystoid macular edema with serous retinal detachment; (d) serous retinal detachment with diffuse retinal thickening; (e) tractional macular edema by epiretinal membrane; (f) tractional macular edema with vitreomacular interface abnormality.

Optical coherence tomography scanning was done for all patients as follows

The pupils have been dilated using 1.0% tropicamide and 2.5% phenylephrine (cyclopherine; Kahira Pharm, Kahira Pharmaceuticals: Cairo, Egypt). The patient data were introduced to the computer. Twelve consecutive line scans were done at equally spaced angular orientations in a radial spoke pattern focused on the fovea. The scan length is 6 or 9 mm.

Retinal thickness data were shown in two ways: a quantitative and a false color topographic display. The macula was divided into nine ETDRS-type regions, including a central disc of 500-μm diameter, and an inner and outer rings, each splitted into four quadrants, with outer radii of 1 and 2 disc diameters, respectively. Each of the nine regions has average retinal thickness.

In the false color display, thickness of the macula was changed to a false color value within 2 disc diameter from the center. The brighter colors indicate increased retinal thickness.

Computer program SPSS 'version 21' (SPSS Inc., Chicago, Illinois, USA), was used to collect and analyze data. Data were expressed as number, percentage, mean, and SD. Man Whitney U Test was used to determine significance for numeric variables, and also analysis of variance test was used. χ^2-test was used to determine significance for categorical variable and Pearson's correlation to determine significance between variables in the same group. The level of significance was set as follows:

$P > 0.05$, no significant.

$^{*}P < 0.05$, mild significant.

$^{**}P < 0.001$, moderate significance.

$^{***}P < 0.0001$, highly significance.

The study was approved and monitored by the Medical Ethics Committee, Assiut Faculty of Medicine, IRB#17100858.

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 form.

Results

The study was done on 60 eyes of 36 patients with a mean age of 57.30 ± 10.48 years (range: 32–83.0 years) (Table 1).

Table 1 Demographic and clinical data in study groups

Age (years)	
Range	32.0-83.0
Mean±SD	57.30±10.48
Sex [*n* (%)]	
Male	33 (55)
Female	27 (45)
DM type [*n* (%)]	
Type 1	9 (15)
Type 2	51 (85)
DM duration (years)	
Range	5.0-30.0
Mean±SD	16.19±5.92
DM treatment [*n* (%)]	
Insulin	34 (56.67)
Oral hypoglycemic drugs	21 (35.)
Both	5 (8.33)

DM, diabetes mellitus.

Table 2 Duration of diabetes mellitus

Duration of diabetes mellitus (years)	*n* (%)
5-9	2 (5.55)
10-14	6 (16.66)
≥15	28 (77.77)
Total	36 (100)

Table 3 Fundus fluorescein angiography of patients in this study

Fundus fluorescein angiography	*n* (%)
Staging FFA	
Mild NPDR	0
Moderate NPDR	44 (73.33)
Severe NPDR	0
PDR	16 (26.67)
Type of leakage in FFA	
Diffuse	36 (60.0)
Focal	24 (40.0)

FFA, fundus fluorescein angiography; PDR, Proliferative Diabetic Retinopathy; NPDRP, Non Proliferative Diabetic Retinopathy

Table 4 Central macular thickness by optical coherence tomography and best-corrected visual acuity by logMAR best-corrected visual acuity logMAR in this study

Items	Descriptive
CMT (μm)	
Range	215.0-612.0
Mean±SD	353.61±96.91
BCVA logMAR	
Range	0.1-1.3
Mean±SD	0.46±0.23

BCVA, best-corrected visual acuity; CMT, central macular thickness.

Age distribution

All patients were between 32 and 83 years of age, with 16 (44.44%) patients in 60–69 years, nine (25%) patients in 50–59 years, six (16%) patients in 40–49 years, three (8.33%) patients in 70–79 years, one (2.77%) patient in 30–39 years, and one (2.77%) patient in more than 80 years (Tables 2 and 3).

Table 5 Central macular thickness in optical coherence tomography patterns of diabetic macular edema study groups

CMT (μm)	Diffuse	CME	CME+SRD	SRD+diffuse	Tractional
Mean±SD	337.92±71.58	408.94±68.36	453.10±98.83	299.0±67.23	415.57±80.45
Compared with					
Diffuse	-	*P*<0.02*	*P*<0.001**	*P*<0.01*	*P*<0.001**
CME	*P*<0.02*	-	*P*=0.275 (NS)	*P*<0.0001***	*P*=0.264 (NS)
CME+SRD	*P*<0.001**	*P*=0.275 (NS)	-	*P*<0.001**	*P*=0.496 (NS)
SRD+diffuse	*P*<0.01*	*P*<0.0001***	*P*<0.001**	-	*P*<0.001**
Tractional	*P*<0.001**	*P*=0.264 (NS)	*P*=0.496 (NS)	*P*<0.001**	-
Correlation with BCVAL log MAR	*P*<0.03*	*P*=0.496 (NS)	*P*=0.206 (NS)	*P*=0.447 (NS)	*P*=0.624 (NS)

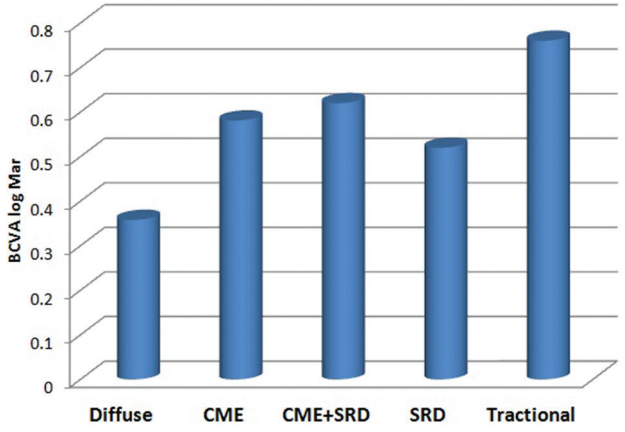
With significant difference (*P*<0.03*) in diffuse thickening group. The higher mean value of CMT was in CME+SRD group vs lower mean value in SRD+diffuse and diffuse thickening group. CME, cystoid macular edema; CMT, central macular thickness; SRD, serous sensory detachment; ** *P*<0.001 moderate significance; *** *P*<0.0001 Highly significance.

Table 6 Best-corrected visual acuity logMAR in optical coherence tomography patterns of diabetic macular edema study groups

BCVA logMAR	Diffuse	CME	CME+SRD	SRD+diffuse	Tractional
Mean±SD	0.358±0.15	0.581±0.29	0.620±0.41	0.520±0.18	0.760±0.36
Compared with					
Diffuse	-	*P*<0.001**	*P*<0.01*	*P*<0.01*	*P*<0.0001***
CME	*P*<0.001**	-	*P*=0.695 (NS)	*P*=0.362 (NS)	*P*<0.02*
CME+SRD	*P*<0.001**	*P*=0.695 (NS)	-	*P*=0.226 (NS)	*P*=0.697 (NS)
SRD+diffuse	*P*<0.01*	*P*=0.362 (NS)	*P*=0.226 (NS)	-	*P*<0.03*
Tractional	*P*<0.0001***	*P*<0.02*	*P*=0.697 (NS)	*P*<0.03*	-

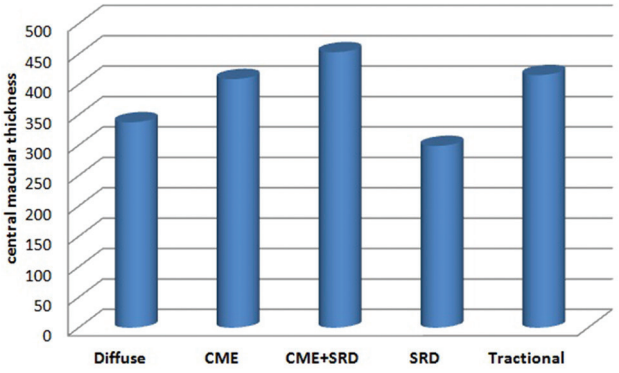
With significant difference between diffuse and CME, and CME+SRD and tractional (*P*<0.05). The higher mean value BCVA logMAR was in tractional and CME+SRD group vs lower mean value in diffuse thickening group. BCVA, best-corrected visual acuity; CME, cystoid macular edema; SRD, serous sensory detachment.

Figure 2



Best-corrected visual acuity logMAR in optical coherence tomography patterns of diabetic macular edema.

Figure 3



Central macular thickness in optical coherence tomography patterns of diabetic macular edema.

We classified DME by OCT into five groups:

(1) Group 1, in which the eyes had noncystoid sponge-like DRT, with intraretinal reflectivity reduction and extended areas of lower reflectivity in the outer retina without CME or SRD. This group included 21 (35%) eyes.

(2) Group 2, in which the eyes had CME defined by the presence of cystic spaces in the retina which appeared as round or oval low reflectivity areas, with highly reflective septa separating the cystic cavities. This group included 16 (26.67%) eyes.

(3) Group 3, in which the eyes had CME and SRD in the same eye. SRD is collection of fluid under fovea and a well-defined outer border of the detached retina without traction. This group included 10 (16.67%) eyes.

(4) Group 4, in which the eyes had DRT with SRD in the same eye. This group included five (8.33%) eyes.

(5) Group 5, in which eyes had tractional macular edema. This traction is either posterior hyaloid traction or epiretinal membrane traction or both. This group included eight (13.33%) eyes (Figs. 1–3 and Tables 4–6).

Discussion

The mean age of all patients was 57.30 ± 10.48 years in our study. The large number of patients were in the age group 60–69 years (44.44% of patients). Sander *et al*. [8] found the mean age of the patients was 57 years (range: 28–71 years), whereas Kang *et al*. [9] found the mean age of patients was 59.9 years (range: 31–86 years).

In this study, of the 36 patients, 20 (55.5%) were males and 16 (44.4%) were females. In the study by Golubovic-Arsovska [10], 55.8% of patients were females, whereas 44.2% were males. Klien *et al*. [11], in the Wisconsin Epidemiologic Study of Diabetic Retinopathy, found that increased incidence of DME associated with female sex.

The duration of diabetes mellitus of the patients in our study ranged from 5 to 30 years. Overall, 77.77% of patients had diabetes for 15 years and more. Mean duration was 16.19 years. Kang *et al*. [9] found the average duration of diabetes in patients having clinically significant maculae edema (CSME) was 15.09 ± 7.49 years, and also TH Chou *et al*. [12] found the mean duration of DM with CSME is 11.2 ± 5.5 years, whereas the study by Zhang *et al*. [13] showed that diabetic maculopathy often occurred within 10 years of diabetes duration, and its severity and incidence increased year by year.

In this study, five OCT-based classification were discussed: group 1 included eyes with diffuse macular edema without cysts (35%). This may represent the swollen Müller cells and Henle's fiber layer [14]. Group 2 included eyes with CME (26.67%), which represents retinal edema persistence and Müller cells necrosis described histopathologically. Group 3 included eyes with CME with SRD (16.67%). SRD is characterized by accumulation of fluid accumulation subretinal with distinct posterior border of detached retina. This appears as a high reflective line attached to the retinal pigment epithelium in the peripheral margin of the subretinal lenticular space by OCT.

Group 4 included eyes with SRD with diffuse thickening (8.33%). Group 5 included eyes with tractional macular edema (13.33%) This traction is either posterior hyaloid traction or epiretinal membrane traction or both.

Otani *et al*. [15] described three patterns of OCT: sponge-like swelling (88%), retinal edema with cystic spaces (47%), and retinal edema with subfoveal fluid accumulation (15%). A classification by Kang *et al*. was reported [9] type 1 thickening with homogenous optical reflectivity (55.2%), type 2 thickening with markedly decreased optical reflectivity in the outer retinal layers (30.3%), and type 3A, with detachment of fovea without traction (14.5%), and type 3B, with detachment of fovea with obvious vitreofoveal traction (2.8%).

Kim *et al*. [6] sat out another classification: DRT (97%), CME (55%), and SRD (2.9%), whereas Murakami *et al*. [16] classification was CME (CME type: 16%), SRD (SRD type: 16.8%), and absence of either CME or SRD (diffuse type: 67.2%).

The prevalence of SRD in eyes with DME in this study either combined with diffuse macular edema or with CME was 25%. This was reported by Otani *et al*. [15] as 15%, Kang *et al*. [9] as (14.5%) and Kim *et al*. [6] as (9.9%), but it was reported by Catier *et al*. [17] as 26% which is near to what was reported in our study. It was thought that SRD is caused by breaking down of the retinal-blood barrier at the level of the retinal capillaries and the retinal pigment epithelium. Fluid and proteins are released, and the anatomical features limit protein and water movement out of retina. The draining vascular system and the retinal pigment epithelium are unable to handle the water load [18].

A relationship between some morphologic patterns of DME and worse visual acuity was found in our study. The visual acuity was significantly the best in group 1 (diffuse macular edema without cysts). On the contrary, BCVA in eyes with CME and CME with SRD was significantly worse.

A study by Yamamoto *et al*. [5] assumed that eyes with diabetic CME have worse visual acuity than eyes with diffuse retinal swelling with no cysts. Moreover, the study by Kang *et al*. [9] found that best visual acuity was in eyes with thickening with homogeneous optical reflectivity.

Electron microscope found intracytoplasmic swelling of Muller cells and secondary neuronal degeneration in eyes with CME [19] and so may have less visual acuity than those with diffuse macular edema. Recently, Sun *et al*. [20] have also discovered that the inner retinal layer disturbance in the 1-mm foveal area leads to worse VA.

The mean central foveal thickness of: group 1 (diffuse macular edema without cysts) was 337.92 ± 71.58, group 2 (CME) was 408.94 ± 68.36, group 3 (CME with SRD) was 453.10 ± 98.83 while Otani *et al*. [15] have found that the mean foveal thickness was 424.6 ± 18 μm in eyes with diffuse macular edema, and 527.6 ± 18 μm in eyes with CME. Yang *et al*. [21] reported a mean foveal thickness of 255.6 μm in eyes

with CSME, and 174.6 μm in eyes without CSME. Yamamoto *et al*. [5] recorded that the mean foveal thickness became 252.7 μm in eyes with diffuse macular edema, and 537.1 μm in eyes with CME.

The current study revealed a reverse correlation between best-corrected VA and CMT of the fovea in patients with diffuse thickening alone, whereas the correlation was not significant in eyes associated with CME or SRD. These results were comparable to previous studies, which showed modest correlation between OCT measured CMT and VA. Kim *et al*. [6] found that the more the increase in retinal thickness, whatever the pattern, the worse the VA, and Otani *et al*. [15] found that the central foveal thickness and the BCVA revealed an intermediate negative correlation, whatever the tomographic features, whereas Murakami *et al*. [16] concluded that CME type had mean VA significantly worse than with the SRD type or diffuse type but found that thickening of fovea was significantly correlated with bad VA in eyes with diffuse macular edema or with CME but not in eyes with SRD.

Recently, Shin *et al*. [22] assumed that integrity of foveal photoreceptor layer was related intimately with the final VA in DME.

Conclusion

OCT has the advantage that it gives quantitative measurements, beside the qualitative assessment done with biomicroscopy or fluorescein angiography. Our study affirmed that OCT is very useful in routine assessment of DME either before or after therapy and in detecting vitreoretinal traction and SRD undetectable on biomicroscopy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Aiello LP, Gardner TW, King GL, Blankenship G, Cavallerano JD, Ferris FLIII, Klein R. Diabetic retinopathy. Technical review. Diabetes Care 1998; 21:143–156.

2 Mohamed Q, Gillies MC, Wong TY. Management of diabetic retinopathy: a systematic review. JAMA 2007; 298:902–916.

3 Klein BE, Klein R, Lee KE. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in beaver dam. Diabetes Care 2002; 25:1790–1794.

4 Zhang X, Bao S, Lai D, Rapkins RW, Gillies MC. Intravitreal triamcinolone acetonide inhibits breakdown of the blood-retinal barrier through differential regulation of VEGF-A and its receptors in early diabetic rat retinas. Diabetes 2008; 57:1026–1033.

5 Yamamoto S, Yamamoto T, Hayashi M, Takeuchi S. Morphological and functional analyses of diabetic macular edema by optical coherence tomography and multifocal electroretinograms. Graefes Arch Clin Exp Ophthalmol 2001; 239:96–101.

6 Kim BY, Smith SD, Kaiser PK. Optical coherence tomographic patterns of diabetic macular edema. Am J Ophthalmol 2006; 142:405–412.

7 Senger DR, Connolly DT, van de Water L, Feder J, Dvorak HF. Purification and NH2-terminal amino acid sequence of guinea pig tumor-secreted vascular permeability factor. Cancer Res 1990; 50:1774–1778.

8 Sander B, Larsen M, Engler C, Strøm C, Moldow B, Larsen N, Lund-Andersen H. Diabetic macular oedema: a comparison of vitreous fluorometry, angiography and retinopathy. Br J Ophthalmol 2002; 86:316–320.

9 Kang SW, Park CY, Ham DI. The correlation between fluorescein angiographic and optical coherence tomographic features in clinically significant diabetic macular edema. Am J Ophthalmol 2004; 137:313–322

10 Golubovic-Arsovska M. Correlation of diabetic maculopathy and level of diabetic retinopathy. Section Biol Med Sci 2006; 27:139–150.

11 Klein R, Klein BEK, Moss SE, Cruickshanks KJ. The WSDR XV. The long-term incidence of macular edema. Ophthalmology 1995; 102:7–16.

12 Chou TH, Wu PC, Kuo JZC, Lai CH, Kuo CN. Relationship of diabetic macular oedema with glycosylated haemoglobin. Eye 2009; 23:1360–1363.

13 Huirong Z, Xinrong L. Classification and visual prognosis of diabetic maculopathy. Chinese Journal of Ocular Fundus Diseases (2000)-03.

14 Fine BS, Brucker AJ. Macular edema and cystoid macular edema. Am J Ophthalmol 1981; 92:466.

15 Otani T, Kishi S, Maruyama Y. Patterns of diabetic macular edema with optical coherence tomography. Am J Ophthalmol 1999; 127:688–693.

16 Murakami T, Nishijima K, Sakamoto A, Ota M, Horii T, Yoshimura N. Association of pathomorphology, photoreceptor status, and retinal thickness with visual acuity in diabetic retinopathy. Am J Ophthalmol 2011; 151:310–317.

17 Catier A, Tadayoni R, Paques M, Erginay A, Haouchine B, Gaudric A, Massin P. Characterisation of macular edema from various etiologies by optical coherence tomography. Am J Ophthalmol 2005; 140:200–206.

18 Nassif N, Cense B, Park BH, Yun SH, Chen TC, Bouma BE, *et al*. *In vivo* human retinal imaging by ultrahigh-speed spectral domain optical coherence tomography. Opt Lett 2004; 29:480–482.

19 Yanoff M, Fine BS, Brucker AJ, Eagle RCJr. Pathology of human cystoid macular edema. Surv Ophthalmol 1984; 28 (Suppl):505–511.

20 Sun JK, Lin MM, Lammer J, Prager S, Sarangi R, Silva PS, Aiello LP. Disorganization of the retinal inner layers as a predictor of visual acuity in eyes with center-involved diabetic macular edema. JAMA Ophthalmol 2014; 132:1309–1316.

21 Yang C, Cheng C, Lee F, Hsu WM, Liu JH. Quantitative assessment of retinal thickness in diabetic patients with and without clinically significant macular edema using optical coherence tomography. Acta Ophthalmol Scand 2001; 79:266–270.

22 Shin HJ, Lee SH, Chung H, Kim HC. Association between photoreceptor integrity and visual outcome in diabetic macular edema. Graefes Arch Clin Exp Ophthalmol 2012; 250:61–70.