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RETINAL DISORDERS

Spectral domain optical coherence tomography classification of diabetic macular edema: a new proposal to clinical practice

Serra Arf[1] · Isil Sayman Muslubas[1] · Mumin Hocaoglu[1] · Mehmet Giray Ersoz[1] · Hakan Ozdemir[2] · Murat Karacorlu[1]

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Abstract

Purpose To classify the types of diabetic macular edema (DME) and evaluate its morphological features on spectral domain optical coherence tomography (SD-OCT) and determine correlations between visual acuity and OCT findings.

Methods We assessed 406 eyes of 309 patients with a diagnosis of DME retrospectively. Three types based on SD-OCT were identified: diffuse macular edema, cystoid macular edema, and cystoid degeneration. Morphological features such as serous macular detachment (SMD), vitreomacular interface abnormalities (VMAI), hard exudates, photoreceptor status, and correlations between visual acuity and those morphological features were also evaluated by SD-OCT.

Results The most common type of DME was cystoid edema (68.5%). No statistically significant difference was found between groups in sex ($P = 0.40$), type of diabetes ($P = 0.50$), or diabetic retinopathy ($P = 0.78$). However, the duration of symptoms and BCVA was significantly lower in the group with cystoid degeneration compared with the group with cystoid edema ($P < 0.001$) and the group with diffuse macular edema ($P < 0.001$). In the group with cystoid degeneration compared with the groups with cystoid and diffuse edema, the central fovea and central subfield were significantly thicker (both ($P < 0.001$), the subfoveal choroid was significantly thinner ($P = 0.049$), rate of serous macular detachment was significantly lower ($P < 0.001$), and the rate of outer retinal damage was significantly higher ($P < 0.001$).

Conclusions Cystoid macular degeneration, which is consistent with poor functional and morphological outcomes, should be differentiated from cystoid macular edema. Serous macular detachment, which is mostly seen in eyes with early stages of DME, should be evaluated as an accompanying morphological finding rather than a type of DME.

Keywords Diabetic macular edema · Serous macular detachment · Cystoid macular edema · Diffuse macular edema · Cystoid macular degeneration · SD-OCT

Introduction

Diabetic macular edema (DME) is caused primarily by the breakdown of the blood-retinal barrier and is characterized by collection of fluid in the central retina [1]. It is the most common reason for visual deterioration in patients with diabetes. Macular edema can be observed at any stage and in any type of diabetic retinopathy (DR) and can cause visual impairment experienced by patients with diabetes [1–3]. The Wisconsin Epidemiologic Study of DR reported that 20.1% of patients with type 1 diabetes, 13.9% of patients with type 2 diabetes not using insulin, and 25.4% of those with type 2 diabetes using insulin develop DME after 10 years from diagnosis [1–3].

To date, many definitions and classifications of DME have been used [2, 3]. The term clinically significant DME is used to be preferred to determine its seriousness, depending primarily on subjective methods such as indirect ophthalmoscopy. Clinically significant macular edema was further classified into focal or diffuse. However, leakage noted on angiography is not always correlated with edema [2, 3].

Recently, optical coherence tomography (OCT) has been widely used as a safe and accurate imaging method for assessing macular anatomy both quantitatively and qualitatively. As well as OCT features of DME, such as spongelike macular swelling, diffuse retinal thickening, cystoid macular edema (CME), serous macular detachment (SMD), and

✉ Murat Karacorlu
mkaracorlu@gmail.com

[1] Istanbul Retina Institute, Hakkı Yeten Cad. Unimed Center No: 19/7 Fulya – Şişli, 34349 Istanbul, Turkey

[2] Department of Ophthalmology, Bezmialem Vakıf University Faculty of Medicine, İstanbul, Turkey

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vitreomacular interface abnormalities (VMIA), correlations between those OCT features and status of foveal photoreceptor and visual acuity have been reported [4–8]. However, it is known that cystoid macular degeneration (CMD), which is a result of chronic macular edema and associated with poor visual acuity, is a finding distinct from CME; CMD and CME should be separated from each other in OCT-based classifications. Also, SMD in DME is visible on OCT as a hyporeflective area beneath the neuroretina. It has a reported prevalence of approximately 15–30% in eyes with DME and has a significant inflammatory component, regardless of the morphologic DME pattern [5, 6].

In this study, CME and CMD were differentiated from each other, and SMD was excluded from the DME types and was considered as a comorbid finding. According to this, we categorized DME as diffuse macular edema, CME, or CMD, using OCT, and investigated whether the type of macular edema and features such as SMD, hard exudates, and vitreomacular interface abnormalities associated with visual acuity.

Methods

Patients with clinically evident DME associated with diabetes were evaluated at Istanbul Retina Institute between January 2010 and December 2018 and assessed retrospectively. Written informed consent was obtained prior to the diagnostic and therapeutic procedures. The study protocol was approved by the Institutional Review Board of Memorial Şişli Hospital, Istanbul. The study adhered to the tenets of the Declaration of Helsinki.

All patients received a comprehensive ophthalmic examination, and the macula was screened by using spectral domain optical coherence tomography device (SD-OCT, Heidelberg Engineering, Heidelberg, Germany), as described previously [9]. The presumed fovea was characterized as the central area in the absence of inner retinal layers, nerve fiber layer, ganglion cell layer, inner plexiform layer, and inner nuclear layer, whether cystoid spaces, retinal swelling, or SMD were present or absent [10]. Central subfield thickness was determined as the average thickness in the central 1-mm diameter circle of the ETDRS grid. The morphologic features within the scanned 1-mm area centered on the fovea were assessed for each eye. The macula was screened by taking 49 sections (512 A-scan) at 120 μm intervals within a 20° × 20° rectangular field by Spectralis HRA + OCT. An average of nine images was obtained for each section. Two high-quality, horizontal, and vertical line scans centered on the fovea were obtained for each eye. One hundred frames were averaged using automatic averaging, and fundus features were saved and tracked automatically to align follow-up scans. Lesions on SD-OCT imaging were evaluated by 2 independent observers (S.A and I.S.M.). EDI-OCT was used for measuring subfoveal choroidal thickness (SCT) in all cases. The SCT was defined as the distance between the base of the RPE and the choroidoscleral boundary. Manual calipers provided with the software of the device were used for measurement. Values for each central foveal choroidal thickness were obtained from horizontal and vertical line scans, and values were averaged.

We classified patients into three types with SD-OCT: type 1, eyes with diffuse edema; type 2, eyes with CME; and type 3, eyes with CMD. Each type was then subdivided into a, b, and c according to presentation of morphological findings. The presence of SMD was graded as "a," presence of VMIA such as vitreomacular traction (VMT) and epiretinal membrane (ERM) was graded as "b," and presence of hard exudate was graded as "c" (Table 1).

Diffuse edema was determined as increased retinal thickness with reduced intraretinal reflectivity and expanded areas of lower reflectivity [7, 8]. The localization of intraretinal cystoid-like spaces that presented as round or oval areas of low reflectivity with highly reflective septa separating the cystoid-like spaces was named as CME. Eyes with cystoid spaces of horizontal diameter ≥ 600 μm were graded as CMD [7, 11]. Although there is no consensus on the definition of CMD, severe CME (the horizontal diameter of cystoid spaces ≥ 600 μm) was accepted as CMD. SMD was considered present if the posterior surface of the retina was elevated over a nonreflective cavity with minimal shadowing of the underlying tissues [5]. VMIA classifications were based on International Vitreomacular Traction Study Group [12]. Intraretinal or subretinal highly reflective spots were identified as hard exudates [13].

The status of outer retinal layers within the central 1 mm (external limiting membrane (ELM) and ellipsoid zone (EZ)) was also evaluated. Eyes with a well-delineated and continuous ELM were classified as intact, and eyes with an interrupted ELM were classified as disrupted. Each eye also was classified on basis of the status of the ellipsoid zone beneath the fovea, by using the same criteria described for the ELM line, that is, ellipsoid zone intact or disrupted.

Eyes with type 1 or 2 diabetes mellitus with clinically evident DME with satisfactory quality OCT images were evaluated in the study. Patients with macular edema due to any cause

Table 1 Classification of diabetic macular edema

Category	SD-OCT appearance
Type 1	Diffuse macular edema
Type 2	Cystoid macular edema
Type 3	Cystoid macular degeneration
a	Serous macular detachment
b	Vitreomacular interface abnormalities*
c	Hard exudates

*Presence of vitreomacular traction or epiretinal membrane

SD-OCT spectral domain optical coherence tomography

other than DM, significant media opacities such as cataract or vitreous hemorrhage, or ocular diseases except diabetic retinopathy were excluded from the study. Patients who had undergone cataract surgery, intravitreal injection, or peripheral argon laser photocoagulation within the last 6 months or had a history of macular focal/grid laser or macular surgery were also excluded from the study. We also excluded eyes with subretinal lipid aggregating within the 1-mm central scanned area.

Data for all 406 eyes were used for statistical analysis. Descriptive statistical methods (mean, standard deviation) were used for characteristics. For comparison of groups, the independent *t* test and one-way ANOVA were used for continuous variables and chi-square test for categorical data. The influence of variables on BCVA was analyzed with multivariate linear regression. Statistical analyses used SPSS Version 20.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

A total of 406 eyes of 309 patients with ages ranging from 19 to 85 were evaluated in the study. The mean duration of diabetes was 15.4 ± 7.1 years, and the mean duration of symptoms was 15.5 ± 13.6 months. Approximately 89% of patients had type 2 diabetes, and 77% of eyes had nonproliferative DR.

Three DME types based on OCT were identified: diffuse edema in 100 eyes of 81 patients (24.6%), CME in 278 eyes of 203 patients (68.5%), and CMD in 28 eyes of 25 patients (6.9%). The most common type of DME was CME. No statistically significant difference was seen between the groups in sex ($P = 0.40$), type of diabetes ($P = 50$), or DR ($P = 0.78$). However, the duration of symptoms and BCVA were significantly different in the group with CMD compared with the groups with CME ($P < 0.001$) and diffuse edema ($P < 0.001$). Patient with recent onset DME were also evaluated. The duration of symptom was 6 months or less in 40 eyes (40%) in the diffuse edema group and in 106 eyes (38%) in the cystoid macular edema group. In the cystoid macular degeneration group, none of the eyes had symptoms less than 6 months. While diffuse edema and cystoid macular edema were seen in patients with recent onset of DME, cystoid macular degeneration was identified in patients with longer duration of symptoms (Table 2).

In the group with CMD compared with the groups with CME and diffuse macular edema, the central fovea and central

Table 2 Patient characteristics

	Diffuse macular edema (type 1)	Cystoid macular edema (type 2)	Cystoid macular degeneration (type 3)	*P*
Number of eyes (%)	100 (24.6)	278 (68.5)	28 (6.9)	< 0.001*
Age, years (range)†	58.5 ± 10.9 (26 to 82)	59.1 ± 10.7 (19 to 85)	63.4 ± 10.7 (32 to 79)	< 0.09*
Female, %	28 (35)	86 (37.4)	9 (36)	0.40§
Duration of diabetes, years (range)††	14.9 ± 7.1 (1 to 38)	15.7 ± 7 (1 to 40)	19.2 ± 6.6 (7 to 30)	0.01*
Duration of symptoms, months (range) •	13.9 ± 11.8 (1 to 48)	14.5 ± 14 (1 to 60)	34.9 ± 15 (12 to 60)	< 0.001*
Type of diabetes, (%)				
Type 1	11 (13.6)	21 (10.4)	3 (12)	0.50§
Type 2	70 (86.4)	182 (89.6)	22 (88)	
Type of diabetic retinopathy, (%)				
Nonproliferative	75 (75)	214 (77)	23 (82.1)	0.78§
Proliferative	25 (25)	64 (23)	5 (17.9)	
BCVA, LogMAR (range) ••	0.36 (1.0 to 0.1)	0.46 (1.0 to 0.0)	0.89 (1.0 to 0.6)	< 0.001*

BCVA best corrected visual acuity, *LogMAR* logarithm of the minimal angle of resolution

Data, except percentages, are mean ± standard deviation (range)

§ Pearson's chi-square test

*One-way ANOVA test

† Cystoid macular edema (CME) vs diffuse macular edema (DME) $P > 0.99$; CME vs cystoid macular degeneration (CMD) $P = 0.14$; DME vs CMD $P = 0.10$, Bonferroni post hoc test

†† CME vs DME $P > 0.99$; CME vs CMD $P = 0.07$; DME vs CMD $P = 0.01$, Bonferroni post hoc test

• CME vs DME $P < 0.99$; CME vs CMD $P < 0.001$; DME vs CMD $P < 0.001$, Bonferroni post hoc test

•• CME vs DME $P = 0.001$; CME vs CMD $P < 0.001$; DME vs CMD $P < 0.001$, Bonferroni post hoc test

subfield were significantly thicker (both $P < 0.001$), the subfoveal choroid was significantly thinner ($P = 0.049$), the rate of presence of SMD was significantly lower ($P < 0.001$), the rate of presence of exudate was significantly lower ($P < 0.001$), and the rate of outer retinal damage was significantly higher ($P < 0.001$) (Table 3).

Multivariable linear regression analyses revealed that BCVA was significantly associated with longer duration of symptoms ($P = 0.004$), increased central subfield thickness ($P = 0.02$), and disruption of the EZ ($P < 0.001$) and ELM ($P = 0.04$). However, there was no association between BCVA and presence of SMD ($P = 0.45$), hard exudate ($P = 0.56$), vitreomacular traction ($P = 0.36$), or epiretinal membrane ($P = 0.06$) (Table 4).

The presence of SMD was lower in eyes with longer duration of symptoms, disrupted ellipsoid zone and ELM, CMD, and epiretinal membrane (all $P < 0.001$). In eyes with epiretinal membrane, the duration of disease was longer ($P = 0.04$), as was the duration of symptoms ($P = 0.001$). In eyes with hard exudate, the rate of presence of SMD was statistically higher, and the rate of presence of an ERM was statistically lower than in eyes with no hard exudate (both $P = 0.001$).

The coexistence of SMD and hard exudate was the most common finding in both diffuse edema and CME, whereas the presence of ERM was the most common finding in the CMD type. The distribution of SMD, VMIA, and hard exudates within types of DME is demonstrated in Table 5, and types of DME are presented in Fig. 1.

Discussion

Various morphological categories of DME based on OCT have been advised [14]. First, Otani et al. [8] reported three structural features of DME: spongelike retinal swelling, CME, and serous retinal detachment. Panozzo et al. [15] classified three main morphologies of DME as simple thickening, cystoid thickening, and neuroepithelial detachment and also graded epiretinal traction as four types. In the study of Kim et al. [7], the presence of VMT was considered, and five OCT patterns, diffuse retinal thickening, CME, serous retinal detachment, posterior hyaloidal traction, and tractional retinal detachment, were identified.

In previous studies, it has been shown that the development of DME is initiated by fluid collection within Müller cells owing to downregulation of the Kir4.1 channels [4, 16, 17]. The subsequent swelling of Müller cells causes Müller cell dysfunction. If fluid continues to accumulate, necrosis of

Table 3 Type of diabetic macular edema and characteristics on optical coherence tomography

Characteristic	Diffuse macular edema (Type 1, *n*:100)	Cystoid macular edema (Type 2, *n*:278)	Cystoid macular degeneration (Type 3, *n*:28)	*P*
Central foveal thickness, μm (range) †	382.2 ± 92.3 (267 to 731)	528.2 ± 145.6 (258 to 987)	699.9 ± 110.2 (523 to 988)	< 0.001*
Central subfield thickness, μm (range) † †	419.9 ± 83.1 (302 to 701)	526.4 ± 125.6 (274 to 973)	664.7 ± 101.7 (487 to 949)	< 0.001*
Subfoveal choroidal thickness, μm (range) •	277 ± 51.7 (162 to 403)	286.8 ± 68.4 (150 to 534)	246.5 ± 50.8 (155 to 313)	0.049*
Serous macular detachment (a) (%)	50 (50)	123 (44.2)	1 (3.6)	< 0.001••
Vitreomacular interface (b) (%)				
Vitreomacular traction	1 (1)	10 (3.6)	0 (0)	0.26••
Epiretinal membrane	24(24)	55 (19.8)	8 (28.6)	0.43••
Exudate (c) (%)	60 (60)	130(46.8)	6(21.4)	0.001••
External limiting membrane status (%)				
Intact	94 (94)	233 (83.8)	1 (3.6)	< 0.001••
Disrupted	6 (6)	45 (16.2)	27 (96.4)	< 0.001••
Ellipsoid zone status (%)				
Intact	91(91)	215 (77.3)	0 (0)	< 0.001••
Disrupted	9 (9)	63 (22.7)	28 (100)	< 0.001••

Data, except percentages, are mean ± standard deviation (range)

•• Pearson's chi-square test

*One-way ANOVA test

† Cystoid macular edema (CME) vs diffuse macular edema (DME) $P < 0.001$; CME vs cystoid macular degeneration (CMD) $P < 0.001$; DME vs CMD $P < 0.001$, Bonferroni post hoc test

†† CME vs DME $P < 0.001$; CME vs CMD $P < 0.001$; DME vs CMD $P < 0.001$, Bonferroni post hoc test

• CME vs DME $P > 0.99$; CME vs CMD $P = 0.05$; DME vs CMD $P = 0.30$, Bonferroni post hoc test

Table 4 Multivariable linear regression analyses for best corrected visual acuity

Variable*	B	95% confidence interval	*P*
Age	−0.033	−0.003 to 0.001	0.50
Duration of disease	−0.7	−0.006 to 0.001	0.10
Duration of symptoms	0.141	0.001 to 0.004	0.004
Central subfield thickness	0.28	0.000 to 0.001	0.02
Subfoveal choroidal thickness	−0.086	−0.001 to 0.000	0.07
Serous macular detachment	0.035	−0.027 to 0.062	0.45
Epiretinal membrane	0.083	−0.001 to 0.105	0.06
Vitreomacular traction	0.039	−0.063 to 0.172	0.36
Exudate	0.025	−0.029 to 0.054	0.56
Ellipsoid zone status	0.443	0.167 to 0.339	< 0.001
External limiting membrane status	0.157	0.003 to 0.195	0.04

B regression coefficient

* Age, duration of disease, duration of symptoms, central subfield thickness, subfoveal choroidal thickness, presence of serous macular detachment, presence of epiretinal membrane, presence of vitreomacular traction, presence of exudate, status of ellipsoid zone, and external limiting membrane were considered

Müller cells may occur [4, 17]. As the swollen Müller cell cytoplasm is associated with the swelling type of DME, liquefaction necrosis of Müller cells leads to cystoid spaces [18]. As a result, death of Müller cells and neuroglia results in the configuration of large cystoid spaces [4]. In the study of Murakami et al. [18], it was concluded that the patterns of foveal pathomorphology, such as CME, SMD, and retinal swelling, represented the stages of progression of DME, and the SMD or retinal swelling types could be chronologically earlier than the CME type. In another study, DME was also classified in terms of the size of cystoid spaces, and cases with cystoid spaces with horizontal diameter ≥ 600 μm were identified as severe CME. It was concluded that the horizontal diameter of the largest cyst could predict poor visual acuity and that an association between the size of cystoid cavities, retinal thickness, and visual acuity was reported [19].

Table 5 Distribution of presence of serous macular detachment, vitreomacular interface abnormalities, and hard exudates within types of diabetic macular edema

Abnormality on SD-OCT (%)	Diffuse macular edema (type 1) (*n*: 100)	Cystoid macular edema (type 2) (*n*: 278)	Cystoid macular degeneration (type 3) (*n*: 28)
None	13 (3.2)	54 (13.3)	15 (3.7)
a	14 (3.4)	46 (11.3)	–
b	11 (2.7)	38 (9.3)	*7 (1.7*
c	21 (5.2)	52 (12.8)	4 (1)
a + b	2 (0.5)	10 (2.5)	–
a + c	*27 (6.7)*	*61 (15)*	1 (0.2)
b + c	5 (1.2)	11 (2.7)	1 (0.2)
a + b + c	7 (1.7)	6 (1.5)	–

a, presence of serous macular detachment; b, presence of vitreomacular interface abnormalities such as vitreomacular traction and epiretinal membrane; c, presence of hard exudate; a + b, presence of serous macular detachment and vitreomacular interface abnormalities; a + c, presence of serous macular detachment and hard exudate; b + c, vitreomacular interface abnormalities and hard exudate; a + b + c, presence of serous macular detachment, vitreomacular interface abnormalities, and hard exudate

In the light of this information, we distinguished CMD—large cystoid cavities with horizontal diameter ≥ 600 μm, consistent with long-term diabetic macular edema—from CME in our study. Three main morphologies of DME were identified. Eyes with SMD, VMIA, or hard exudates were evaluated separately and included in the classification. The duration of symptoms was shorter, BCVA was better, and central subfield thickness was lower in the diffuse macular edema group than in the CME group. Also, the rates of intact ELM and EZ were higher in eyes with diffuse macular edema than eyes with CME. Furthermore, the duration of symptoms was longer, BCVA was worse, central subfield thickness was greater, and rate of outer retinal damage was higher in the group with CMD compared with the group with CME and diffuse macular edema. Similar to previous reports, it could be concluded that diffuse macular edema is the earliest type of DME. However, CMD is the chronic form of DME and is chronologically much later than CME.

The configuration of SMD was not related with the duration or severity of DME in the study of Gaucher et al. [11]. However, Campos et al. [20] suggested that SMD was more likely to occur in early-onset DME associated with increased choroidal thickness, increased choriocapillaris permeability, and outer blood-retinal barrier dysfunction. The rate of presence of SMD was lower in eyes with longer duration of symptoms, which was different from the findings of Gaucher et al. The rate of presence of SMD was lower in eyes with CMD than in eyes with diffuse edema and CME. SMD was detected in eyes with diffuse edema and CME, without statistically difference between two groups.

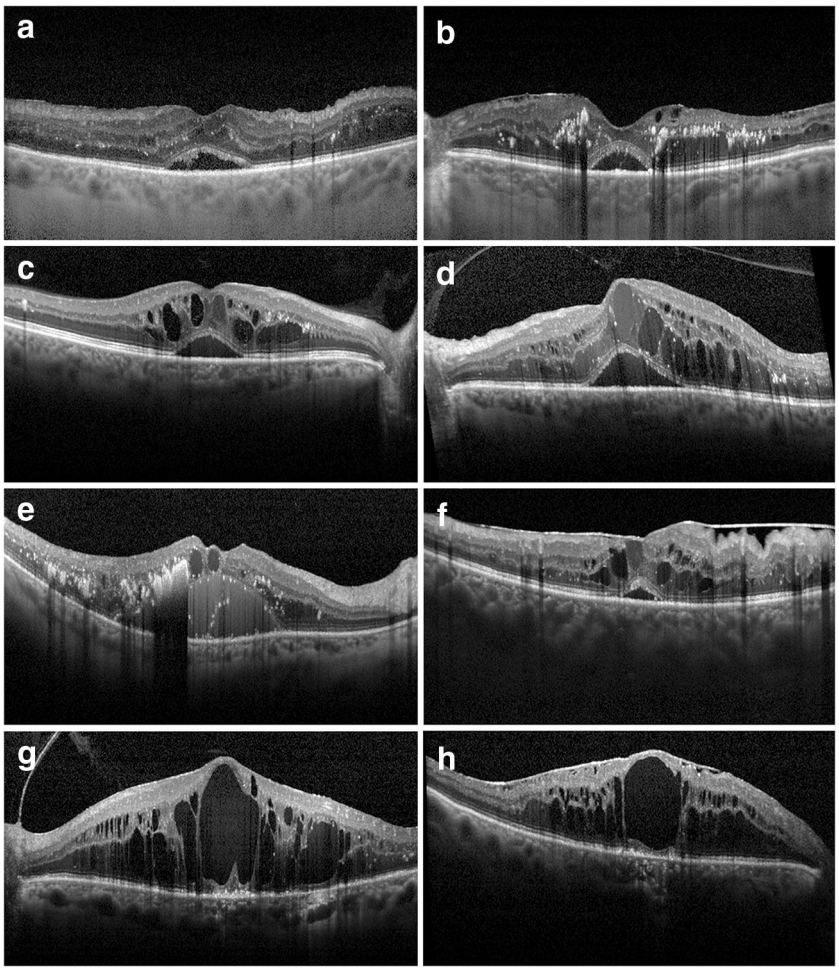

Fig. 1 Types of diabetic macular edema. Patient with diffuse macular edema with serous macular detachment (Type 1 a) (**a**). Patient with diffuse macular edema with serous macular detachment and hard exudate (Type 1 a + c) (**b**). Patient with cystoid macular edema with serous macular detachment (Type 2 a) (**c**). Patient with cystoid macular edema with serous macular detachment and vitreomacular traction (Type 2 a + b) (**d**). Patient with cystoid macular edema with serous macular detachment and hard exudate (Type 2 a + c) (**e**). Patient with cystoid macular edema with serous macular detachment and epiretinal membrane (Type 2 a + b) (**f**). Patient with cystoid macular degeneration (Type 3) (**g**). Patient with cystoid macular degeneration and epiretinal membrane (Type 3 b) (**h**)

In the study of Vujosevic et al. [6], morphologic and functional characteristics of eyes with DME and SMD vs DME without SMD were assessed, and it was reported that BCVA was not different between the two groups, but DME with SMD correlated with interruption of the ELM, greater choroidal thickness, and macular impairment. In the present study, there was also no association between visual acuity and presence of SMD. However, the rate of SMD was lower in eyes with a disrupted EZ and ELM, different from previous study.

Hard exudates can be frequently seen in eyes with DR along with macular edema and are composed of lipids and proteinaceous material, such as fibrinogen and albumin that leak from microaneurysms and dilated capillaries [21, 22]. It has been demonstrated that increasing amounts of hard exudates are related with a risk of visual deterioration and degradation of submacular hard exudates, causing a severe reduce in visual acuity in patients with DME [23]. In the present study, hard exudates were observed, especially in eyes with early stages of DME, as expected, but there was no association between BCVA and presence of hard exudates because we excluded eyes with subretinal aggregates within the 1-mm central scanned area, unlike previous studies.

The prevalence of VMT, including eyes with taut thickened posterior hyaloid and vitreoretinal adhesion, ranges between 4 and 25% in eyes with DME. Studies have reported a prevalence of ERM between 13 and 34% in eyes with DME [24, 25]. In the study of Mikhail et al. [25], 146 eyes with DME were evaluated, and 19 (13%) of those had an ERM, 8 (5.5%) had VMT, and one (0.7%) had both. A statistically significant difference in mean BCVA was observed between patients with and without VMIA; patients with these abnormalities had worse vision [25]. In the present study, 87 (21.4%) of the 406 eyes with DME had an ERM, and 11 (2.7%) had VMT. Unlike the study by Mikhail et al. [25], there was no association between BCVA and presence of an ERM or VMT.

Impairment of the EZ has been correlated with increased severity of DR [14]. It is known that loss of the ELM and the EZ is closely associated to poor visual acuity in cases with DME [10, 14, 18, 26]. This was demonstrated also in our study. Murakami et al. [10] found that an intact ELM represented better visual acuity in eyes of the CME type and diffuse type but not in eyes with the serous retinal detachment type in DR. In our study, although there was no association between SMD and visual

acuity, the presence of SMD was lower in eyes with EZ and ELM disruption. Also, both EZ and ELM disruption were correlated with presence of CMD, as expected.

Strengths of this study include the well-defined cohort and large sample size. The study also has some limitations, including the lack of treatment results, lack of macular angiographic features (dye-based angiographic or OCTA), and retrospective design.

In conclusion, diffuse macular edema is the earliest type of DME. However, CMD is the chronic form of DME and is chronologically much later than CME. CMD, which is consistent with poor functional and morphological outcomes, should be differentiated from CME. Serous macular detachment, which is mostly seen in eyes with early stages of DME, should be evaluated as an accompanying morphological finding rather than a type of DME. However, the presence of hard exudates is mostly seen in eyes with early stages of DME, similar to SMD. The presence of an ERM is correlated with duration of DME. The coexistence of SMD and hard exudate was the most common finding in both diffuse edema and CME, whereas the presence of ERM was the most common finding in the CMD type.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent licensing arrangements), or nonfinancial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name the institution/committee) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. "For this type of study formal consent is not required."

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