Société Française d'Ophtalmologie

DIABETIC MACULAR EDEMA: DIAGNOSIS AND PRETREATMENT ASSESSMENT

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Diabetic macular edema (DME) is still the leading cause of visual impairment in diabetic retinopathy (DR)(1). The therapeutic arsenal of DME has nevertheless been considerably enhanced in recent years because several molecules have been approved for the treatment of DME.
DME pathogenesis is complex and is not fully understood. It involves several interrelated mechanisms (breakdown of the blood-retinal barrier, impairment in retinal dehydration mechanisms) and DME may be exacerbated by systemic factors such as high blood pressure or ocular factors, including vitreomacular traction. Before considering the treatment of DME, it is therefore essential to perform an exhaustive pretreatment assessment to potentially identify the major mechanism, and determine the best therapeutic indication.

DEFINITION OF DME

According to the International classification of the American Academy of Ophthalmology, DME is defined by the presence of any retinal thickening or hard exudate on the posterior pole in diabetic patients with diabetic retinopathy (2).

PRETREATMENT ASSESSMENT

The pretreatment assessment aims at assessing the functional impact of DME, determining DME phenotype, investigating aggravating (including systemic) factors for DME, and assessing factors influencing the therapeutic decision.

1. Anamnesis

Collection of clinical data on

The patient:

- patient age,
- type of diabetes, its duration and its treatment
- quality of the blood glucose control (HbA1c)
- blood pressure control and treatment
- renal function (proteinuria, renal function)
- existence of dyslipidemia (cholesterol, triglyceridemia)
- existence of sleep apnea
- patient general condition, difficulty moving, pregnancy, recent cardiovascular history, associated glaucoma and its treatment

DME:

- time since diagnosis
- previous treatments

2. **Functional impact: measurement of the best-corrected visual acuity**

3. **Biomicroscopy and fundus examination:**

    - Lens condition, measurement of intraocular pressure
    - Macular thickening, presence of exudates
    - Investigating a complete vitreous detachment
    - Severity of associated diabetic retinopathy
    - Optic disc, assessment of the cup-to-disc ratio

4. **Additional examinations**

- **Optical Coherence Tomography (OCT)** is the reference diagnostic examination for DME. It is more sensitive than biomicroscopy for the early detection of DME. It allows assessing the macular thickening, precisely locating and quantifying it. It also allows analyzing changes in the intraretinal structures associated with DME and in the vitreomacular interface. OCT will therefore allow assessing the presence of negative predictive factors for visual acuity (for example, extended photoreceptor cell atrophy or thinning of the inner retina), vitreomacular traction or epimacular membrane (thin or thick with retinal folds).
- **Color fundus photographs** of the posterior pole and retinal periphery allow visualizing retinal lesions with a greater sensitivity than fundus examination and quantifying the severity of RD associated with DME.
- In DME, **fluorescein angiography** is useful to identify the sources of leakage responsible for DME, as well as the severity of macular capillary occlusions associated with DME, an important prognostic factor.

CLASSIFICATION OF DME

Once these examinations performed, it will be possible to determine DME severity and type according to its classification. Several DME classifications have been proposed. The international ETDRS classification remains the reference classification. It is based on DME location from the macula center, assessed on stereoscopic fundus color photographs (3). The disadvantage of the ETDRS classification is that it is too complex for routine practice. That is why a simplified ETDRS classification has been proposed: the International classification of the American Academy of Ophthalmology (2), which is based on the location of the edema from the macula center. It is assessed on photographs of the posterior pole: the closer from the center the edema is, the greater the visual threat is.

The angiographic classification into focal, diffuse and mixed DME, depending on the source of leakage, is controversial. There is no international consensus on the definitions of focal and

diffuse DME (4) and clinical studies have failed to demonstrate the prognostic value of this classification.

Finally, although OCT allows assessing many retinal anomalies associated with DME, there is, to date, no internationally accepted DME classification based on OCT. Indeed, there is no strict correlation between the macular thickness and the visual acuity, therefore DME severity cannot be described based only on this parameter. As for most retinal anomalies assessed by OCT, their prognostic value has not yet been clearly demonstrated.

However to date, a "modern" classification of DME may be proposed based on the international AAO classification, by adding the signs known to be associated with negative functional outcomes.

MODERN CLASSIFICATION OF DME

MILD diabetic macular edema	retinal thickening or hard exudates **at the posterior pole but remote from the fovea center**
MODERATE diabetic macular edema	retinal thickening or hard exudates **in the vicinity of the macula center but not reaching the center**
SEVERE diabetic macular edema	retinal thickening or hard exudates **reaching the macula center**
TRACTIONAL diabetic macular edema	macular thickening associated with **a vitreomacular traction* or epimacular membrane****
FACTORS FOR NEGATIVE OUTCOMES	- macular ischemia: extended occlusion of the macular capillaries, with at least a doubling of the normal diameter of the foveal avascular zone - retrofoveal exudative plaques - photoreceptor cell atrophy extended to the macula center ***

***: vitreomacular traction is suspected on biomicroscopy based on the absence of** posterior vitreous detachment and a bright and tight aspect of the posterior vitreous cortex. OCT confirms the traction: the top of the edema is at or below the posterior vitreous cortex on OCT, the vitreous cortex is generally thickened, the vitreous adherence may be single or multiple, focal (width less than 1500 microns) with an acute or more extended sharp retinal profile leading to a table-top appearance. It may be isolated or associated with a thin epiretinal membrane.
This aspect should be differentiated from vitreomacular adherence: the posterior vitreous cortex is still adherent to the top of the edema but is rarely thickened, and most importantly, it runs on from both sides of the edema.
** **epimacular membrane**: thick epimacular membrane, resulting in retinal folds
*** extended disruption of the junction line between the photoreceptor inner and outer segments (ellipsoid line)

Conclusion

DME pretreatment assessment is based on the collection of the personal and ocular history, the functional (visual acuity) and anatomical (fundus examination, OCT) assessment of the retinal condition. Both color retinophotography and angiography allow better assessing the peripheral retina condition and macular ischemia. Once these examinations performed, DME classification allows determining whether the macular involvement is central and tractional.

Conflict of interest:

Pascale Massin: consultant or clinical investigator or speaker for Alimera, Allergan, Bayer, Novartis
Stéphanie Baillif: clinical investigator or speaker for Alcon, Allergan, Bayer, Novartis
Franck Fajnkuchen: consultant for Allergan, Bayer, Novartis
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Catherine Creuzot: consultant or clinical investigator or speaker for Alcon, Allergan, Bayer, Bausch &Lomb, Novartis, Théa

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