Correlation between Diabetic Macular Edema and Best Corrected Visual Acuity in Different Categories of Diabetic Retinopathy

Thesis

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ عَلَيْكَ
الْكِتَابَ وَالْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ وَكَانَ
فَضْلُ اللهِ عَلَيْكَ
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Elsayed Akef Abdelhafiz Mohamed

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List of Abbreviations

Abb.	Full term
µm	*Micrometer*
AGEs	*Advanced glycation end products*
BCVA	*Best corrected visual acuity*
BRB	*Blood-retinal barrier*
CME	*Cystoid macular edema*
CMT	*Central Macular thickness*
CSME	*Clinically significant diabetic macular edema*
DAG	*Diacylglycerol*
DCCT	*Diabetes Control and Complications Trial*
DM	*Diabetes mellitus*
DME	*Diabetic macular edema*
DR	*Diabetic Retinopathy*
eNOS	*Endothelial nitric oxide synthase*
ETDRS	*Early Treatment Diabetic Retinopathy Study*
FAZ	*Fovea avascular zone*
HB	*Hemoglobin*
HRC's	*High-risk characteristics*
IGF-1	*Insulin-like growth factor-1*
IOP	*Intra ocular pressure*
IPL	*Inner plexifom layer*
IQR	*Inter quartile range*
IRMA	*Intraretinal micro vascular abnormalities*
IVI	*Intra vitreal injection*
JAMs	*Junctional adhesion molecules*
MAR	*Minimal angle of resolution*
mm	*Millimeter*
NO	*Nitric oxide*
NPDR	*Non-proliferative diabetic retinopathy*
NSD	*Neurosensory retinal detachment*
NVD	*New vessels at disc*
NVE	*New vessels elsewhere*

List of Abbreviations cont...

Abb.	Full term
OCT	*Optical Coherence Tomography*
OPL	*Outer Plexiform Layer*
PDR	*Proliferative diabetic retinopathy*
PKC	*Protein kinase C*
PRP	*Pan retinal photocoagulation*
RAAS	*Renin-angiotensin-aldosterone system*
RAGE	*Receptor Advanced glycation end-products*
RFT	*Renal function test*
ROS	*Reactive oxygen species*
RPE	*Retinal pigment epithelium*
SD-OCT	*Spectral-domain Optical Coherence Tomography*
SPSS	*Statistical Package for the Social Sciences*
TD-OCT	*Time-domain Optical Coherence Tomography*
UKPDS	*United Kingdom Prospective Diabetes Study*
VEGF	*Vascular endothelial growth factor*
VTDR	*Vision-threatening diabetic retinopathy*
WESDR	*Wisconsin Epidemiologic Study of Diabetic Retinopathy*
ZO-1	*Zonula occludens-1*

INTRODUCTION

Diabetic retinopathy (DR) is a major cause of vision loss in the working age population and people with diabetes are 25 times more likely than the general population to go blind. (1)

Diabetic macular edema (DME) is a major cause of visual acuity loss in diabetes, it affects central vision from the early stages of retinopathy, and it is the most frequent sight-threatening complication of diabetic retinopathy, particularly in older type 2 diabetic patients. (2)

DME prevalence, indicated in the Wisconsin Epidemiologic Study of Diabetic Retinopathy done at Wisconsin university USA 1994, is only about 3% in mild non proliferative diabetic retinopathy (NPDR), but increases to 38% in moderate to severe NPDR and to 71% in eyes with proliferative diabetic retinopathy (PDR). (3)

Diabetic macular edema (DME) is manifested as retinal thickening caused by the accumulation of intraretinal fluid, primarily in the inner and outer plexiform layers. It is believed to be a result of hyper permeability of the retinal vasculature.

The Early Treatment Diabetic Retinopathy Study Group (ETDRS) defined DME (based on clinical grounds) as an increase in retinal thickness at or within one disc diameter of

the foveal center whether focal or diffuse, with or without hard exudates, sometimes associated with cysts. [4] [5]

The term "clinically significant macular edema" (CSME) characterize the severity of the disease:

1. Increase in retinal thickness 500 μ of the center of the fovea
2. Hard exudates 500 μ of the center of the fovea with increased retinal thickness.
3. Increase in retinal thickness one disc diameter within one disc diameter at the center of the fovea. [6]

DME leads to distortion of visual images and may cause a significant decrease in visual acuity even in the absence of severe retinopathy, although macular edema is a common and characteristic complication of diabetic retinopathy and shows apparent association with the systemic metabolic alterations of diabetes, it does not necessarily fit the regular course of diabetic retinopathy progression. It may occur at any stage of diabetic retinopathy. [7]

Patients with DME present with a range of visual symptoms depending on the degree to which the fovea is involved and the chronicity of the edema. If the macula center is not involved patients are rarely symptomatic; only a few very observant individuals may notice relative paracentral scotomas corresponding to focal edema and hard exudates. Some patients

with central macular involvement have excellent acuity and no visual complains, presumably because of only recent involvement of the center. Over time, patients experience a gradual progressive vision loss over weeks to month. Patients may complain of loss of color vision, poor night vision and washing-out of vision in bright sunlight with poor dark-light adaptation. [8][9]

Visual acuity is defined as the "spatial resolving capacity" of the eye or, put another way, the size of an object that can be resolved with an eye. It can be measured by identifying the angle subtended at the eye by the smallest recognizable optotype.

Visual Acuity Measurement

The most common approach is based on the detailed and rigorous refraction and VA protocols of the Early Treatment Diabetic Retinopathy Study (ETDRS), widely considered the gold standard for assessing VA in the ophthalmic clinical research setting. These protocols include specific requirements for refraction and VA lanes, acuity chart type, lighting and chart height, and careful, protocol-defined algorithms for performing refraction and VA measurement. [10, 11]

The ETDRS protocol of the National Eye Institute is widely accepted as the "gold standard". This protocol combines a logarithmic progression of letter sizes (first proposed by

Green in 1868) with a standardized, proportional layout proposed by Bailey and Lovie (1976).

OCT is a digital optical instrument that generates cross sectional images (tomograms) of the retina by optical-coherence interferometry,a procedure analogous to ultrasound, except for using light(abroad bandwidth near infrared light beam at 840nm) rather than sound, and measures the echo delay time of light reflected and backscattered from the retina. It produces reliable, reproducible, and objective cross sectional images of the retinal structures and the vitreoretinal interface and allows quantitative measurements of retinal thickness (RT). (12,13)

OCT classification of DME:

Type 1: diffuse macular edema without cysts.

Type 2: cystoid macular edema.

Type 3: tractional macular edema.

Type 4: serous retinal detachments.

This classification seems to be exhaustive exposing the whole aspects of DME. It is useful to disclose the pathogenic phenomena of DME, Tractional forces on the fovea can be caused not only by the posterior hyaloid but also by an epiretinal membrane or sometimes by the two structures at the time. (14, 15)

OCT allows a quantitative diagnosis of DME, as it is used to obtain numerical representation of the retinal thickness. CSME may be diagnosed using only biomicroscopy, but CSME with minimal increase in retinal thickness is difficult to recognize without OCT. Different studies demonstrated that OCT may identify DME in patients with normal biomicroscopy. [16,17,18]

In diabetic patients with increased retinal thickness between 200and 300μm, considering abnormal values if they are above 200 μm, only 14% are detected by ophthalmoscopy. It corresponds to a subclinical form of macular edema [19].