Correlation between Visual Functions and Optical Coherence Tomography, Fundus Auto Fluorescence and Fundus Fluorescein Angiography Findings in Treatment-Naive Diabetic Macular Edema

Thesis

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Sara Samy Gamal El Din

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List of Abbreviations

Abb.	Full term
11-cis RAL	11-cis Retinal
11-cis ROL	11-cis Retinol
A2 E	Bioretinoids (N-retinylidene-N-retinylethanolamine)
ABCR	ATP binding cassette Transporter
ACE inhibitors	Angiotensin converting enzyme inhibitors
At RDH	All-trans Retinal Dehydrogense
BCVA	Best Corrected Visual Acuity
BRB	Blood Retinal Barrier
CPFT	Central Point Foveal Thickness
CME	Cystoid Macular Edema
CRT	Central Retinal Thickness
CSCR	Central Serous Chorioretinopathy
CSFT	Central Subfield Foveal Thickness
cSLO	Confocal Scanning Laser Ophthalmoscope
CSME	Clinically Significant Macular Edema
DCP	Deep Capillary Plexus
DRCR	Diabetic Retinopathy Clinical Research
DRIL	Disorganization of Retinal Inner Layer

Abb.	Full term
DM	Diabetes Mellitus
DME	Diabetic Macular edema
DMI	Diabetic Macular Ischemia
DNA	Deoxyribonucleic acid
DR	Diabetic Retinopathy
EDI	Enhanced Depth Imaging
ELM	External Limiting Membrane
ETDRS	Early Treatment Diabetic Retinopathy Study
EZ	Ellipsoid Zone
FAF	Fundus Autofluorescence
FAZ	Foveal Avascular Zone
FFA	Fundus Fluorescein Angiography
GAT	Goldmann Applanation Tonometer
GCC	Ganglion Cell Complex
HbA1c	Hemoglobin A1C
HRS/HRF	Hyper Reflective Spots/Foci
HTN	Hypertension
ICC	Intraclass Correlation Coefficient
IL-1β	Interleukin 1 beta
INL	Inner Nuclear Layer
IPL	Inner Plexiform Layer
IRMA	Intraretinal Microvascular Abnormalities
LBs	Lipid Bisretinoids

Abb.	Full term
LF	Lipofusin
LMP	Lysosomal Membrane Permeabilization
Log MAR	Logarithm of the Minimum Angle of Resolution
LRAT	Lecithin Retinol Acyl Transferase
MAs	Microaneurysms
Mtorc 1	Mammalian Target of Rapamycin
nAMD	Neovascular Age-related Macular Degeneration
N- ret PE	N-retinylidene phosphatidyl anolamine
NALP3	Cryopyrin
NPDR	Non Proliferative Diabetic Retinopathy
NSD	Neurosensory Detachment
NVDs	New Vessels at the Disc
NVEs	New Vessels Else where
OCT	Optical Coherence Tomography
OCTA	Optical Coherence Tomography Angiography
ONL	Outer Nuclear Layer
OPL	Outer Plexiform Layer
OS-IS	Outer Segment –Inner Segment
PCV	Polypoidal Choroidal Vasculopathy
PDR	Proliferative Diabetic Retinopathy
PKc	Protein Kinase C

Abb.	Full term
POS	Photoreceptor Outer Segment
PVD	Posterior Vitreous Detachment
RNFL	Retinal Nerve Fiber Layer
RPE	Retinal Pigment Epithelium
SCP	Superficial Capillary Plexus
SD	Standard Deviation
SD-OCT	Spectral-Domain Optical Coherence Tomography
SS-OCT	Swept- Source Optical Coherence Tomography
SFCT	SubFoveal Choroidal Thickness
SRD	Serous Retinal Detachment
TFEB	Transcription Factor EB
VEGF	Vascular endothelial growth factor
VKH	Vogt Koyanagi Harada
VMT	Vitreomacular Traction
WESDR	Wisconsin Epidemiologic Study of Diabetic Retinopathy

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Correlation between Visual Functions and Optical Coherence Tomography, Fundus Auto Fluorescence and Fundus Fluorescein Angiography Findings in Treatment-Naive Diabetic Macular Edema

Abstract

Background: Diabetic macular edema (DME) is a sight-threatening consequence of diabetic retinopathy. Available treatment modalities for DME involve repeated and invasive intraocular injection of anti-VEGF and other substances, placing heavy burdens on the patient and the health care facilities**.**So, identifying reliable methods for DME prognosis is actually very helpful. Multimodal retinal imaging tools provide us with these predictive prognostic biomarkers

Aim of the Work: To correlate between visual functions (visual acuity and color vision) with macular features of OCT, FAF and FFA in patients with untreated (treatment-naive) DME as a guide for visual prognosis of these patients.

Patients and Methods: Fifty eyes of 35 diabetic patients with untreated clinically significant macular edema (CSME) underwent best corrected visual acuity (BCVA) determination (logMAR), slit lamp biomicroscopy; fluorescein angiography (FFA;FAZ size, macular leakage pattern, areas of capillary dropout) optical coherence tomography (OCT; central point foveal thickness [CPFT], volume, outer and inner retinal layers intergrity [ONL, INL], hyper-reflective foci[HRF], subfoiveal choroidal thickness[SFCT]); fundus autofluorescence (Hyper FAF; absent or increased (FAF, single or multiple spots). Linear correlation and three-way analysis of covariance were used for statistics.

Results: In OCT, we found that CPFT & ORL integrity is significantly well correlated to visual function (BCVA, color vision). However, CSFT was only correlated to visual acuity but not color vision. Regarding FFA parameters, especially (FAZ size, areas of capillary drop out), we found that these parameters are correlated significantly to visual acuity but not color vision. On the other hand, we found that the presence of hyper FAF spots was not related significantly to visual acuity but related to a significant level to color vision. However, a number of spots were not correlated to visual acuity or color vision. There was significant correlation between retinal thickness in OCT and type of leakage in FFA. Also, large cystoid spaces and FAF spots in the fovea were significantly correlated together. However, there was no correlation between retinal thickness and subfoveal choroidal thickness in OCT.

Conclusions:

- Multimodal retinal imaging is of great benefit not only in diagnosis but also in its prognosis.
- Integration between different retinal imaging tools helps in finding alternative and less invasive way in diagnosis.
- FAF is simple non-invasive imaging mode to assess RPE function with evolving application in DME.

Keywords: Diabetic Macular Edema, Best Corrected Visual Acuity, Optical Coherence Tomography, Fundus Auto Fluorescence, Fundus Fluorescein Angiography.

Introduction

Diabetes mellitus (DM) is a major health problem that affects 415 million people all over the world, and this number is estimated to reach 642 million by 2040 ***(Cho et al., 2018).***

Due to this high prevalence of DM, it is not surprising that Diabetic Retinopathy (DR) is one of main causes of vision loss in adults aged 20–74 years. DR ranked as the fifth most common cause of preventable blindness. Over one-third of diabetics had signs of DR, and a third of these were afflicted with diabetic vision-threatening complications ***(Lee et al., 2015).***

Diabetic Macular Edema (DME) involves accumulation of excess fluid and lipids in the macula due to breakdown in the Blood Retinal Barrier (BRB). When this fluid extends into the fovea, the patient becomes symptomatic with metamorphopsia and drop of vision. ***(Antonetti et al., 1999).***

Most important risk factors for DME are the type of diabetes (type I or II), the treatment method (insulin, oral hypoglycemic drugs, or diet only), and the mean duration of diabetes. Other risk factors include high levels of

hemoglobin A1c (HbA1c), hypertension and hyperlipidemia, smoking, pregnancy, physical inactivity and renal disease, while use of angiotensin converting enzyme (ACE) inhibitors has a regressive effect on DR ***(Muni et al., 2013).***

In the **Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)**, the 10-year rate of developing DME was 20.1% in patients with type I diabetes, 13.9% in patients with type II diabetes not using insulin, and 25.4% in type II diabetes patients using insulin ***(Klein et al., 2009).***

DME can develop at any given stage of DR. However, its prevalence increases with the severity of DR; it affects 3% of eyes with mild non-proliferative diabetic retinopathy (NPDR), increases to 38% of eyes with moderate to severe NPDR, and reaches 71% of eyes with proliferative diabetic retinopathy (PDR) (Figure 1**)** ***(Bandello et al., 2017).***