Advances for Early Diagnosis of Primary Open Angle Glaucoma

An Essay submitted for partial fullfillment of Master Degree of Ophthalmology

By

Ereny Magdy Halim Dawood , **MB. BCh.**

Under supervision of

Prof.Dr. Nadia Mohammed Ismail El-Mowafy

Professor of Ophthalmology

Faculty of Medicine - Ain-Shams University

Dr. Karim Magdi Naguib

Lecturer in Ophthalmology

Faculty of Medicine - Ain-Shams University

Faculty of Medicine

Ain-Shams University

Cairo,Egypt

2013

Acknowledgement

First of all, I would like to thank God because without him I cannot do anything in my life. I thank God for helping me to finish this work and for all his blessings and gifts throughout my life.

I would like to express my deepest gratitude and appreciation to ***Prof. Dr.*** **Nadia Mohammed Ismail El-Mowafy**, Professor of Ophthalmology, Faculty of Medicine, Ain Shams University, for her invaluable guidance, support and encouragement throughout this work. I am very fortunate to be one of her students.

I also wish to express my gratefulness to ***Dr. Karim Magdi Naguib***, Lecturer of Ophthalmology, Faculty of Medicine, Ain Shams University, for his outstanding efforts, fruitful suggestions, honest assistance and patience that allowed me to accomplish this work.

I am indebted as well to my father, my mother, my brothers and friends for their loving care, confidence and consistent support and I seize this opportunity to thank them all for everything they have done for me.

Ereny Magdy

المُستحدَث فى التشخيص المُبكر للجلوكوما ذات الزاوية المفتوحة

رسالة كجزء تكميلى للحصول على درجة الماجستير فى طب وجراحة العيون

مقدمة من

الطبيبة/ ايرينى مجدى حليم داود
بكالوريوس الطب والجراحه

تحت اشراف

أ.د./ نادية محمد اسماعيل الموافى
أستاذ طب وجراحة العيون
كلية الطب – جامعة عين شمس

د./ كريم مجدى نجيب
مدرس طب وجراحة العيون
كلية الطب – جامعة عين شمس

كلية الطب
جامعة عين شمس
القاهرة - مصر
2013

Contents

LIST OF ABBREVIATIONS

ARPs.......................... Atypical Retardation Patterns
Asb...........................Apostilb
AUC............................Area Under Curve
BL ....Border Line
CA...............................Cup Area
CI................................Confidence Interval
CpRNFL ....Circumpapillary Retinal Nerve Fiber Layer
CPSD ....Corrected Pattern Standard Deviation
CSLO ....Confocal Scanning Laser Ophthalmoscopy
CV...............................Cup Volume
dB................................Decibel
FDT.............................Frequency doubling technology
FE................................Fellow Eye
FL................................Fixation losses
FNs..............................False Negatives
FPs...............................False Positives
GDx ECC ....Enhanced Corneal Compensation
GDxFCC....................Fixed Corneal Compensator
GDxVCC....................Variable Corneal Compensation
GHT...........................Glaucoma Hemifield Test
GPA ....Guided Progression Analysis
GPS ....Glaucoma Probability Score
HFA ....Humphrey Field Analyzer
HM ....High Myopia
HRT............................Heidelberg Retina Tomograph
IOP ....Intraocular Pressure
IPL..............................Inner Plexiform Layer
MD.............................Mean Deviation
MGCC.......................Macular Ganglion Cell Complex
MRA...........................Moorfields Regression Analysis
My cells....................Magnocellular Ganglion Cells
NFI ....Nerve Fiber Index
NRA............................Neuroretinal Rim Area
NTG.........................Normal Tension Glaucoma

OCT..........................Optical Coherence Tomography
ODA.........................Optic Disc Area
OHT.......................Ocular Hyper Tension
ONH ....Optic Nerve Head
ONL ....Outside Normal Limits
P................................Probability Values
PCO..........................Posterior Capsular Opacification
POAG.......................Primary Open Angle Glaucoma
PPG..........................Preperimetric Glaucoma
PSD...........................Pattern Standard Deviation
Py cells...................Paravocellular Cells
RNFL ....Retinal Nerve Fiber Layer
RPE......................... Retinal Pigmented Epithelium
SAP..........................Standard Automated Perimetry
SD.............................Standard Deviation
SD-OCT...................Spectral Domain OCT
SF.............................Short-Term Fluctuation
SITA........................Swedish Interactive Threshold Algorithm
SLP..........................Scanning laser polarimetry
SN ....Signal-to-Noise Ratio
SVM ....Support Vector Machine
SWAP.....................Short-Wavelength Automated Perimetry
TDOCT..................Time Domain-OCT
TSNIT.....................Temporal–Superior–Nasal–Inferior–Temporal
TSS..........................Typical Scan Score
WNL ....Within Normal Limits

List of Tables

List of Figures

Introduction

Glaucoma is characterized by progressive degeneration of retinal ganglion cells and their axons that leads to nerve fiber layer loss, optic disc cupping and concecutive glaucomatous visual field changes. (1)

Early glaucoma detection is crucial for the prognosis of the disease and treatment by preventing the progression of irreversible restriction of the visual field. (2)

Standard automated white-on-white perimetry (SAP), frequency-doubling technology (FDT) perimetry, and short wavelength automated perimetry (SWAP) are three of the prevailing visual field testing technologies in use in clinical practice. Although SAP is considered the reference standard for detecting visual field loss in glaucoma, there is evidence suggesting that FDT perimetry and SWAP detect visual field changes earlier than SAP does. (3)

Combination of FDT and OCT seem to be useful for detecting possible preperimetric glaucoma (both structural and functional abnormalities) in disc suspects and OHT eyes , and may be useful tools for identifying those individuals who warrant close follow-up for detecting glaucoma by SAP. (4)

The deterioration of the optic nerve head (ONH) and retinal nerve fiber layer (RNFL) often precede the visual field loss detected by perimetry. Imaging technologies for evaluation of the ONH and RNFL are useful in the differentiation between glaucomatous and normal eyes. (5)

Computer-based devices such as confocal scanning laser ophthalmoscopy, scanning laser polarimetry, and optical coherence tomography provide quantitative assessments of structural damage to ONH and RNFL. (6)

Confocal Scanning Laser Ophthalmoscopy (CSLO) is used to evaluate topographic changes in the ONH and in neuroretinal rim area (RA) in glaucoma patients . (5)

The latest generation of CSLO is the Heidelberg retina tomograph III (HRT III) that provides numerous stereometric parameters, including disc area, rim area, and cup area that assist clinicians in assessing the anatomical features of the optic disc. (7)

Classification indices such as the Moorfields regression analysis (MRA) and the glaucoma probability score (GPS) which highlight regions as "outside normal limits" are among the HRT tools currently used to discriminate between healthy and glaucomatous discs.(7)

Scanning Laser Polarimetry (SLP) measures RNFL thickness. The available SLP instruments are the GDx VCC (variable cornea compensation) and the latest GDx ECC (enhanced corneal compensation). The GDx has been shown to discriminate well between glaucomatous and healthy eyes in earlier stages of disease . (7)

Optical coherence tomography (OCT) provides high resolution cross-sectional images of the RNFL and ONH that give accurate and objective anatomic diagnosis of glaucoma . several SDOCT devices as the RTVue, the Spectralis OCT, the 3D OCT can discriminate between healthy eyes and those with perimetric glaucoma . (8,7)

Finally, Interpretation of instrument results for detection of glaucoma and monitoring its progression remains a challenge . (7)

Aim of this essay

To review the advances in early diagnosis of open angle glaucoma **.**

PRIMARY OPEN ANGLE GLAUCOMA

Primary open angle glaucoma (POAG) is still one of the major causes of blindness in the world. Glaucoma is defined clinically as progressive optic neuropathy characterized by cupping of the optic nerve head, focal or diffuse thinning of the retinal nerve fiber layer and subsequently followed by characteristic visual field loss.(1)

The main clinical features of POAG are an open iridocorneal angle and cupping of the optic nerve head (ONH) (or optic disc), with corresponding loss of visual field. It is also characterized by abscance of signs of secondary glaucoma or a non glaucomatous cause for the optic neuropathy. Elevated intraocular pressure (IOP) is not part of the clinical definition because POAG can occur when IOP is normal (typically 10 to 21 mmHg). Nevertheless, elevated IOP is an important risk factor and is also considered to be a causative factor in glaucoma. (2)

Other risk factors are old age, race and positive family history. At the genetic level, a distinction between juvenile onset (age at diagnosis 10–35 years) and adult onset (age at diagnosis above 35 years) has been made. Many juvenile onset cases have autosomal dominant inheritance whilst adult onset cases are typically multi factorial. Other factors include increased glutamate levels, alterations in nitric oxide (NO) metabolism, vascular alterations and oxidative damage caused by reactive oxygen species (ROS). (3,4)

It has been demonstrated that 20-40% of optic nerve axons can be lost before irreversible visual field defects are observed in standardized automated perimetry. Thus detection of optic nerve head and retinal nerve fiber layer (RNFL) damage is crucial for the diagnosis of glaucoma in its early stages.(5)

Evaluation of the relationship between anatomical structure (optic nerve and retinal nerve fiber layer [RNFL]) and function (visual sensitivity) in glaucoma can aid in assessing the relative efficacy of structural and functional tests in detecting glaucomatous damage and in their optimal use. Although a significant relationship is expected between structure and function because both provide related information, studies using the available measurement methods have shown that this relationship is modest at best. One reason for this imperfect relationship may be the variability associated with measurements obtained using currently available methods. (6)

White-on-white standard automated perimetry (SAP) has been most widely used for assessment and followup of functional damage in glaucomatous eyes. Its result is, however, known to be relatively insensitive to functional damage of retinal ganglion cells (RGCs) in the early stage of glaucoma, although recent studies indicated that functional damage can also occur before structural damage. (7)

Frequency doubling technology (FDT) was developed based on a phenomenon first demonstrated by Kelley, the frequency doubling illusion, which occurs when a low spatial frequency (0.25 cycles per degree) sinusoidal grating undergoes rapid (25 Hz) counterphase flicker. (8)

Several studies have shown that FDT stimulus predominantly stimulates the M-cells representing about 10% of all RGCs with axons projecting into the magnocellular layer of the lateral geniculate nucleus, with partial contribution of input from other RGCs and cortical mechanism. In contrast to the first generation of FDT, the Matrix FDT perimeter increases the spatial resolution by adopting a 24-2 testing pattern similar to SAP.(9)

Short-Wavelength Automated Perimetry (SWAP) generates a blue-violet (440-nm wavelength) stimulus over a bright yellow background and may preferentially stimulate the RGCs in the koniocellular pathway. The Swedish Interactive Thresholding Algorithm (SITA) has been incorporated into SWAP to shorten test duration and improve test–retest variability. These