Changes in Ganglion Cell Complex and Nerve Fiber Layer in correlation to perimetry changes in early open angle glaucoma

Thesis

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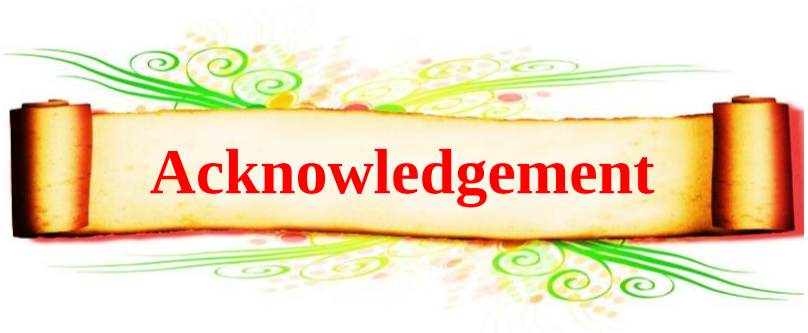

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Contents

List of Abbreviations

AAO	**:** American academy of ophthalmology
AC	**:** Anterior chamber
ADP	**:** Adenosine diphosphate
AIF	**:** *Acquired image frame*
AL	**:** *Axial length*
Asb	**:** Apostilbs
ATP	**:** Adenosine triphosphate
AUROC	**:** Area under **receiver operating characteristic curve**
BCVA	**:** Best corrected visual acuity
BM	**:** Bruch's Menbrane
BMO	**:** Bruch's Membrane Opening
CB	**:** Ciliary body
cpRNFL	**:** Circum-papillary retinal nerve fiber layer
CSFI	**:** Combined index of structure and function
ELM	**:** External limiting membrane
ERM	**:** Epiretinal membrane
FAZ	**:** Foveal vascular zone
FD-OCT	**:** Fourier domain optical coherence tomograghy
FDT	**:** Frequency doubling technology
FT	**:** Full threshold strategy
GCC	**:** Ganglion cell complex
GCIPL	**:** Ganglion cell-inner plexiform layer
GCL	**:** Ganglion cell layer
GHT	**:** Glaucoma hemifield test
GPA	**:** Guided progression analysis
HD-OCT	**:** High definition optical coherence tomograghy
HS	**:** Highly significant
ILM	**:** Inner limiting membrane
INL	**:** Inner nuclear layer
IOP	**:** Intraocular pressure
IPL	**:** Inner plexiform layer
IS/OS	**:** Boundary between the photoreceptor inner and outer segments
LGB	**:** Lateral geniculate body
M-Cells	**:** Magnocellular cells
MD	**:** Mean deviation
MDB	**:** Minimum distance band
NFL	**:** Nerve fiber layer
NPE	**:** Non Pigmented epithelium
NS	**:** Non-significant

OAG	**:** Open angle glaucoma
OCT	**:** Optical coherence tomograghy
OHT	**:** Ocular hypertension
OLM	**:** Outer limiting membrane
ON	**:** Optic nerve
ONH	**:** Optic nerve head
ONL	**:** Outer nuclear layer
OPL	**:** Outer plexiform layer
POAG	**:** Primary open angle glaucoma
PC	**:** Personal computer
PE	**:** Pigmented epithelium
PR	**:** Photoreceptors
PSD	**:** Pattern standard deviation
pRNFL)	**:** Peripapillary retinal nerve fiber layer
PSD	**:** Pattern standard deviation
RGC-AC	**: Retinal ganglion cell–axonal complex**
RGCs	**:** Retinal ganglion cells
RNFL	**:** Retinal nerve fiber layer
RPE	**:** Retinal pigment epithelium
RPE/CH	**:** Retinal pigment epithelium and choriocapillaris
S	**:** Significant
SAP	**:** Standard automated perimetry
SC	**:** Schlemm's canal
SD	**:** Standard deviation
SD OCT	**:** Spectral domain optical coherence tomography
SF	**:** SITA Fast
SITA	**:** Swedish interactive thresholding algorithm strategy
SLO	**:** Scanning Laser ophthalmoscope
SLO/OCT	**:** spectral domain scanning laser ophthalmoscope/ OCT
SPSS	**:** Statistical Package for Social Science
SS	**:** SITA Standard
SWAP	**:** short-wavelength automated perimetry
TDOCT	**:** time domain optical coherence tomography
TM	**:** Trabecular meshwork
VF	**:** Visual field
VFI	**:** Visual field index

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Abstract

Background: Glaucoma is an optic neuropathy that is characterized by the loss of retinal ganglion cells and the retinal nerve fiber layer. There is a diversity of factors that may lead to glaucoma but the main issues in common are the effect on the retinal ganglion cells and potentially devastating visual loss.

Aim of work: The aim of the present study is to assess the macular ganglion cell layer (GCL) and peripapillary retinal nerve fiber layer (pRNFL) using OCT. This is to demonstrate the structural damage that occurs in early glaucoma patients. Also to correlate those changes with the functional changes seen in Standard Automated Perimetry (SAP).

Patients and Methods: This is a reterograde cross-sectional observational study conducted in Ain Shams University hospitals. This present study aimed at analyzing the data of 40 patients with early open angle glaucoma to the outpatient clinic of both Ain Shams University Hospitals and Memorial Institute of Ophthalmology over a year period from November 2016 to December 2017.

Results: Our study found that both GCC and pRNFL thickness are highly significant when comparing patient and control groups. Our results also showed better diagnostic capability of GCC over pRNFL to detect early glaucomatous changes. We also found that total GCIPL is the best macular parameter with AUC 0.840 while the total pRNFL AUC 0.791. Also we found a low correlation of structural damage with functional damage and this is in agreement with other studies that proved RGC dysfunction may precede axonal numerical loss in the presence of normal structures.

Conclusion: the assessment of GCC parameters plays an important role in diagnosis and monitoring of glaucoma. Our study showed that SDOCT is a useful ancillary diagnostic tool for evaluation of early macular and circumpapillary structural changes in glaucomatous eyes.

Keywords: ganglion cell complex, peripapillary retinal nerve fiber layer, pattern standard deviation, standard automated perimetry.

INTRODUCTION

Glaucoma is a neurodegenerative disease associated with progressive loss of retinal ganglion cells (RGCs) and their axons. RGC complex is defined as a set of neighboring ganglion cells in the RGC layer together with their axons forming a nerve fiber bundle in the retinal nerve fiber layer (RNFL) until their exit from the eye in the optic nerve head. The goal of glaucoma management is to slow down the rate of progressive neural loss to preserve visual function throughout the patient's life. Assessment of visual function in clinical practice is traditionally performed with Standard Automated Perimetry (SAP). Although SAP testing has been widely used for diagnosis, staging, and monitoring of the disease, it has become increasingly evident that a substantial number of RGCs may be lost before damage to SAP becomes statistically significant ***(Bach and Hoffmann, 2008)***

Glaucomatous visual field (VF) defects include an early paracentral scotoma, which may slowly merge and form an arcuate defect that continues to the blind spot. A nasal step may be present and one hemifield more depressed than the other. The visual field defect should correspond to the RNFL loss. As clinical examination is subjective and clinician dependent, early glaucoma signs can be overlooked from time to time. Early treatment opportunities may be missed if relying primarily on a visual field defect. This is because a substantial reduction in RGC

population can occur before clinically significant visual field defect can be detected. Since the introduction of optical coherence tomography (OCT), the technology has assisted clinicians in the detection of RNFL loss associated with glaucoma. Due to advances in OCT technology, we can now acquire a 6 x 6 mm cube of data in the peripapillary region in less than 1.5 seconds. Using OCT ONH scan to analyze peripapillary retinal nerve fiber layer (pRNFL) is now a widely employed parameter for diagnosing glaucoma. ***(Quigley* et al., *1990)***

Studies comparing high-resolution imaging of anatomical structures with SAP have shown that OCT may detect a large number of glaucoma patients with early and/or progressive damage compared with SAP. ***(Lee* et al., *2012)***

Optical coherence tomography (OCT) has become a staple in noninvasive imaging of ophthalmology. This strategy provides quantitative as well as qualitative clinical measures, and also provides information about various ocular pathologies. With the use of spectral-domain OCT technology, which has a higher scanning speed and improved axial resolution compared to time-domain OCT, It is now possible to perform 3-D volumetric scans of the retina and obtain detailed retinal layer analysis in an objective and reproducible fashion. The cpRNFL thickness measurement has become a well-established and widely used biomarker in glaucoma assessment since the

introduction of OCT. In addition to its excellent glaucoma discriminating performance, cpRNFL may offer equivalent performance in glaucoma progression assessment, but this statement remains the subject of debate. As it measures the thickness along a circle close to the optic nerve head (ONH) margin, cpRNFL covers all the axons of the ganglion cell distributed in the entire retina, but it is not a direct measurement of the glaucoma insult to retinal ganglion cells (RGCs). Instead, cpRNFL is an indirect measure of the consequence of the ganglion cell body damage. ***(Kerrigan* et al.,** ***2000)***

Peripapillary retinal nerve fiber layer (pRNFL) thickness varies significantly with degree of myopia, age, ethnicity, axial length (AL), and optic disc area. Consequently, the thickness measurements of particular retinal layers in the macula could offer glaucoma detection ability comparable or superior to that of pRNFL thickness in highly myopic patients. Macular thickness may theoretically reflect RGC loss better, because more than 50% of all RGCs are concentrated and multilayered in this region, and RGC bodies are 10 to 20-fold the diameter of their axons. In addition, since the macula lies along the globe's optical axis, the macula maybe less affected by globe AL than the optic disc and peripapillary structures. ***(Ishikawa* et al.,** ***2012)***

So the measurement of the peri-macular ganglion cell layer has emerged as a new diagnostic parameter in

glaucoma with spectral domain OCT (SDOCT). Various OCT machines now use this technique to capture the thickness of the innermost three retinal layers around the macula. These three layers, known as the macular ganglion cell complex (GCC), they are the retinal nerve fibre layer, ganglion cell layer and inner-plexiform layer. The GCC contain the axons, cell bodies and dendrites of the ganglion cells, respectively, which have been shown to be preferentially affected by glaucoma. This new parameter may assist early glaucoma detection, especially in cases where the ganglion cell loss is predominately macular rather than peripheral. ***(Nakano, Hangai and Nakanishi, 2012)***