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Original Research Article

Evaluation of retinal nerve fibre layer, optic nerve head, and macular ganglion cell analysis measurements for early glaucoma detection using spectral domain optical coherence tomography

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ABSTRACT

Background: Glaucoma is the leading cause of irreversible blindness worldwide. It is very important to diagnose glaucoma in early stages so that timely management can be done. Spectral domain optical coherence tomography (SD-OCT), is a newer device which helps to diagnose glaucoma early. The aim of our study was to evaluate the RNFL, ONH, and mGCA (GCL+IPL) measurements for early glaucoma detection using spectral domain optical coherence tomography (SD-OCT).
Methods: Total 30, POAG (primary open angle glaucoma) suspects were compared with 30 normal controls. The Cirrus HD-OCT optic disc cube 200 × 200 protocol was used to measure ONH, RNFL and macular parameters.
Results: The average cpRNFL thickness of all quadrants was significantly lower in POAG suspects, (84.13±7.42 µm versus 103.85±8.95 µm, p<0.001). The superior GCL+IPL thickness of POAG suspects and controls was 75.75±2.60 µm and 80.05±1.74 µm, respectively, (p<0.001). The inferior GCL+IPL thickness of POAG suspects and controls was 75.98±2.59 µm and 80.00±1.79 µm, respectively, (p<0.001).
Conclusions: The SD-OCT is an important device to diagnose POAG suspects, early. The GCA measurements and average RNFL (especially superior and inferior) measurements, both are equally good to discriminate between glaucoma suspects and normal controls.

Keywords: Macular ganglion cell analysis (mGCA), Retinal nerve fibre layer, Spectral domain optical coherence tomography

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide.[1] Glaucoma is a progressive optic neuropathy resulting in characteristic structural damage and associated visual field loss. In addition to ophthalmoscopy, optic nerve imaging and perimetry are used to aid in the diagnosis and surveillance of glaucoma. However, standard achromatic perimetry (SAP), lacks the resolution to detect early glaucomatous damage as greater than 35% of the retinal ganglion cells can be lost before detection of any visual field defects.[2] It has been observed, that structural changes precede detectable functional deficits, has led to an increased interest in imaging technology. Retinal ganglion cells (RGCs) are the cells that die in glaucoma. Retinal nerve fiber layer (RNFL), is made up of RGC axons and exit the eye through the optic nerve. On SD-OCT, progression of glaucomatous optic neuropathy can be seen by increased optic nerve cupping, peri-papillary RNFL thinning and macular ganglionic cell loss. More than 50% of RGC bodies reside within ~5 mm or 16° of the fovea.[3] Cell bodies are stacked up to six layers thick.[3] Thus, small losses of ganglion cell bodies are detectable by analysing total retinal thickness. The ganglion cell bodies along

with RNFL constitutes more than 30% of the retinal thickness.

Macular thickness by SD-OCT is a highly reproducible measurement (intra-visit and inter-visit coefficients of variation of <1%).[4-6] Ganglion cell-IPL (GCIPL), also shows good reproducibility.[5] Thus glaucomatous progression can be detected easily with high reproducibility. Macular thickness has been correlated both with optic nerve cupping and peripapillary RNFL thickness in glaucoma.[8,9] Macula thickness losses in glaucomatous patients have been correlated with estimated RGC count and Humphrey Visual Field (HVF) parameters in both glaucomatous and normal eyes.[7,8,10-12] SD-OCT macular thickness maps compare both intra eye asymmetry and inter eye asymmetry.[13,14]

The macular RGC + IPL (GCIPL) thickness for glaucoma diagnosis has shown to produce results similar to peripapillary RNFL thick-ness.[15] Macular layer (GCIPL) asymmetry has also been shown to be effective in the diagnosis of early glaucoma.[16-18] The macular GCIPL have shown to be correlated with visual field defects.[17] In advance disease macular GCIPL may also perform better than RNFL.[19] The measurement of extra macular ganglion cell complex thickness or the ratio of ganglion cell complex to total macular thickness are other strategies.[20,21] The most informative OCT parameters in differentiating pre-perimetric glaucoma included GCC average thickness, inferior quadrant RNFL thickness, inferior GCC thickness and superior GCC thickness.[22-24]

The aim of our study was to evaluate the RNFL, ONH, and mGCA (GCL+IPL) measurements for early glaucoma detection using spectral domain optical coherence tomography (SD-OCT).

METHODS

This was a hospital based, prospective, observational, cross-sectional study, included sixty patients, out of which 30 were primary open angle glaucoma (POAG) suspect and 30 were healthy control subjects.

The study was approved by the Institutional Review Board of the parent institution and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients. This study was done from 1st January 2019 to 31st December 2019, over one year of period.

Comprehensive ophthalmic examinations included best corrected visual acuity (BCVA) measurement, refraction, IOP measurement by Goldmann applanation tonometer, slit-lamp bio microscopy, gonioscopy, fundus examination, peripheral retinal examination and automated Humphrey SITA standard 24-2 visual field test. Systemic and ocular medical history of each subject was also recorded. Each patient's central corneal thickness (CCT) was measured using an ultrasonic pachymeter. The average of five CCT values was taken. Color stereoscopic optic disc photographs and red-free nerve fiber layer photographs were taken on fundus camera.

Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, California, USA) was performed following pupillary dilation. The Cirrus HD-OCT Optic Disc Cube 200 × 200 protocol was used to measure vertical C/D, cup volume, average circum-papillary RNFL (cpRNFL) thickness, and cpRNFL thickness in quadrants and in 12 clock-hour sectors. The macular cube 200 × 200 protocol was used to calculate average, minimum, and regional GCIPL thickness in six wedge-shaped sectors. Zeiss' Cirrus HD-OCT provides the ganglion cell and inner plexiform layers (GCL+IPL) in its ganglion cell analysis (GCA) software.

A primary open angle glaucoma (POAG) suspect is defined as an individual with open anterior chamber angle and who has one of the following findings in at least one eye: 1) an optic nerve or nerve fiber layer defect suggestive of glaucoma (enlarged cup-disc ratio, asymmetric cup-disc ratio, notching or narrowing of the neuroretinal rim, a disc hemorrhage, or suspicious alteration in the nerve fiber layer), 2) a visual field abnormality consistent with glaucoma, 3) ocular hypertension (OHT) an elevated IOP greater than 21 mmHg, without evidence of structural or functional damage by standard clinical tests.

This study included POAG suspects and normal controls. The criteria for diagnoses in each group were as follows:

Inclusion criteria for POAG suspects

BCVA 20/40 or more; refractive error between ±5.0 D spherical and ±3.0 D cylinder; IOP <22 mmHg (on at least 2 successive occasions and at 2 weeks interval); gonioscopy showed open angles; optic disc suspicious for glaucoma defined as having features suggestive of glaucomatous optic neuropathy such as cup-disc ratio >0.6, any diffuse or focal neuroretinal rim thinning, any disc hemorrhage, and/or any RNFL defects on the red-free photograph; normal visual fields defined as that with a mean deviation (MD) and pattern standard deviation (PSD) values within 95% normal confidence limits and a glaucoma hemi field test (GHT) classified as "within normal limits."

Inclusion criteria for ocular hypertension (OHT)

BCVA 20/40 or more; Refractive error between ±5.0 D spherical and ±3.0 D cylinder; IOP >22 mmHg and <32 mmHg (on at least 2 successive occasions and at 2 weeks interval); gonioscopy showed open angles; normal optic disc and normal visual fields.

Exclusion criteria

Patients with media opacity precluding good-quality OCT scans such as corneal opacity, cataracts, history of intraocular diseases, complicated intraocular surgery, non-glaucomatous secondary causes of elevated IOP, coexisting retinal disease, other diseases affecting visual field, with medications known to affect visual field sensitivity or with problems other than glaucoma affecting color vision, were excluded from this study. Patients with moderate or advanced glaucoma (MD worse than -6 dB) were excluded from the study.

All statistical analyses were done at 5% significance using Graph Pad Instat version 3.0 and Microsoft Excel 2019. Descriptive analysis such as mean and standard deviation were used to exhibit the clinical parameters.

RESULTS

Out of sixty (60), patients included in this study, 30 patients (60 eyes), were diagnosed as POAG suspects and 30 patients (60 eyes), were age and gender matched normal patients and assigned in control group. The average age of POAG suspects and control group patients was 56.83±4.76 years and 55.43±5.80 years (p=0.311), respectively, (Table 1). The male to female (M:F) ratio was 2:1 and 3.28:1 respectively (Table 1).

Table 1: General characteristics of study candidates.

Variables	POAG suspect	Control group	P value
Number of patients	30	30	
Age (mean±SD) in years	56.83±4.76	55.43±5.80	0.311
Males/females	20/10	23/7	
M:F ratio	2:1	3.2:1	

Table 2: Investigation findings.

Variables	POAG suspect	Control group	P value
IOP (mmHg)	17.6±2.97	12.08 ±1.26	<0.001
CCT (µm)	525.08±37.15	531.1±30.5	0.334
Vertical C:D ratio	0.60±0.11	0.42±0.04	<0.001
Cup volume (mm^3)	0.346±0.232	0.229±0.042	<0.001
VF(MD)	0.070±3.163	0.689±4.136	0.359
VF(PSD)	3.392±2.344	2.890±1.789	0.189
VF(VFI)	94.51±5.321	95.63±5.372	0.254
Central MT (µm)	239.55±12.42	247.7±8.32	<0.001

IOP- intra ocular pressure, CCT- central corneal thickness, C:D- cup to disc ratio, VF- visual field, MD- mean deviation, PSD- pattern standard deviation, VFI- visual field index, MT- macular thickness.

The mean IOP in POAG suspects and control group was 17.6±2.97 mmHg and 17.6±2.97 mmHg, (p<0.001), respectively. The mean central corneal thickness (CCT) was 525.08±37.15 µm in POAG suspect and 531.1±30.5 µm in controls, (p=0.334). The vertical C:D ratio was 0.60±0.11 in POAG suspects and 0.42±0.04 in controls, (p<0.001). The cup volume was 0.346±0.232 mm^2 in POAG suspects and 0.229±0.042 mm^2 in controls, (p<0.001). The mean deviation (MD) on HVF, in POAG suspects and controls was 0.070±3.163 and 0.689±4.136 respectively, (p=0.359). The pattern standard deviation (PSD) in POAG suspects and controls was 3.392±2.344 and 2.890±1.789 respectively (p=0.189). The visual field index (VFI) in POAG suspects was 94.51±5.321 and in controls was 95.63±5.372, (p=0.254). The central macular thickness of POAG suspects and controls was 239.55±12.42 µm and 247.7±8.32 µm, respectively (p<0.001) (Table 2).

T Table 3: Circum-papillary Retinal Nerve Fiber Layer (cpRNFL) thickness by SD-OCT.

RNFL thickness (µm)	POAG Suspect	Control group	P value
All quadrants	84.13±7.42	103.85±8.95	<0.001
Superior quadrant	114.45±16.93	128.81±11.12	<0.001
Inferior quadrant	109.96±23.05	134.73±8.61	<0.001
Nasal quadrant	72.93±16.69	77.08±9.28	0.096
Temporal quadrant	58.28±11.14	66.45±6.57	<0.001

The average cpRNFL thickness of POAG suspects and controls was 84.13±7.42 µm 103.85±8.95 µm, respectively (p<0.001). The superior quadrant RNFL thickness of POAG suspects and controls was 114.45±16.93 µm and 128.81±11.12 µm, respectively, (p<0.001). The inferior quadrant RNFL thickness of POAG suspects and controls was 109.96±23.05 µm and 134.73±8.61 µm, respectively (p<0.001). The nasal quadrant RNFL thickness of POAG suspects and controls was 72.93±16.69 µm and 77.08±9.28 µm, respectively (p=0.096). The temporal quadrant RNFL thickness of POAG suspects and controls was 58.28±11.14 µm and 66.45±6.57 µm, respectively (p<0.001) (Table 3).

Table 4: Macular ganglion cell analysis (mGCA), by SD-OCT.

mGCA (µm) (GCL+IPL)	POAG suspect	Control group	P value
(Sup. + Inf.) GCL+IPL	74.98±2.53	80.09±1.65	<0.001
Superior GCL+IPL	75.75±2.60	80.05±1.74	<0.001
Inferior GCL+IPL	75.98±2.59	80.00±1.79	<0.001

mGCA - macular ganglion cell analysis, GCL-ganglion cell layer, IPL- inner plexiform layer

Table 4 shows the mGCA (GCL+IPL) thickness in study patients. The combined (superior+inferior) average

GCL+IPL thickness of POAG suspects and controls was 74.98±2.53 µm 80.09±1.65 µm, respectively (p<0.001). The superior GCL+IPL thickness of POAG suspects and controls was 75.75±2.60 µm and 80.05±1.74 µm, respectively (p<0.001). The inferior GCL+IPL thickness of POAG suspects and controls was 75.98±2.59 µm and 80.00±1.79 µm, respectively (p<0.001) (Table 4).

DISCUSSION

The objective of our study was to evaluate the RNFL, ONH, and mGCA (GCL+IPL) measurements for early glaucoma detection using SD-OCT and we found that there was no statistically significant difference between POAG suspects and controls, (56.83±4.76 versus 55.43±5.80 years, p value-0.311). Out of total 30 POAG suspects 20 (66.66%) were male and 10 (33.33%) were female. The total 30 controls were approximately age and gender matched.

In our study, POAG suspects had significantly high IOP as compared to normal controls, (17.6± 2.97 versus 12.08±1.26 mmHg, p<0.001). Glaucoma suspects may have elevated intraocular pressure (IOP) with other findings consistent with glaucoma.[25]

The CCT was not significantly lower in POAG suspects in our study, (525.08±37.15 versus 531.1±30.5 µm, p=0.334). In one study, the mean CCT values were 533 µm (POAG), 530 µm (NTG), 550 µm (GS), and 565 µm (OH).[26] This is not verified if CCT is regarded as a risk factor because of its effect on IOP measurements or an independent risk factor unrelated to IOP. Currently, no linear correction formula for the two parameters is available.[27]

The vertical C:D ratio and cup volume both were significantly larger (p<0.001) in POAG suspect as compared to normal controls. Larger cup-to-disc ratio is a risk factor for the progression of glaucoma.[28,29]

There was no statistically significant difference in MD, PSD and VFI, between POAG suspects and control group, (p values- 0.359, 0.189, 0.254), in this study. At least 25% of retinal ganglion cells are lost before a significant change is seen on white-on-white perimetry.[30] In one study the VF progression was estimated using the MD and VF index, considering VF rapid progression an MD slope ≥0.5 dB/year or VF index ≥1%/year.[31]

In our study central macular thickness was significantly lower in POAG suspects than to normal controls, (239.55±12.42 versus 247.7±8.32 µm, p<0.001).

In this study, the average cpRNFL thickness of all quadrants was significantly lower in POAG suspects, (84.13±7.42 µm versus 103.85±8.95 µm, p<0.001). The RNFL thickness in superior, inferior and temporal quadrants was also significantly lower in POAG suspects as compared to normal controls (p<0.001). There was no significant difference in nasal quadrant RNFL thickness between POAG suspect and controls (72.93±16.69 µm versus 77.08±9.28 µm, p=0.096). Karti et al, reported significantly lower RNFL and ganglion cell complex measurements in normal looking discs of individuals who had a history of POAG in their first-degree relatives, compared to individuals without a family history.[32]

On mGCA, the superior and inferior GCL+IPL thickness was significantly thin in POAG suspects as compared to normal controls, in our study, (p<0.001). All three innermost retinal layers potentially involved in the glaucomatous damage (RNFL, GCL and IPL).[33,34]

The diagnostic ability of the GCIPL parameters was similar to that of the RNFL and ONH parameters to differentiate from PPG from controls, as Sung et al and Kim et al.[35,36]

CONCLUSION

The SD-OCT is an important device to diagnose POAG suspects, early. The GCA measurements and average RNFL (especially superior and inferior) measurements, both are equally good to discriminate between glaucoma suspects and normal controls.

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