A Comparative Analysis of Ganglion Cell Complex Parameters in Nigerian Negroes with Glaucoma and Macular Disease

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ABSTRACT

Aim: To evaluate the differences between ganglion cell complex (GCC) of primary open angle glaucoma and ocular disorders affecting the macula.

Methods and Materials: Forty-seven patients diagnosed with primary open angle glaucoma and 27 patients with macular diseases of different aetiology were enrolled in this pilot study. All patients underwent direct GCC analysis with the optical coherence tomographic scan, using the Optovue Fourier Domain RTVue-version. A comparison of the average GCC thickness, focal loss volume (FLV) and the global loss volume (GLV) of the two groups was made.

Results: A total of 74 pairs of eyes were included in the study. This comprised 48 males and 26 females with a mean age of 53.8 ± 11.3 among glaucoma patients and 59.8 ± 9.8 among patients with macular disease. Eyes with macular disease (33.3%) and eyes with glaucoma (42.6%) had abnormal average GCC parameters. However, the mean average GCC value was significantly higher in eyes with macular disease (87.50 ± 20.73) when compared with eyes with glaucoma (76.55 ± 12.51) (p=0.01). A significantly higher percentage of eyes with macular disease (43.3%) had GLV values within normal range when compared with eyes with glaucoma (21.3%) (p=0.03). Abnormal FLV values were seen in both eyes with macular disease (83.3%) and eyes with glaucoma (80.9%) but the differences were not of statistical significance (p= 0.24).

Conclusion: This pilot study demonstrated abnormal OCT GCC values in eyes with glaucoma as well as in eyes with macular disease. However, eyes with macular disease had significantly higher mean average GCC parameters but GLV parameters that were within normal values.

Key words: glaucoma, macular disease, ganglion cell complex

INTRODUCTION

One of the leading causes of blindness worldwide is glaucoma, an optic neuropathy characterized by progressive loss of optic nerve function. Glaucoma affects 3 main areas in the eyes, the optic nerve head, nerve fibre layer and retinal ganglion cells. Retinal ganglion cells encompass three layers in the retina: 1) the retinal nerve fibre layer (NFL) made up of ganglion cell axons, 2) the ganglion cell layer (GCL) made up of ganglion cell bodies, and 3) the inner-plexiform layer (IPL) made up of the ganglion cell dendrites. All three layers, collectively known as the ganglion cell complex (GCC), become thinner as the ganglion cells die from glaucoma.[1]

The GCC is now increasingly being evaluated for early glaucomatous changes.[1] Structural changes in the optic nerve head and retinal nerve fibre layer also occur.[2,3] New diagnostic tools for glaucoma focus on providing quantitative, reproducible, and objective measurements of optic nerve head, retinal nerve fibre layer (RNFL) thickness and GCC. Some of these new investigational tools include confocal scanning laser ophthalmoscopy (CSLO), scanning laser polarimetry (SLP), and optical coherence tomography (OCT).[4] Of the three tools, the OCT was found to have significantly better diagnostic accuracy.

Optical coherence tomography (OCT) is a non invasive and relatively safe imaging technique valuable for analysis of the optic nerve head and the retinal nerve fibre layer in glaucoma. It is also valuable for evaluating the retinal anatomy in several macular diseases, including macular hole, age-related macular degeneration and macular oedema. OCT provides high resolution and reproducible images of the RNFL that discriminate glaucomatous from healthy subjects.[5, 6, 7] Ganglion cell loss is best analysed around the macular region as it contains about 50% of all retinal ganglion cells. However, the GCC is also affected in various disorders affecting the retina. For instance, Cabrera DeBuc D et al found reduced thickness of ganglion cell/inner plexiform layer (GCL+IPL) complex in the pericentral region of the macula in eyes with mild diabetic retinopathy.[8]

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The RTVue, a recent Fourier-domain OCT from Optovue, directly measures the thickness of the 3 layers that constitute the GCC and provides a unique analysis of the percentage loss of these layers compared to an extensive normative database. The high depth resolution available in the RTVue enables a complete separation of the GCC from other areas and enables better analysis. GCC analysis has been found to significantly correlate with visual field damage and can accurately distinguish between normal and glaucomatous eyes.[8,9] Anecdotal evidence also suggests that the GCC may manifest damage before the peri-papillary RNFL measurements, however this possibility requires further clinical validation and studies.

Focal loss volume (FLV) and global loss volume (GLV) are two important diagnostic tools available on the version 4 soft ware of the RTVue and are suggested to provide the most sensitive detection of GCC thinning.[10] FLV provides a quantitative measure of the amount of significant GCC loss. It is the total sum of significant GCC loss (in volume) divided by the map area, as such it provides the percentage of significant tissue loss for volume. Early study results suggest that FLV is the most accurate parameter to differentiate normal from glaucomatous eyes, being better than the average GCC thickness parameter.[10]

Few studies have evaluated the effect of diseases of the macula on GCC parameters. Based on the above evidence, this study designed a pilot study to investigate the OCT GCC characteristics for both glaucoma and different macular diseases. The FLV, GLV and Av GCC parameters were measured for both groups of eyes and a comparison was made.

AIM

To evaluate the differences between ganglion cell complex parameters in primary open angle glaucoma and ocular disorders affecting the macula.

METHODS AND MATERIALS

Forty-seven patients who had been diagnosed with primary open angle glaucoma and 27 patients with macular diseases of different aetiology between January and December 2009 were enrolled in this study. All patients underwent direct ganglion cell (GCC) analysis with the optical coherence tomographic scans, using the Optovue Fourier Domain RTVue-version. The RTVue-100 (Optovue, Inc., Fremont, CA) with software version 2.0.4.0, uses a scanning laser diode to emit a scan beam with a wavelength of 820 nm to provide images of ocular microstructures. The GCC protocol is a 7mm raster scan composed of one horizontal B scan with 800 A scans, and 17 vertical B scans with 934 A scans. A well-trained operator obtained good-quality OCT images with pupillary dilation in all eyes. The criteria for determining scan quality were signal strength of at least 50 or more (as suggested by the manufacturer), a clear fundus image allowing a foveal pit, even and dense colour saturation throughout all retinal layers with red colour visible in the retinal pigment epithelium without interruptions, and a continuous scan pattern without missing or blank areas. As indicated by the manufacturer, results from the scans are colour coded; abnormal values show up in red while borderline values are yellow, and normal values are green. A comparison of the average GCC thickness, focal loss volume (FLV), and global loss volume (GLV) was made between the two groups and statistical analysis was done with the Epi Info software. Data were presented as the mean SD. The two-tailed paired t-test was performed to evaluate the difference between the two groups of parameters (macular disease and glaucoma).

RESULTS

A total of 74 pairs of eyes were included in the study. The characteristics of the study patients are shown in table 1; 48 males and 26 females with mean ages of 53.8 ± 11.3 among glaucoma patients, and 59.8 ± 9.8 among patients with macular disease. Age, sex and eye affected were not significantly different for both groups of patients. Five eyes (18.5%) with macular disease had macular oedema secondary to retinal vein occlusions. Another 5 eyes (18.5%) had macular oedema secondary to diabetic retinopathy while yet another 5 eyes (18.5%) had wet age related macular degeneration. A further 7 eyes (26%) had macular holes and 4 eyes (14.8%) had polypoidal choroidal vasculopathy affecting the macula. An old macular toxoplasma scar was seen in 1 eye (3.7%).

The mean FLV value was 9.34 ± 7.98 among eyes with glaucoma when compared with 10.23 ± 8.18 in eyes with macular disease. This difference was not statistically significant (p= 0.64). The difference in the mean GLV values between eyes with glaucoma (18.07 ± 12.86) and eyes with macular disease (17.99 ± 13.69) was also not statistically significant (p=0.98). Eyes with macular disease (33.3%) and eyes with glaucoma (42.6%) had abnormal average GCC parameters but the mean average GCC value was significantly higher in eyes with macular disease (87.50 ± 20.73) when compared with eyes with glaucoma (76.55 ± 12.51) (p=0.01). A significantly higher percentage of eyes with macular disease (43.3%) had GLV values within normal range when compared with eyes with glaucoma (21.3%) (p=0.03). Abnormal FLV values were seen in both eyes with macular disease (83.3%) and eyes with glaucoma (80.9%), but the differences were not of statistical significance (p= 0.24) table 2.

Table 1. Distribution of age, sex and the affected eye colour

Variable	Glaucoma		Macular disease		χ^2	df	P
	Frequency	%	Frequency	%			
Age (years)							
< 50	14	29.8	5	16.7	3.72	2	0.15
50 – 59	18	38.3	8	30.0			
≥ 60	15	31.9	14	53.3			
Total	47	100	27	100			
Mean age	53.8 ± 11.3		59.8 ± 9.8				
Student's t statistic = 2.29, p = 0.03*							
Sex							
Male	28	59.6	20	66.7	0.39	1	0.53
Female	19	40.4	10	33.3			
Total	47	100	27	100			
Affected eye							
Right	26	55.3	19	633	0.48	1	0.49
Left	21	44.7	11	36.7			
Total	47	100	27	100			

Table 2. Analysis of ganglion cell complex parameters in eyes with glaucoma and macular disease

Variable	Glaucoma		Macular		χ^2	df	P
	Frequency	%	Frequency	%			
FLV							
Normal	5	10.6	5	16.7	3.08	2	0.24†
Abnormal	38	80.9	25	83.3			
Borderline	4	8.5	0	0 .0			
Total	47	100.0	30	100.0			
GLV							
Normal	10	21.3	13	43.3	7.17	2	0.03†*
Abnormal	27	57.4	16	53.3			
Borderline	10	21.3	1	3.3			
Total	47	100 .0	30	100.0			
Average GCC							
Normal	15	31.9	16	53.3	3.82	2	0.15
Abnormal	20	42.6	10	33.3			
Borderline	12	25.5	4	13.3			
Total	47	100.0	30	100.0			

†Fisher exact p, *Significant

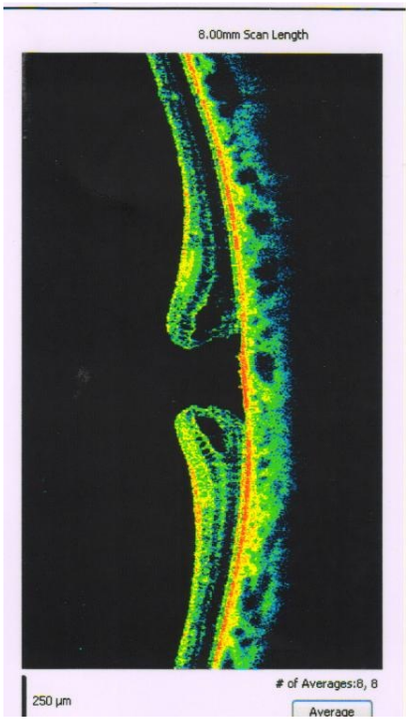
DISCUSSION

The idea that the macula is a good site to test for glaucomatous changes has gradually become more acceptable over the years.[11-16] Landmark studies by Zeimer, Asrani and colleagues[17, 18] have demonstrated damage in the macula and showed that evaluation of the macula may be more effective for detecting early glaucoma than evaluation in the peri-papillary region. Macular evaluation for glaucoma is centred around the GCC, which has been reported to be damaged early in glaucoma. Selective evaluation of the macular GCC therefore is expected to be more sensitive for detecting glaucoma even when compared with evaluation of the retinal nerve fibre layer (RNFL).[19] The GCC is however only abnormal in situations where structural damage has occurred. A recent study to evaluate the capability of Fourier-domain optical coherence tomography (FD-OCT) to detect structural damage in patients with preperimetric glaucoma, concluded that FD-OCT does not seem to be decisive for early detection of structural damage in patients with no functional impairment.[20]

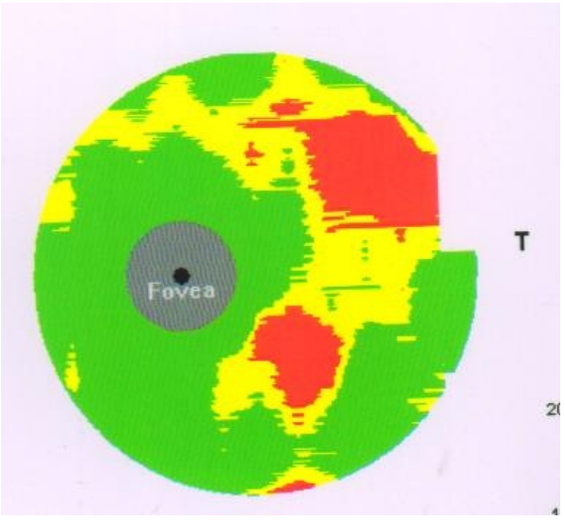
The concern of the present study is the effect of other macular pathologies on GCC measurements for glaucoma. Similar concerns have been raised about the peri-papillary region. A recent study[21] showed that macular GCC parameters may be better diagnostic indicators in cases of non-glaucomatous conditions with reduced RNFL thickness, such as extensive peri-papillary atrophy in high myopia. With this in view, this study considers that the macula area may actually have more confounders when evaluating for glaucoma than the peri-papillary region.

The study utilized the Optovue RTVue Fourier domain OCT which directly measures the GCC and provides a unique analysis of the percentage loss compared to an extensive normative database of mixed races. The results are presented as a significant loss from the normal, which makes clinical interpretation straightforward. Both eyes with glaucoma (42.6%) and eyes with macular disease (33.3%) had abnormal average GCC values. Mean average GCC value was higher in eyes with macular disease (87.50 ± 20.73) than in glaucomatous eyes (76.55 ± 12.51); this difference was statistically significant (p=0.01). Since many eyes with macular disease had abnormal average GCC values, there are concerns that macular disorders may be confounders of glaucoma evaluation. However, more clinical studies are required as this is only a pilot study.

Definite reductions in the foveal retinal nerve fibre layer have been reported in the diabetic retina as a result of neurodegeneration.[8] Macular oedema can also result in extensive thickening of the retina, while full thickness macular holes affect retinal evaluation in the macula. Figure 1 shows the results of the GCC analysis carried out on one of the patients with a macular hole. The patient examined has a macular hole in the left eye; the corresponding GCC images show central areas of abnormal values, the FLV and GLV values are also abnormal even though the patient is not a glaucoma patient. The optic nerve head analysis and TSNIT (temporal, superior, nasal inferior, temporal direction) graph also show that the optic nerve is not glaucomatous.



A



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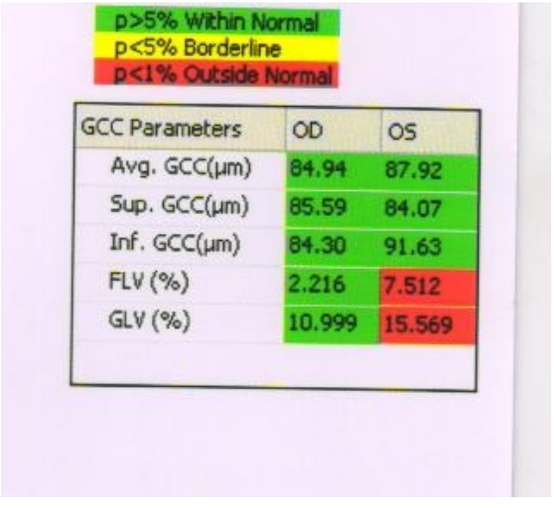

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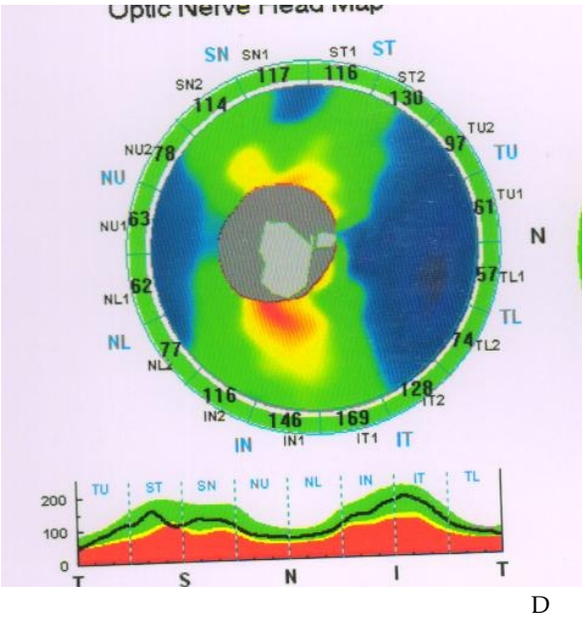

D

Figure 1. Optical coherence tomographic pictures of a 52-year-old male with a macular hole in the left eye.
A. OCT line scan of the macula; B. Ganglion cell complex significance map; C. GCC parameters revealing the abnormal FLV and GLV values; and D. Optic nerve head map and TSNIT significance graphs.

Figure 2 (A to C) shows abnormal GCC significance images in a 54-year-old female with advanced glaucoma. A normal GCC significance map is shown in figure 2 D. The FLV and GLV values as well as the optic nerve head map and TSNIT curve are also grossly abnormal. In patients that have both glaucoma and macular disease, the use of macular GCC to evaluate the severity of glaucoma may be misleading: both conditions can give abnormal GCC readings, hence an erroneous impression of the severity of the glaucoma may be given from superimposed effects of the changes from macular disease. In other macular diseases like macular oedema where therapeutic interventions may improve the oedema, other OCT analytical protocols like the grid, MM5 and line scans may be used to assess the contribution of the macular disease to the GCC changes. Repeat scans after therapeutic interventions can also aid decision making.

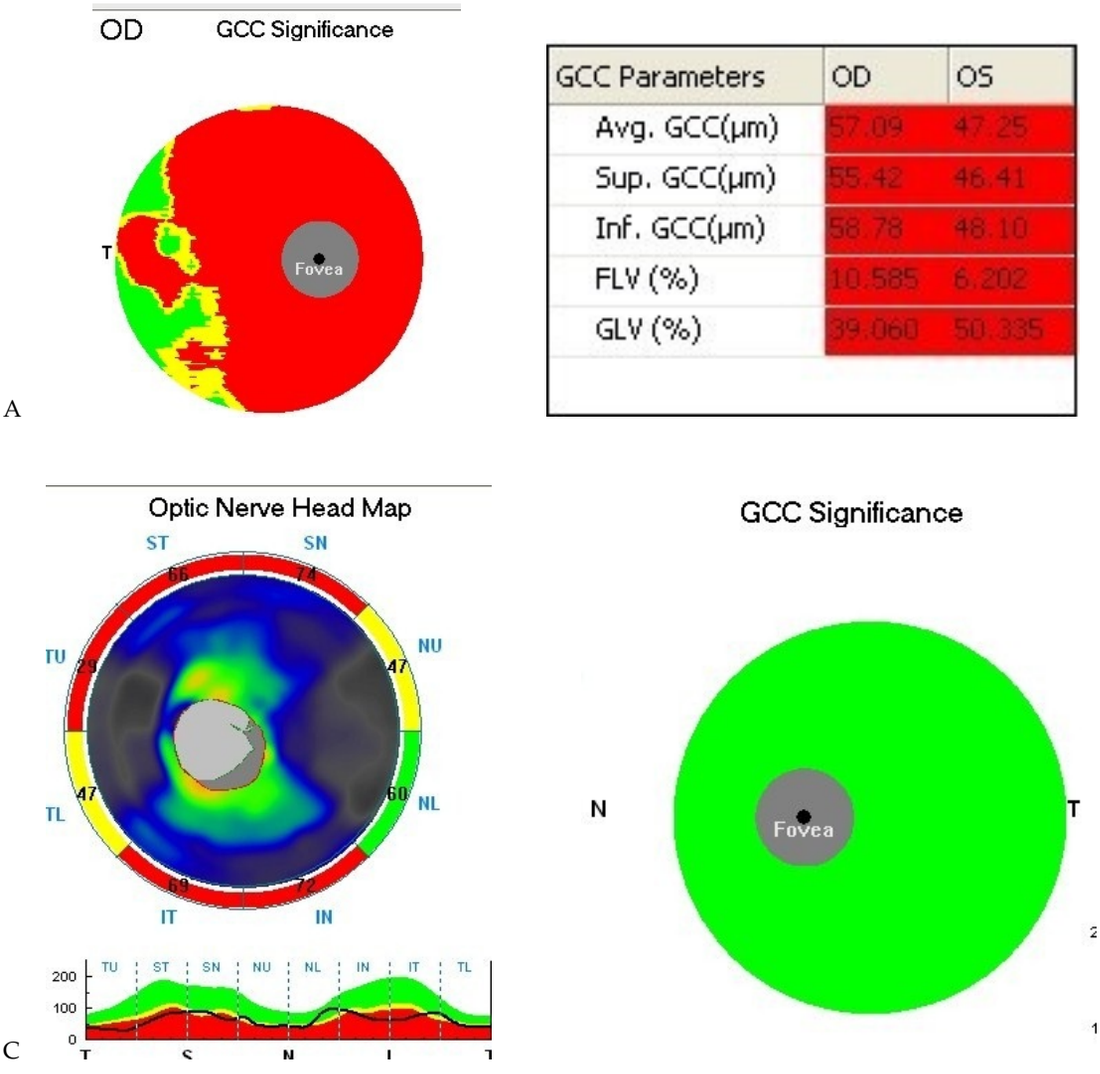

Figure 2. Optical coherence tomographic pictures of a 54-year-old female with advanced glaucoma in the right eye.
A. Abnormal – The ganglion cell complex significance map; B. GCC parameters revealing abnormal FLV and GLV values; C. Optic nerve head map and TSNIT significance graphs; D GCC significance map for a normal patient.

The focal loss volume (FLV) and global loss volume (GLV) parameters both sum up the volume of the GCC loss in the macula, however they give different levels of focality. The FLV is a highly sensitive analytic tool and is able to differentiate between glaucomatous and normal eyes as it correlates well with the visual field index (VFI) as both parameters are most likely influenced by visual field focal defects.[22,23] FLV also has a higher diagnostic accuracy for perimetric glaucoma than the simple GCC average.[24] In this study results, the FLV was found to be equally abnormal in glaucoma (80.9%) as well as in macular diseases (83.3%), implying that this statistical tool may not be highly sensitive in differentiating these two unique disorders. Focal volume losses of the GCC may also occur in macular disorders. In this study, 57.4% of eyes with glaucoma and 53.5% of eyes with macular diseases had abnormal GLV values and this difference was statistically significant. This may suggest that global loss of GCC volume is more likely to be seen in glaucoma than in macular disease.

Ganglion cell complex analysis was designed mainly to differentiate glaucomatous from normal eyes. The literature on the use of this tool to analyse macular disease is not rich. As a direct consequence of this, studies comparable to this are not easily available. Evaluating the RNFL in the region of the macular is less sensitive for detecting glaucoma than evaluating the GCC,[25] but macular disease may actually be a confounder when using macular GCC to evaluate glaucomatous changes, and there may be more confounding lesions in the macula than in the peri-papillary region or the nerve fibre layer.

CONCLUSION

This pilot study demonstrated abnormal OCT GCC values in eyes with glaucoma as well as in eyes with macular disease. Eyes with macular disease showed significantly higher mean average GCC parameters, but had GLV parameters that were within normal values.

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