World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: http://www.wjpsonline.org/
Original Article

Comparing gangion cell complex and retinal nerve fibre layer for the early diagnosis of glaucoma

[1]Dr. Ashok H. Madan, [2]Dr. Minal Vyawahare, [3]Dr. Smital M. Metange and [2]Dr. Nilesh Gaddewar

[1]Professor and Head of the Department, [2]Assistant Professor, [3]Junior Resident, Department of Ophthalmology, Government Medical College, Nagpur, Maharashtra

Received: 22-08-2018 / Revised Accepted: 02-10-2018 / Published: 26-10-2018

ABSTRACT

Context: With the newertechnologies like Optical Coherence Tomography (OCT**)**, it's time to rethink whether Retinal Nerve Fibre Layer (RNFL) thickness is the earliest tool for glaucoma detection or Ganglion Cell Complex (GCC) needs a reconsideration as we know that the cell bodies die prior to their processes.
Purpose: To evaluate and compare the early glaucoma detection abilities of circumpapillary RNFL (cpRNFL) and macular GCC (mGCC) retrospectively on the OCT.
Patients and Methods: 60 preperimetric glaucoma patients and 80 controls in an age group of 18-60 years were enrolled in this cross- sectional study. The cpRNFL thickness and mGCC of each patient were measured.
Results: The Area under receiver operating characteristic curve (AUROC) curve was significantly higher for mGCC than that for cpRNFL. It was noted that the mGCC loss occurs prior to the decrease in the cpRNFL thickness.
Conclusion: Prior studies have labelled GCC as just being complementary to RNFL in early detection of glaucoma but our study detected GCC to be superior. Thus the mGCC analysis though commonly performed needs recognition as an early detection tool for glaucoma.

Keywords: Glaucoma, Optical Coherence Tomography, Retinal Nerve Fibre Layer**,** Ganglion Cell Complex

Address for Correspondence: Dr. Ashok H. Madan, Professor and Head of the Department, Department of Ophthalmology, Government Medical College, Nagpur, Maharashtra; Email: dr.ashokmadan@gmail.com

How to Cite this Article: Dr. Ashok H. Madan, Dr. Minal Vyawahare, Dr. Smital M. Metange and Dr. Nilesh Gaddewar. Comparing gangion cell complex and retinal nerve fibre layer for the early diagnosis of glaucoma. World J Pharm Sci 2018; 6(11): 62-66.

INTRODUCTION

Glaucoma is characterised by the underlying progressive optic neuropathy[1] which leads to irreversible blindness. By 2020, India will become 2nd overall in number with glaucoma [2] which will have significant health and economic consequences on the developing country. But the fact that the blindness due to glaucoma is preventable and the key to prevention lies in early detection & prompt treatment, warrants further research in this grey zone thus reducing blindness due to glaucoma.

Although visual field analysis has been gold standard for glaucoma diagnosis, it has been documented that 40% of the RNFL maybe lost prior to a defect in the visual fields.[3] Thus, Retinal Nerve Fibre Layer (RNFL) loss precedes visual field defects thereby detecting glaucoma early i.e. pre-perimetric detection.But, as RNFL loss is preceded by retinal ganglion cell death represented by Ganglion Cell Complex(GCC) and in cases of high myopia where RNFL progressively thins out, the optic neuropathy i.e. the ganglion cell loss can be depicted more effectively by GCC as compared to RNFL.[4] The early detection of ganglion cell loss will result in early intervention in pre – perimetric glaucoma patients even before the RNFL loss sets in.

As the ganglion cell layer is thickest at the macula & RNFL increases in thickness towards the disc[5], macular GCC (mGCC) and circumpapillary RNFL (cpRNFL) were compared in this study which gave their respective best results for the early glaucoma diagnosis. The objective of the study was to compare mGCC and cpRNFL for the early diagnosis of glaucoma.

SUBJECTS AND METHODS

The study was conducted in Government Medical College, Nagpur, a tertiary care centre in the Central India.It was an observational study involving 140 subjects (80 controls and 60 pre-perimetric glaucoma patients) who were in the age group from 18-60 years. One eye of each subject was enrolled. The study period was from July 2016-2017. The procedures followed the tenets of the Declaration of Helsinki.

The participants were informed and the consent was taken. They were subjected to complete ophthalmic examination which included visual acuity, Best Corrected Visual Acuity (BCVA), refractive error, slit lamp examination, Intraocular Pressure (IOP) measurement through Applanation Tonometry, Gonioscopy, Ultrasound Pachymetry, slit lamp biomicroscopy using 90 D lens, Colour optic disc photography on fundus camera, visual field analysis by Standard perimetry using 24-2 protocol and GCC and RNFL analysis by the Optical Coherence Tomography (OCT).

Inclusion criteria: The controls had an IOP <21 mmHg, open angles on gonioscopy and werenot having the optic nerve head changes, visual field defects, the family history of glaucoma or any neurologic/ systemic disease that would have influenced the results. The pre- perimetric glaucoma patients included patients with IOP >/=21mm Hg with the optic nerve head changes without the visual field changes i.e.Mean Deviation better than -6 dB, <25 % of the points in Total Deviation Plot having P=5% &<10% points having P=1% & no point in the central 5 degree having sensitivity <15 dB.

***Exclusion criteria*:** Patients having corneal opacities, high refractive errors, retinal and macular diseases, history of intra- ocular surgery , non – glaucomatous secondary causes of raised intra-ocular pressure, diseases affecting visual fields and medications known to affect the visual field sensitivity - which would have influenced the two important variants of the study, were excluded from the study. Patients with moderate to advanced glaucoma i.e. Mean Deviation worse than -6 dB on the visual fields were also excluded.

mGCC and cpRNFL measurements over OCT- Spectral domain- OCT (Fourier based Optovue) was performed by a single experienced examiner after dilating the pupil with 0.5%tropicamide eye drops. Internal fixation was achievedand scans were obtained. OCT scans underwent quality check and only those with the Signal Strength Index more than 35 were included. Unclear scans, scans not properly centred and those scans having missing areas due to blinks or eye motion were discarded.

The mGCC scan sampled macula in 0.6 secs to reduce the problems of eye movements and corneal dryness. The scan pattern consisted of 128*512 pixel taken in 6*6mm sq. area. The cpRNFL thickness was calculated in 3.45mm radius ring centred on the optic disc. The global and quandrant- wise mGCC and cpRNFL measurements were obtained from a built- in software.

The data obtained was tabulated in Microsoft Excel. The Area under receiver operating characteristic (AUROC) curves were obtained and compared using the 17.8 version of Medcalc Software. The results were considered statistically significant at $P < 0.001$.

RESULTS

Out of 140 participants enrolled for the study 60 eyes (participants) were pre-perimetric glaucoma cases and 80 were controls. The mean age of pre-perimetric glaucoma patients was 48 years and that of the controls was 37 years. In the pre- perimetric group 27 were male & 33 were female patients and in the controls there were 41 males & 39 females.

The data obtained had normal distribution. The differences of means for cpRNFL was statistically significant for the controls and pre- perimetric glaucoma groups. The same was true for mGCC as well. (Table 1)

The AUROC depicted the ability of each parameter to discriminate the cases from controls. The comparison of AUROC's of the average mGCC and the cpRNFL is shown in the Figure 1& Table 2. It shows that the AUROC of mGCC is significantly greater than cpRNFL.(Table 3)The highest sensitivity and specificity for mGCC are 88.33 & 96.25 whereas that for cpRNFL are 76.67 & 77.50. The cpRNFL didn't detect any of the pre-perimetric glaucomatous eyes that were not detected by mGCC loss.

DISCUSSION

The management of glaucoma has ideally been based on the combination of Intraocular Pressure measurement, Optic Nerve Head (ONH) analysis and the visual field assessment. We now know that the diagnosis of glaucoma is delayed using these tests & that they do not provide a diagnosis in time for providing appropriate care. The advances like OCT in diagnosing glaucoma has made it possible to detect the retinal ganglion cell layer death which is an early process in the evolution of glaucoma.

Thus, OCT which gives high resolution imaging of the RNFL, optic nerve head and the macula besides being non- invasive and rapid, is increasingly being used in the early diagnosis of glaucoma whereby treatment can be instituted in time. The RNFL is measured around the disc where it is better evaluated as the nerves converge on the disc before leaving the eye. Whereas GCC is measured at the macula since macula has almost 50% of the retinal ganglion cells thus rendering mGCC to be better in evaluating GCC than anywhere else in the retina. Compared to cpRNFL, mGCC shows less inter-individual anatomic variability.

As the earlier studies showed no advantage of macular thickness evaluation over RNFL thickness assessment in terms of glaucoma detection[6,7], RNFL thickness has long being used to detect initial signs of glaucoma development prior to visual field changes.[8-10]However, GCC measurement has a theoretical advantage in glaucoma diagnostics as retinal ganglion cell loss occurs early in the pathogenesis of disease than RNFL loss. Furthermore, macular GCC appears to be more reliable particularly in certain clinical settings such as pathological myopia, optic disc size variability or deformation like ONH hypoplasia or coloboma where the accuracy of cpRNFL is reduced.[11, 12] There are some studies that have reported comparable diagnostic capabilities of GCC and RNFL in pre- perimetric glaucoma detection.[13, 14]Saha M et al in his study reported that macular thickness measured exhibited high discriminating power between controls, glaucoma suspects & glaucoma patients comparable with cpRNFL thickness parameters.[14] But since the advent of GCC imaging in the OCT, GCC analysis has only been a supplementary tool for glaucoma evaluation. But with the knowledge that the GCC is 1st to get affected in glaucoma &the studies mentioning utility of GCC imaging in early diagnosis of glaucoma [15, 16], it becomes necessary to compare RNFL and GCC for the early detection of glaucoma.

In the present study, we found that mGCC and cpRNFL both were reduced in pre- perimetric glaucoma patients, but mGCC appears to detect glaucoma earlier than cpRNFL and is not just supplementary but better than cpRNFL in the early detection of glaucoma.The ability of GCC to detect glaucoma early as compared to RNFL is found to be slightly better in some studies[17]. And the addition of GCC data to RNFL data has been found to enhance the detection of glaucoma in both pre-perimetricand perimetric groups[18]but it is still not utilised as the primary modality for the early glaucoma detection.
Besides all the pros, the cons are those of the macular diseases like ARMD hindering the usefulness of GCC. The study had limitations as it was a retrospective study, patients couldn't be followed and there was exclusion of patients having macular diseases, refractive errors and visual field defects.

CONCLUSION

The study showed that mGCC can be primarily and independently be utilised for the early diagnosis of glaucoma. It also appears to be valuable in monitoring the progression of glaucoma.

Table 1: Comparative OCT data for study group.

Diagnosis	cpRNFL	mGCC
CONTROLS		
Mean	112.0375	100.4691
No. of controls	80	80
Std. deviation	8.8209	6.1316
95% CONF interval	110.0745 to 114.0005	99.1046 to 101.8336
CASES		
Mean	95.1333	84.7305
No. of cases	60	60
Std. deviation	13.3828	8.6594
95% CONF interval	91.6762 to 98.5905	82.4935 to 86.9675

Table 2: Comparison of diagnostic accuracy of the corresponding thickness parameters using the area under receiver-operating characteristics curve

Variable	AUROC	Std Error[a]	95% Confidence Interval [b]
mGCC	0.944	0.0255	0.891 to 0.975
cpRNFL	0.839	0.0340	0.768 to 0.896

[a] DeLong et al., 1988 [b] Binomial exact

Table 3: Pairwise comparison of AUROC curves

mGCC ~ cpRNFL

Difference between areas	0.104
Standard Error	0.0404
95% Confidence Interval	0.0253 to 0.184
z statistic	2.586
Significance level	P = 0.0097(i.e.<0.001)

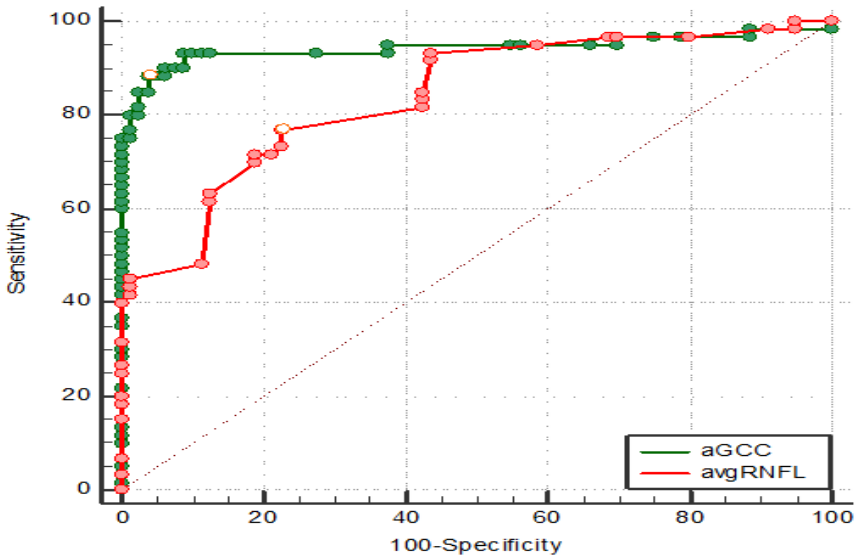

Figure 1. Receiver operating characteristic curves of average macular GCC (aGCC) & average cpRNFL (avgRNFL).

REFERENCES

1. Van Bushirk EM et al. Glaucomatous optic neuropathy. Am J Ophth 1992;113(4): 447.
2. H A Quigley, A T Broman. The number of people with glaucoma worldwide in 2010 & 2020. Br J Ophthalmology 2006 Mar;90(3): 262-267.
3. Mansoori T et al. Quantification of retinal nerve fibre layer thickness using spectral domain optical coherence tomography in normal Indian population. Indian J Ophthalmol 2012;60:555-8.
4. Kita Y et al. Circumpapillary ganglion cell complex thickness to diagnose glaucoma- A pilot study. Indian J Ophthalmol 2017; 65:41-7.
5. Curcio CA, Allen KA. Topography of ganglion cells in human retina. J Comp Neurol 1990;300:5‑25.
6. Jeoung JW et al. Macular ganglion cell imaging study: Glaucoma diagnostic accuracy of spectral domain OCT. Invest Ophthalmol Vis Sci 2013;54:4422-9.
7. Kim MJ et al. Topography profiles of retinal nerve fibre layer defects affect the diagnostic performance of macular scans in pre-perimetric glaucoma. Invest Ophthalmol Vis Sci 2014;55:2079-87.
8. Leite MT et al. Comparison of the diagnostic accuracies of the Spectralis, Cirrus, and RTVue optical coherence tomography devices in glaucoma. Ophthalmology 2011;118:1334‑9.
9. Kim NR et al. Comparing the ganglion cell complex and retinal nerve fibre layer measurements by Fourier domain OCT to detect glaucoma in high myopia. Br J Ophthalmol 2011;95:1115‑21.
10. Seong M et al. Macular and peripapillary retinal nerve fibre layer measurements by spectral domain optical coherence tomography in normal‑tension glaucoma. Invest Ophthalmol Vis Sci 2010;51:1446‑52.
11. Shoji T et al. Assessment of glaucomatous changes in subjects with high myopia using spectral domain optical coherence tomography. Invest Ophthalmol Vis Sci 2011; 52: 1098‑102.
12. Holló G et al. Evaluation of a new software version of the RTVue optical coherence tomograph for image segmentation and detection of glaucoma in high myopia. J Glaucoma 2016; 25: 615‑9.
13. Karti O et al. The assessment of optical coherence tomographic parameters in subjects with a positive family history of glaucoma. Clin Exp Ophthalmol 2017;100:663-7
14. Saha M et al. Comparative analysis of macular & peripapillary RNFL thickness in normal, glaucoma suspect & glaucomatous eyes by OCT. Nepal J Ophthalmol 2016;8:110-8.
15. Falsini B et al. Structure-function relationship in ocular hypertension and glaucoma: interindividual and interocular analysis by OCT and pattern ERG. Graefes Arch Clin Exp Ophthalmol 2008;246:1153–62.
16. Hwang YH et al. Diagnostic ability of macular ganglion cell asymmetry for glaucoma. Clin Exp Ophthalmol 2015;43:720-6
17. Azusa Akashi AK et al. Comparative assessment for the ability of cirrus RTVue and 3D OCT to diagnose glaucoma. Invest Ophthalmol Vis Sci 2013;54:4478–84.
18. Sung MS et al. Diagnostic validity of macular ganglion cell-inner plexiform layer thickness deviation map algorithm using cirrus HD-OCT in preperimetric and early glaucoma. J Glaucoma 2014; 23(8): 144–51.