INTERNATIONAL JOURNAL OF INNOVATIVE RESEARCH & DEVELOPMENT

ISSN: 2278 – 0211 (Online)

Analysis Of Difference In Central Macular Thickness By Oct In Normal, Glaucoma Suspects And Glaucomatous Patients And Establishing Whether Asymmetry In Horizontal Macular Hemifield Thickness (MHT) Can Detect Early Glaucoma

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Abstract:
Aim: Analysis of difference in Central Macular Thickness (CMT) by time domain Optical Coherence Tomography (OCT) in normal, glaucoma suspects and glaucomatous patients and establishing whether asymmetry in horizontal macular hemifield thickness (MHT) can detect early glaucoma.
Methods: From a macular thickness map of OCT, difference of values vertically just beyond the centre (called DMT1) and the topmost-lowermost values of the macular thickness map (DMT2) were calculated for normal patients to establish a normative database. The number of glaucomatous patients and glaucoma suspects with either of the two DMT values outside 95% CI (+-1.96 SD) was also calculated.
Results: 200 healthy eyes, 105 eyes of glaucoma suspects and 65 glaucomatous eyes (45 early(EG) and 20 moderate-severe(M-SG)) were included in the study of whom 6.5%, 33.3%, 82.2% and 70% respectively had abnormal MHT(DMT values outside 95% CI). The M-SG group had the overall lowest macular thickness which was statistically significantly lower than healthy and glaucoma suspect groups ($p<0.001$). The sensitivity of MHT was higher that RNFLT in EG ($p<0.05$).
Conclusions: CMT is lower in glaucomatous eyes. Asymmetric horizontal MHT aids in early diagnosis of glaucoma.

Key words: *Central Macular Thickness, Macular Hemifield Thickness, Optical Coherence Tomography, Glaucoma.*

1.Introduction

Circumpapillary retinal nerve fibre layer (cRNFL) thickness, measured using Optical Coherence Tomography (OCT), is the primary structural assessment strategy used in glaucoma diagnosis. However, because glaucomatous damage involves progressive loss of retinal ganglion cells (RGCs), observation of macular changes has additionally been considered for structural assessment of glaucoma. The concept of measuring retinal thickness at the macular region in evaluating glaucomatous damage has received increasing attention since it was hypothesized by Zeimer et al.[2]

The anatomic macula measuring approximately 6 mm is recognized histologically by the presence of xanthophyll pigment and multilayered ganglion cells. There are up to 7 layers of ganglion cell bodies in the central retina or macula and as few as 1 cell layer in the peripheral retina. The macula is the retinal area concerned with central vision and contains approximately 50% of all RGCs. [3]

Therefore, it is conceivable that loss of retinal ganglion cells, the primary pathology of glaucoma, can be more readily detected over the macular region than the peripheral retina. [4] Therefore, macular thickness measurement can be a good target for assessment of glaucomatous structural damage.

Our study aims to analyze the difference in Cntral Macular Thickness (CMT) by time domain OCT in normal, glaucoma suspects and glaucomatous patients and to investigate whether asymmetry in horizontal macular hemifield thickness(MHT) can detect early glaucoma.

2.Materials And Methods

Institutional Ethics Committee clearance was obtained for performing this study. Patients fulfilling laid down study inclusion criteria underwent complete ophthalmic examination along with time domain OCT (macular thickness and fast retinal nerve fibre layer thickness (RNFLT) assessment) and Automated Perimetry (AP) by Humphrey Field Analyser (Carl Zeiss, USA) using the 24-2 SITA Fast Protocol.

All patients in the study group had Central Corneal Thickness (CCT) corrected Intraocular Pressure (IOP) of > 21mm in the selected eye. CCT was obtained using the contact method (Ocuscan, Alcon Lab, USA) and CCT corrected IOP was calculated by the Ocuscan machine using the Henderson's formula.

Glaucomatous eyes were defined as those in which glaucomatous Visual Field (VF) defects were confirmed on at least two VF examinations yielding reliable data, and by the presence of a glaucomatous optic disc that showed an increase in cupping (vertical cup–disc ratio >0.6), a difference in the vertical cup–disc ratio of >0.2 between the eyes, diffuse or focal neural rim thinning, or haemorrhage.

Eyes with glaucomatous VF defects were defined as those with a GHT result outside normal limits or a pattern SD (PSD) outside 95% of normal limits. Additionally, a cluster of three points with probabilities of <5% on the pattern deviation map in at least one hemifield, including at

Least one point with a probability of <1%; or a cluster of two points with a probability of <1% was needed.

The Glaucomatous eyes were further divided into those with Early Glaucoma (EG) and those with Moderate to Severe Glaucoma (M-SG) loosely using the Bascom Palmer (Hodapp-Anderson-Parrish) Glaucoma Severity Scale. [5]

Glaucoma-suspect eyes included those with a glaucomatous disc but with a normal VF.

Relatives or attendants accompanying the subjects with CCT corrected IOP <21mm of Hg, no significant ocular or medical history and a normal GHT on VF examination and normal optic nerve head on slit lamp biomicroscopy were included in the group with "Healthy Eyes".

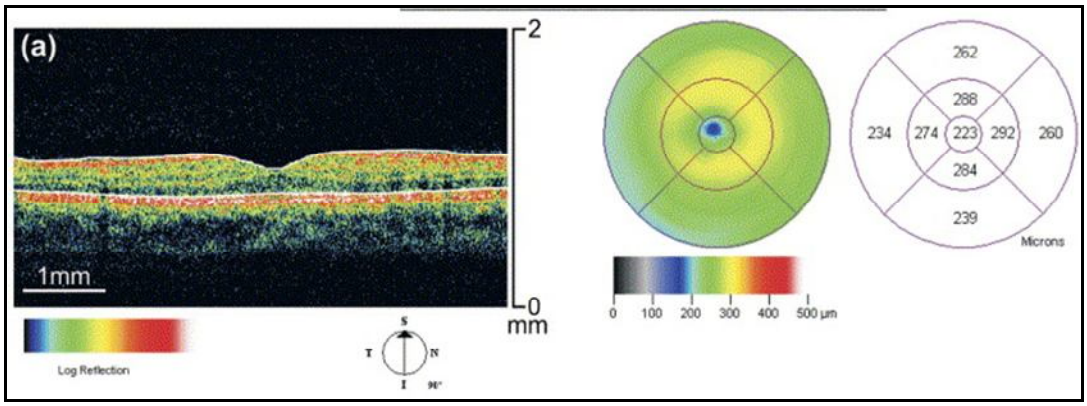

Figure 1: Macular Thickness Map on Time Domain Optical Coherence Tomography

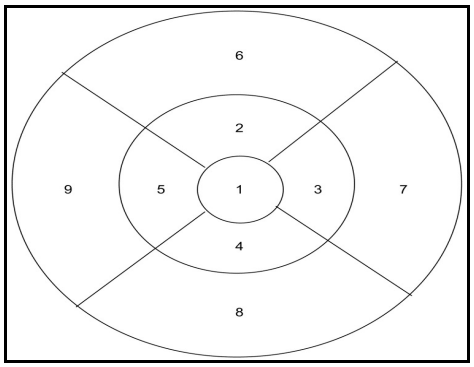

Figure 2: DMT 1 = |2-4| and DMT2 = |6-8|

From the macular thickness map, as shown in Figures 1 and 2, the difference of the two values vertically just beyond the central macular thickness (called DMT1) and the two topmost and lower most value of the macular thickness map (DMT2) was calculated for all patients and normal subjects. The values from the group with "Healthy Eyes" was used to establish a normative database. The number of glaucomatous patients and glaucoma suspects with either of the two DMT values outside 95% CI (+- 1.96 SD) was also calculated.

	Healthy Eyes (200)	**Glaucoma Suspects (105)**	**Early Glaucoma (EG) (45)**	**Moderate-Severe Glaucoma (M-SG) (20)**
Age	52.5	51	52.8	54.4
HVF MD	-1.27(±1.5)dB	-2.52(±1.8)dB	-6.4(±1.94)dB	-9.12(±1.95)dB

	Healthy Eyes (200)	Glaucoma Suspects (105)	Early Glaucoma (EG) (45)	Moderate-Severe Glaucoma (M-SG) (20)
HVF PSD	1.5(±1.28)dB	2.78(±1.65)dB	4.86(±1.44)dB	6.75(±1.11)dB
Average RNFLT	124(±12.62)	112(±13.4)	94(±8.68)	74(±7.82)
Average CMT	210(±15.54)	194(±12.62)	182(±9.84)	169(±8.04)

Table 1: Age Distribution, Mean Deviation (MD), Pattern Standard Deviation (PSD), Average RNFLT And CMT Values Of The Various Study Groups

3.Result

200 healthy eyes were included for building the "Normative Database" for DMT. 105 eyes of glaucoma suspects and 65 glaucomatous eyes (45 early(EG) and 20 moderate-severe(M-SG)) were included in the study. Table 1 shows the age distribution, Mean Deviation (MD) and Pattern Standard Deviation (PSD) on Humphrey Visual Field (HVF) testing as well as average RNFLT and CMT obtained by OCT among the various groups.

Average DMT1 in "Healthy Eyes" was 4.6±3.9µ whereas average DMT2 in "Healthy Eyes" was 6.2±5.6µ. Subjects were deemed to have "abnormal MHT" when either DMT1 and/or DMT2 value was outside 95% confidence interval (±1.96SD). 6.5% (n=13)of the "Healthy Eyes" had abnormal MHT, whereas 33.3% (n=35) of the Glaucoma Suspects, 82.2 % (n=37) of EG and 70% (n=14) of M-SG had abnormal MHT.

Abnormal RNFLT on OCT was defined as average RNFLT value of any one of four quadrants to be less than 5% of normative database. By this definition, 63.8% (n=67) of Glaucoma Suspects, 62.2 % (n=28) of EG and 80 % (n=16) of M-SG had abnormal RNFLT.

Tables 2 and 3 show the sensitivity and specificity of abnormal MHT and abnormal RNFLT respectively.

	Sensitivity	Specificity
Glaucoma Suspects	40.7 %	17.65 %
EG	43.02 %	90.4 %
M-SG	16.28 %	92.86 %

Table 2: Sensitivity And Specificity Of Abnormal MHT

	Sensitivity	Specificity
Glaucoma Suspects	60.36 %	35.6 %
EG	25.23 %	71.19 %
M-SG	14.41 %	93.22 %

Table 3: Sensitivity And Specificity Of Abnormal RNFLT

The M-SG group had the overall lowest CMT which was statistically significantly lower than healthy and glaucoma suspect groups ($p<0.001$). However the sensitivity of asymmetry in MHT was higher than RNFLT analysis in EG ($p<0.05$).

4.Discussion And Conclusion

Glaucoma is associated with characteristic structural changes in the optic nerve head and the RNFL, accompanied by functional VF loss. Thus, both structural and functional assessments are mandatory in glaucoma diagnosis.[3] Often, structural change precedes functional deficit, as assessed by standard automated perimetry. [6] Thus, structural evaluation of the optic disc

And RNFL has been used to detect early glaucomatous changes. El Beltagi et al [7] found that localized retinal NFL thinning as measured by OCT was related to localized visual field defects topographically. The optical coherence tomography measurement of peripapillary RNFL thickness also discriminated very well between glaucoma and normal but was less sensitive for glaucoma suspects.[8]

The loss of ganglion cells and nerve fibre thickness were also observed involving the posterior pole in glaucoma. [2] The macula has the highest density of ganglion cells, with a peak at 750 to 1100 microns from the foveal centre. [9] Ganglion cell loss in glaucoma may result in a decrease in macular cellularity and macular thickness. Lederer et al [10] reported a significant reduction in macular volume, as measured by OCT with standard macular thickness scan covering a circular
The area centred at the fovea, in early and advanced glaucoma but not in glaucoma suspect eyes in a prospective case– control studies. Greenfield et al [11] also demonstrated that macular thickness was significantly thinner in a group of 30 glaucoma eyes than in a group of 29 normal eyes. The changes correlated closely with the peripapillary NFL thickness.
Johnson et al.[12] have documented the high sensitivity and specificity of a GHT result "outside normal limits" in the detection of early glaucomatous functional damage. An abnormal GHT result is very helpful in the diagnosis of glaucomatous change. In particular, an abnormal GHT result is a sensitive indicator of early-stage disease. [12] This is because the characteristic symmetric distribution of retinal nerve fibers with reference to the horizontal raphe is perturbed when glaucoma develops. Thus, asymmetric development of a defect in either the superior or inferior hemifield is indicative of glaucomatous change. Because structural change is often accompanied by functional deficit, it is hypothesized that the rate of macular thickness loss might differ in the superior and inferior hemispheres, as is apparent when VF assessment is
performed using the GHT.
Our study concludes that both CMT and RNFLT is lower in glaucomatous eyes as compared to Healthy Eyes. The order of values, as shown in Table 1, are Healthy>GS>EG>M-SG. Further, it is observed that the decrease from Healthy to GS is not Statistically Significant in *both CMT and RNFLT groups* ($p>0.05$). But the decrease from Healthy to EG statistically significant for *RNFLT only* ($p<0.05$) whereas the decrease from Healthy to M-SG statistically significant for both groups($p<0.05$).
Further it is seen subjects with abnormal MHT is maximum in EG (82.2%), followed by M-SG(70%) and finally GS(33.3%). These findings are similar to those of Um et al[3] . However subjects with abnormal RNFLT is the most in M-SG (80%) and followed by GS (63.8%) and EG(62.2%).
Our study therefore concludes that abnormal MHT has maximum sensitivity and very high specificity for the EG group and is also highly sensitive for GS as well. Hence evaluating MHT values will prove to be an important indicator for the structural status of Glaucoma and will hence be an useful aid in early detection of Glaucoma. This will in turn allow early initiation of appropriate anti glaucoma treatment, and will hence be able to arrest the irreversible loss of retinal nerve fibres and ganglion cells. Further studies with Spectral Domain OCT and evaluation of hemifield "Ganglionic Cell Complex" thickness will further tune the results of our present study.
It can be thus be summarized that that asymmetric horizontal macular hemifield thickness assessment will emerge as a very important non invasive and inexpensive tool in the early diagnosis of glaucoma, particularly early glaucoma and will also help to monitor the progress of this "Silent Thief of Sight".

5.References

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