Diagnosis of Pre-perimetric Glaucoma using Optical Coherence Tomography

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Abstract

Objective: To study the efficacy of Optical Coherence Tomography in pre perimetric glaucoma.

Methods: 76 glaucoma suspects with normal or borderline white on white visual fields underwent RNFL analysis with Optical Coherence Tomography (Stratus OCT version 4).

Outcome measure: Borderline or definite RNFL thinning in the inferior or superior quadrants was taken as the main outcome measure.

Results: Six out of seventy six glaucoma suspects showed RNFL changes in OCT suggestive of glaucoma giving the test a specificity of 92 %. All six patients had cup disc ratio of 0.6 or more and five out of six patients had IOP of 18 or more and positive family history of glaucoma.

Conclusion: Optical Coherence Tomography is an useful tool for diagnosis of pre perimetry glaucoma especially in the presence of other risk factors like raised IOP, enlarged cup and family history of glaucoma.

Introduction

Glaucoma is an optic neuropathy characterized by a specific and progressive injury to the optic nerve and retinal nerve fiber layer. Because the injury due to glaucoma is irreversible, early detection and prevention of glaucomatous RNFL loss is of vital importance. Examination of the optic nerve head and its surrounding nerve fiber layer is considered essential in both detection and monitoring of glaucoma. Damage to the RNFL has been shown to precede visual field loss. Upto 30-50 % nerve fibre loss might have occurred before the first detectable field defect. Hence, objective methods of measuring these structures will aid ophthalmologists in making an accurate diagnosis.

Optical Coherence Tomography (OCT) which was first described in 1991, is a high resolution cross sectional imaging technique that allows accurate measurement of the retinal nerve fiber layer. With the ability to quantify the thickness of the RNFL with a resolution of 8 to 10 microns, clinicians potentially have a more objective tool in helping to diagnose glaucoma much earlier than visual fields. However, white on white perimetry is still considered the gold standard for diagnosis of glaucoma. AAO Preferred Practice Patterns still mentions that the diagnosis of glaucoma is based on appearance of the optic disc and standard achromatic perimetry. In this current study glaucoma suspects who had normal or
Materials and Method

The study was designed as a retrospective observational case series which included glaucoma suspects attending a tertiary care glaucoma centre.

**Study Population:** 103 glaucoma suspects who underwent RNFL analysis on Optical Coherence Tomography were initially enrolled, out of which 76 eyes of 76 patients fulfilled all criteria and were finally included in the study. Only one eye per person was included in the study. If one eye had abnormal fields and the other eye normal, the normal eye was included in the study. If both eyes were normal or both were borderline, the eye with the better PSD value on HFA was selected and assigned to the study.

Complete ophthalmic examination including visual acuity, intraocular pressure, gonioscopy and optic disc evaluation was performed. All patients initially underwent either 30-2 full threshold or SITA - standard white on white perimetry. The time gap between perimetry and OCT was not more than two weeks. Patients with spherical refractive errors of more than 6D, astigmatism more than 3 Dioptres, visual acuity worse than 6/12 were excluded from the study. Other exclusion criteria were secondary causes of raised IOP, abnormal disc appearance such as tilted discs and suspected neurological diseases which are likely to affect the field testing. Those patients with extensive peripapillary atrophy were also excluded from the study.

**Definition of glaucoma suspect:** For the purpose of this study a glaucoma suspect was defined as the presence of an abnormal disc appearance consistent with glaucoma as determined by an experienced clinician. Disc asymmetry of 0.2 or more was also included in the definition of glaucoma suspect.

**Observation procedures:** All selected patients had a reliable visual field on Humphrey Visual Field Analyzer. Reliable fields were defined as fixation loss rate of less than 33 % and false positive and false negative error rates of less than 20 %. Normal and borderline definitions were based on the glaucoma hemi field test.

**OCT measurements:** The test was performed after dilation of the pupil to at least 5 millimetre. Three measurements were performed for each eye. Only measurements with signal strengths of six or more were accepted as reliable for this study.

**Outcome Measures:** Definite RNFL thinning (shaded as red) or borderline RNFL thinning (shaded as yellow) in either the inferior or superior portion of the disc was taken as the main outcome measure. Charts with only temporal or nasal thinning were excluded from the study.

**Statistical Analysis:** The Fisher exact test was used to assess the statistical significance of glaucomatous changes in OCT in the presence of other risk factors like raised IOP, family history of glaucoma and enlarged cup-disc ratio. Odds ratio was also calculated for the above mentioned risk factors.

Results

After all exclusions, 76 eyes of 76 patients were enrolled in the study, of which 51 were males and 25 were females. The age group distribution is shown in Figure1.

A total of 6 patients had abnormal OCT among the 76 patients enrolled in the study.15 patients had a positive family history of glaucoma in either their first degree or second-degree relative and out of these 5 had abnormal OCT. Only one person with abnormal OCT had no family history of glaucoma. The difference between the positive family history group and the negative family history group was statistically significant (p value 0.001, Fisher exact test). The odds of having an abnormal OCT was 36 times in persons having a positive family history of glaucoma.

A total of 47 persons had a CDR of 0.6 or more, out of which 17 had CDR of more than 0.8 (Figure 2). 5 out of 6 OCT positive persons had a CDR of 0.8 or more, and one had a CDR of 0.7. When a CDR of 0.6 was taken as the cut-off, the chance for having an
abnormal OCT was not statistically significant (p value 0.0768, Fisher exact test). But when CDR of 0.8 was taken as the cut-off, the chances of having an abnormal OCT was statistically significant (p value 0.0017, Fisher exact test). Persons with a CDR of 0.8 or more are 22 times more likely to have an abnormal OCT, compared to those having a CDR of 0.7 or less.

The mean IOP of the 76 eyes enrolled in the study was 16.29. 26 patients had an IOP of 18 or more, out of which only 7 eyes had an IOP of 22 mm Hg or more (Figure 3). 5 out of the 6 patients who had an abnormal OCT had IOP more than 18 mm Hg. With 18 mm Hg as the cut-off, the chance of having an abnormal OCT was statistically significant (p value 0.0161, Fisher exact test). The odds of having an abnormal OCT was 11 times more in persons with an IOP of more than 18 when compared to those with IOP of 17 or less.

OCT in glaucoma is a very effective tool in identifying the true negatives. It shows that 70 out of 76 eyes was proven as not having glaucomatous damage. This gives the test a specificity of 92 %.

4 eyes had inferior thinning and 2 had superior thinning. No biarcuate thinning was seen in any of the six cases. 5 eyes out of 6 had definite thinning of RNFL (shaded as red) and I had borderline thinning (shaded as yellow).

Table 1 showing mean superior and inferior RNFL thickness in patients with normal and abnormal OCT values were 79 and 75.33 respectively in the 6 patients with abnormal OCT. (Table 1)

### Discussion

We have studied 76 eyes of 76 patients who were clinically found to have some suspicion of Glaucoma. The numbers were slightly smaller compared to a few other studies\(^5,6\). Ours was an observational study and there was no control group, which were used in other studies\(^5,6\). In the study by Kanamori et al\(^6\) normal population, glaucoma suspects, ocular Hypertensives and glaucoma patients were included in the study and compared. We were only studying the ability of the OCT in picking up Pre perimetric glaucoma in suspected cases.

The role of family history has been highlighted in many studies\(^7,8,9\) although the incidence of MYOC mutation among Indian primary open angle glaucoma patients has been found to be lower compared to certain other parts of the world\(^10\). In our study, in glaucoma suspects with normal fields, those with positive family history of glaucoma are 36 times more likely to have an abnormality in OCT when compared to those with no family history of glaucoma.

Cup – disc ratio has been used to define glaucoma suspects in many other studies\(^11\). Lalezary et al\(^11\) have...
used stereo photographs to classify the study population into normal and glaucoma suspects. In our study the classification has been done by an experienced glaucoma specialist by using 78 D lens biomicroscopy.

In our study, the specificity was a healthy 92 %, which means the OCT is a good tool to rule out disease. Sensitivity was not calculated in our study since this requires a normal age-matched control group. Budenz et al showed a sensitivity of 84 % and a specificity of 98 % in their study on perimetric glaucomas 12.

As expected the mean RNFL thickness in the inferior and superior quadrant was significantly lower in the abnormal OCT group compared to the normal OCT group. Kanamori et al have studied the temporal and nasal thickness also along with the superior and inferior 6. We felt that many errors may crop up if the nasal and temporal thickness was included. Also the inferior and superior poles were the first affected in early glaucoma. The normal OCT showed the characteristic double-hump pattern which is in agreement with other human 6 and histologic studies 13.

**Self assessment of this study – STARD guidelines**

Standards for Reporting of Diagnostic Accuracy (STARD) is an internationally accepted method of assessing a study conducted on a diagnostic equipment. A recent report on the quality of reporting of diagnostic accuracy was conducted with 30 published articles. The STARD guideline consists of 25 points which are to be fulfilled for a good diagnostic study 14. In this meta analysis only 26 % of the papers reported more than half of the STARD items. Our study has reported 11 out of the 25 STARD items, and this compares well with many published articles on diagnostic accuracy of OCT in diagnosis of early glaucoma.

**Conclusion**

Optical Coherence Tomography is a useful tool for pre perimetric diagnosis of glaucoma. The usefulness of this tool increases in the presence of other risk factors like family history of glaucoma, large cup disc ratio and high intra ocular pressure. The specificity of this tool in our study was 92 % which makes it a good tool to rule out those who do not have glaucoma. Comparative studies with the other imaging tools like HRT and GDx are needed in our population to determine which is the best tool for diagnosis of early glaucoma.

**References**