



OPTICAL COHERENCE TOMOGRAPHY; DIAGNOSTIC ACCURACY OF OCT IN DETECTION OF GLAUCOMA BY TAKING PERIMETRY AS GOLD STANDARD

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Article received on:

24/05/2016

Accepted for publication:

01/08/2016

Received after proof reading:

10/09/2016

ABSTRACT: "Glaucoma an optic neuropathy is a caused by progressive retinal ganglion cell (RGC) loss associated with characteristic structural changes in the optic nerve and retinal nerve fiber layer (RNFL). Glaucoma induced damage causes the retinal ganglion cells loss that can result in functional loss and decrease in vision of patient · Measurement of intraocular pressure by Tonometry, characteristics of the optic nerve head changes and associated visual field loss are used for diagnosis of Glaucoma. **Objectives:** To determine the diagnostic accuracy of Optical Coherence Tomography in detection of glaucoma taking perimetry as gold standard. **Study Design:** Cross sectional (validation). **Period:** Six months from 17-02-2014 to 16-08-2014. **Material and Method:** Regarding the Inclusion Criteria patients of glaucoma suspects that meet the criteria mentioned in operational definition of either gender with age range between 35- 60 years were included while patients having refractive errors, hazy media, pupil size less than 4mm after dilation were not included in this study. Also patients with history diabetes mellitus, refractive or retinal surgery were also excluded. All the data was entered and analyzed by using SPSS V-16. **Results:** A total of 100 patients were included in this study during the study period .Majority of the patients were between 35-45 years of age and minimum patients were 56- 60 years old. Mean age of the patients was 47.10 ± 8.02 years. Males and females were 50 (50%). At OCT glaucoma was present in 71 patients while at perimetry glaucoma was present in 69 patients .Sensitivity, specificity and diagnostic accuracy of OCT was 92.7%, 77.4%, 88.0%, respectively .Positive predictive value and negative predictive value of OCT was 90.1% and 82.7%, respectively. **Discussion:** Regarding the pathogenesis of Glaucoma induced damage is due to result of retinal ganglion cell (RGC) death with progressive loss of axons located in the retinal nerve fiber layer (RNFL). Many clinical studies showed that optic nerve head (ONH) damage and thinning of the RNFL occur earlier than the appearance of Glaucoma induced visual field defects; **Conclusion:** In conclusion, glaucoma suspects undergoing the OCT can be assessed for the presence of glaucoma based purely on the results of the OCT.

Key Words: Glaucoma, Optical coherence tomography, Perimetry.

Article Citation: Ahmad F, Hussain MU. Optical coherence tomography; Diagnostic accuracy of oct in detection of glaucoma by taking perimetry as gold standard. Professional Med J 2016;23(9):1149-1156. DOI: 10.17957/TPMJ/16.3457

INTRODUCTION

"Glaucoma is an optic neuropathy caused by progressive retinal ganglion cell (RGC) loss which causes characteristic structural changes in the optic nerve and retinal nerve fiber layer (RNFL) that leads to specific visual field changes on perimetry.; In Glaucomatous patients, glaucoma induced damage can be assessed subjectively by clinically examining the optic nerve head (ONH) and peripapillary retinal nerve fiber layer (RNFL) thickness. Glaucoma may be open angle or closed angle. Open-angle glaucoma (POAG) is considered as having different etiologies and

progressive optic neuropathy with a specific acquired loss of optic nerve fibers. Such damage occurs in the presence of an open angle and raise intraocular pressure, which affects the hemodynamic circulation of Optic nerve head and axon cells transport in posterior segment. POAG has an slow onset and causes irreversible visual loss.¹

In glaucoma there is a relatively slow loss of retinal ganglion cell axons that mostly effect midperipheral visual field. However glaucoma becomes symptomatic when central vision is

affected that occurs in relatively late stage of disease. As the visual damage in glaucoma is irreversible, it can usually be arrested, if early diagnosis has to be made.²

Tonometry for Measurement of intraocular pressure, the optic nerve head changes along associated visual field loss are used for diagnosis of Glaucoma. However In normal or low tension Glaucoma intraocular pressure is normal. So irrespective of IOP, specific changes in optic head with visual field changes are necessary for Glaucoma Diagnosis.³

After Diabetic retinopathy and cataract induced blindness, Glaucoma is the third most common cause of blindness in the world and 10% of blindness are produced due to glaucoma worldwide. In 2020 80 million people will be affected by glaucoma. In Glaucoma First of all vision loss begins in the peripheral visual field followed by central vision loss in its advanced stages. With advancement of medical technology, there have been revolutionary changes in the understanding, diagnosis, and management of glaucoma. In glaucoma patient, Standard automated perimetry (SAP) is the most commonly used method for diagnosis of Glaucoma. Patient Subjective response is observed in automated perimetry. The Standard automated perimetry (SAP) test involves the detection of a stimulus the luminance by the patients which is greater than that of the background of a given constant luminance.⁴

Standard automated perimetry is one excellent test for diagnosis of glaucoma.⁵ Sensitivity is 93% and specificity is 91% in various studies conducted for standard automated perimetry.⁶

Unfortunately our current examination techniques and tests do not allow us to detect the disease early and we often rely on changes of visual field to diagnose glaucoma. Standard Automated Perimetry, (SAP) has poor sensitivity for detecting early glaucoma.⁷

Histological studies as well as postmortem studies

showed that that up to 40% axonal loss may occur before detectable visual field changes.^{8,9}

Similarly in 55% of ocular hypertensive eyes that converted to glaucoma, optic disk structural damage without coexisting visual field changes on SAP had been documented.¹⁰ Sommer et al. reported that evidence of RNFL loss in patients of ocular hypertension 6 years before a detectable change on SAP.¹¹

Advanced imaging technology enabled the detection of structural changes before the development of SAP abnormality.¹²

Optical coherence tomography (OCT), first time described by Huang et al in 1991.¹³

Optical coherence tomography (OCT) is a rapidly developing new technology with significant clinical impact in field of ophthalmology.¹⁴

Recently new available OCT technology, spectral domain (SD)-OCT, has theoretical advantages in glaucoma diagnosis as compared to earlier generation of time domain (TD)-OCT due to increased axial resolution and faster scanning speed that causes to lower susceptibility to eye movement artifacts. Normally, SD-OCT in glaucoma has primarily focused on the evaluation RNFL parameters, however due to variability surrounding structures along with coexisting pathology may cause non reliable measurement. But due to enhanced performance of SD-OCT allows measurements all macular parameters as macula has highest concentration (50 % more RGC cells) of retinal ganglions cells in retina and loss of RGC cells may be easily detected in macular area by SD-OCT.¹⁵

Optical coherence tomography (OCT) is an imaging technology similar to B- scan ultrasound imaging. However OCT used light instead of sound to acquire high-resolution images of retina. OCT uses principle of low coherence Interferometry in which light backscattered from ocular structures. By using OCT cross-sectional images of the optic nerve head, peripapillary retina and the macula

can be obtained. OCT software finally artificially color-coded images in which less reflective tissue has darker colors such as black and blue while High reflective tissue, such as the RNFL, appears green and yellow. In OCT light of Infra-red wavelength (about 840 nm) is used.¹⁶

Regarding role of OCT in Glaucoma It is used for assessment retinal nerve fiber layer (RNFL) thickness in area of circumpapillary and macula regions. The glaucomatous loss of neural axons results in thinning of the retinal nerve fibre layer. With help of OCT the extent and location of these defects can diagnosed. The advantage of OCT for ophthalmologist is that it is fast scanning method that allows three-dimensional (3D) volume scanning of the retina, due to which detailed and accurate quantitative analysis of the retinal structure is possible.⁶ In a study prevalence of glaucoma was 38.8% (111 out of 286 eyes) with 83% sensitivity and 88% specificity on OCT.^{17,18}

Similarly Optic nerve head (ONH) parameters found on OCT scan have excellent ability to discriminate between normal eyes and eyes with even mild glaucoma. These Parameters includes vertical rim thickness, rim area, and vertical cup to disc ratio. These Parameters have the greatest diagnostic capability. These ONH parameters were found to be as good as RNFL thickness parameters in diagnosing glaucoma.¹⁹

OBJECTIVE

Objective of the study was:

To determine the diagnostic accuracy of Optical Coherence Tomography in detection of glaucoma taking perimetry as gold standard.

Operational Definitions

Glaucoma on OCT

The patient was labeled as having glaucoma when average retinal nerve fibre layer thickness will be < 87 μm .

Glaucoma on SAP

"If the patient has visual field defects in perimetry, the patient is diagnosed as a case of glaucoma. Glaucomatous VF defects have to meet at least

two of the following criteria:

1. A cluster of three points with a probability of <5% on a 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%.
2. Glaucoma hemi field test results outside normal limits. The GHT compares five corresponding areas on the superior and inferior fields (as glaucomatous change is typically vertically asymmetrical). Results are given automatically by built in software.;
3. A pattern SD (PSD) < 5%.

Sensitivity: It is the ability of OCT to diagnose patients having glaucoma.

Specificity: It is the ability of OCT not to diagnose patients having glaucoma.

Positive predictive value: It is the probability of negative OCT in patients who actually do not have glaucoma.

Negative predictive value: It is the probability of positive OCT in patients who actually have glaucoma.

True positive: Patients with positive OCT who also have positive perimetry.

True negative: Patients with negative OCT who also have negative perimetry.

False positive: Patients with positive OCT who also have negative perimetry.

False negative: Patients with negative OCT who also have positive perimetry.

MATERIAL AND METHOD

Study design

Cross sectional (validation) study.

Setting

Department of ophthalmology, Independent University Hospital and Allied hospital, Faisalabad.

Duration of Study

Study was carried out over a period of six months from 17-02-2014 to 16-08-2014.

Sample Size

"By using WHO sample size calculator for

sensitivity and specificity.

Sensitivity = 83%, Specificity = 88%
 Prevalence = 38.8%, Confidence interval = 95%
 Precision for sensitivity = 10%, for specificity = 100%
 Sample size = 100"

Sampling Technique

Non probability consecutive sampling.

Sample Selection

Regarding the Inclusion Criteria patients of glaucoma suspects that meet the criteria mentioned in operational definition of either gender with age range between 35- 60 years were included while patients having refractive errors, hazy media, pupil size less than 4mm after dilation were not included in this study. Also patients with history diabetes mellitus, refractive or retinal surgery were also excluded.

Data Collection Procedure

OPD patients fulfilling the inclusion criteria were enrolled and after explaining all the procedure to the patient informed consent was taken. In case of any refractive error of patient, correction was done followed by dilatation of the pupil with 1% tropicamide eye drops.

After explaining the protocol of the tests every subject will undergo automated perimetry (human visual field analyzer) and optical coherence tomography (RT-100 OCT machine, RTVue) on the same day.

All data printout was taken and subjected to separate reviewing by authors that labeled printouts as positive or negative. All the information was recorded on study Performa.

Data Analysis Procedure

All the data was entered and analyzed by using SPSS V-16. Descriptive statistics was calculated for all the variables. Mean and standard deviation was calculated for all the quantitative variables like age. Frequency and percentage was calculated for all qualitative variables like gender and true positives. Sensitivity, specificity, Positive predictive value (PPV) and Negative predictive value (NPV) was calculated by constructing 2×2 table taking perimetry as gold standard as follows

$$\text{Sensitivity} = \text{TP} / \text{TP} + \text{FN} \times 100$$

$$\text{Specificity} = \text{TN} / \text{FP} + \text{TN} \times 100$$

$$\text{PPV} = \text{TP} / \text{TP} + \text{FP} \times 100$$

$$\text{NPV} = \text{TN} / \text{TN} + \text{FN} \times 100$$

$$\text{Diagnostic Accuracy} =$$

$$\text{TP} + \text{TN} / \text{TP} + \text{FN} + \text{FP} + \text{TN} \times 100$$

RESULTS

A total of 100 patients were included in this study during the study period of six months from 17-02-2014 to 16-08-2014.

Majority of the patients were between 35-45 years of age and minimum patients were 56-60 years old. Mean age of the patients was 47.10 ± 8.02 years (Table-I). Males and females were 50 (50%) (Table-II).

Age (Year)	Number	Percentage
35-45	45	45.0
46-55	37	37.0
56-60	18	18.0
Total	100	100.0
Mean ± SD	47.10 ± 8.02	

Table-I. Distribution of cases by age

OCT	PERIMETRY		Total
	Present	Absent	
Present	True positive (TP)	False positive (FP)	
Absent	False negative (FN)	True negative (TN)	
Total			

Gender	Number	Percentage
Male	50	50.0
Female	50	50.0
Total	100	100.0

Table-II. Distribution of cases by gender

OCT	Perimetry		Total
	Present	Absent	
Present	64 (TP)	7 (FP)	71
Absent	5 (FN)	24 (TN)	29
Total	69	31	100

Table-III. Comparison of glaucoma at OCT findings vs glaucoma at perimetry
 Key:
 TP = True positive, FP = False positive,
 FN = False negative, TN = True negative

At OCT glaucoma was present in 71 patients while at perimetry glaucoma was present in 69 patients (Table-III).

Sensitivity, specificity and diagnostic accuracy of OCT was 92.7%, 77.4%, 88.0%, respectively (Table-IV).

Sensitivity rate	$\frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}}$	x 100 =
	$\frac{64}{64 + 5}$	x 100 = 92.7%
Specificity rate	$\frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}}$	x 100
	$\frac{24}{24 + 7}$	x 100 = 77.4%
Diagnostic Accuracy	$\frac{\text{True Positive} + \text{True Negative}}{\text{True Positive} + \text{True Negative} + \text{False Positive} + \text{False Negative}}$	x 100
	$\frac{64 + 24}{64 + 24 + 7 + 5}$	x 100 = 88.0%

Table-IV. Sensitivity, Specificity and diagnostic accuracy of OCT

Predictive value of Positive test	$\frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}}$	x 100 =
	$\frac{64}{64 + 7}$	x 100 = 90.1%
Predictive value of Negative test	$\frac{\text{True Negative}}{\text{True Negative} + \text{False Negative}}$	x 100
	$\frac{24}{24 + 5}$	x 100 = 82.7%

Table-V. Positive predictive value and negative predictive value of OCT

DISCUSSION

Regarding the pathogenesis of Glaucoma induced damage is due to result of retinal ganglion cell (RGC) death with progressive loss of axons located in the retinal nerve fiber layer (RNFL). Many clinical studies showed that optic nerve head (ONH) damage and thinning of the RNFL occur earlier than the appearance of Glaucoma induced visual field defects.²⁰

The European Glaucoma Society (EGS) stated in the 2008 Clinical Practice Guidelines that at least 50% of patients with glaucoma remain undiagnosed while more than 50% of patients currently receiving treatment for glaucoma do not actually have glaucoma. The EGS cited the need to improve on the sensitivity and specificity of diagnostic tests for glaucoma.²¹

In glaucoma patients, optical coherence tomography (OCT) that is one of the latest diagnostic modality, is used for detection of presence of decreased thickness of the retinal nerve fiber layer (RNFL) around the area optic nerve head. So by using the OCT glaucomatous eyes can be differentiated from normal eyes by measuring and analyzing RNFL thickness and ONH parameters because OCT is an accurate and reproducible method in such patients. OCT superior to other imaging techniques, such as scanning laser polarimetry and Heidelberg retina tomography to diagnosis a specific pattern of reduction in retinal nerve layer thickness. Stratus OCT software-provided parameters showed that RNFL measures and ONH topography parameters have the highest power to differentiate glaucomatous from healthy eyes of the patients.²²

In its most recent technology assessment published in 2007, the American Academy of Ophthalmology reviewed the evidence from articles related to the diagnosis of glaucoma using the OCT and other imaging devices like scanning laser polarimetry and Heidelberg retina tomography. A review of 159 articles on diagnostic studies showed that OCT provide more objective, quantitative, and reproducible images of the ONH and RNFL, both of which are effected in glaucoma

before visual field loss occur.²³

The early models of the OCT had a dilemma of deriving the abnormal value using the quantitative data available from the OCT. A study by Budenz using the fast RNFL protocol on 109 normal and 63 glaucoma subjects determined the sensitivity and specificity of the OCT RNFL thickness measurements in diagnosing glaucoma using the standard automatic perimetry as the gold standard.²⁴

In present study, optical coherence tomography sensitivity was 92.7%, specificity 77.4%, diagnostic accuracy 88.0%, positive predictive value 90.1% and negative predictive value was 82.7%. Our results are consistent with previous studies carried out by Hougard (72% sensitivity and 95% specificity)²⁵ and Budenz (68% sensitivity and 100% specificity).²⁴ Our results are also close to the studies conducted by Garas et al and Chang et al.^{17,18}

However the quality of an OCT scan as well as the strength of the signal are some limitations regarding the use OCT in glaucoma patients. Factors that can impaired the strength of signals are dry eyes, tilted discs, staphylomas, epiretinal membranes, posterior vitreous detachments and media opacities such as cataract. For example, Cataracts can affect RNFL thickness measurements. One study found that after cataract surgery 4.8 μm increase in RNFL thickness measurement. This effect is mostly seen in cortical cataracts, followed by posterior subcapsular cataracts and no effect in nuclear cataracts.^{26,27}

CONCLUSION

In conclusion, glaucoma suspects undergoing the OCT can be assessed for the presence of glaucoma based purely on the results of the OCT. The OCT gave categorical results with high sensitivity and specificity. So OCT may be useful as a screening test for glaucoma suspects.

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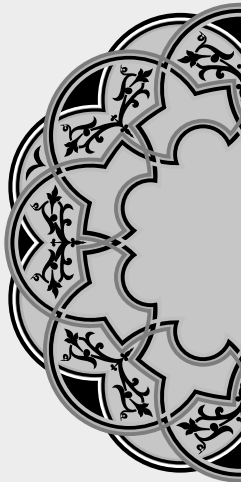
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PREVIOUS RELATED STUDY

Muhammad Firdous. GLAUCOMA CAPSULARE; (ROLE OF FILTRATION SURGERY). (Original) Prof Med Jour 16(3) 406-409 Jul, Aug, Sep, 2009.



*“Never be afraid to try something new.
Remember, amateurs built the ark.
Professionals built the titanic.”*

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Faheem Ahmad	Concept & design, critical expertise & writing, Final approval	
2	Dr. M. Usman Hussian	Concept & data collection	