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Research Article

A Prospective Analysis of Macular Volume and Thickness Parameters in Primary Open Angle Glaucoma Suspects and in Patients with Primary Open Angle Glaucoma Using Optical Coherence Tomography

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Abstract

The study was conducted to analyze and establish the structure functional relationship between OCT macular volume /thickness parameters in patients with POAG SUSPECTS and POAG patients and to correlate macular thickness and RNFL thickness in primary open angle glaucoma suspects and primary open angle glaucoma patients using STRATUS OPTICAL COHERENCE TOMOGRAPHY (OCT).

A prospective study was undertaken in the department of glaucoma services, ARAVIND EYE HOSPITAL, MADURAI between November 2004 and September 2005, a total of 290 eyes of 146 patients were studied and analyzed.

It was found that the RNFL thickness showed a slightly stronger relationship with the disease compared to the macular retinal thickness in POAG. The OUTER RING macular thickness with our prototype OCT provided better correlation than did the INNER RING macular thickness in both the study groups. Thus more peripheral areas of the macula showed a stronger association with glaucoma than did the more central macula.

Conclusion: The study results supported zeimer., et al's hypothesis that macular thickness is reduced in glaucoma. Conversely, we found that peripapillary NFL thickness is a more sensitive indicator of the presence or absence of glaucoma than was macular thickness. Nevertheless, macular thickness assessment clearly may have a role in the assessment and diagnosis of glaucoma.

Keywords: Thickness; Glaucoma Suspects; Coherence Tomography; Patients

Introduction

Glaucoma is one of the leading causes of irreversible blindness in the developing countries and a major health problem in developed countries [1].

WHO statistics indicates that glaucoma accounts for 5.1 million blind people which is 13.5% of global blindness in the world [2].

There will be 60.5 million people with OAG and ACG in 2010, increasing to 79.6 million by 2020 and of these, 74% will have OAG. Women will comprise 55% of OAG, 70% of ACG and 59% of all glaucoma in 2010. Asians will represent 47% of those with glaucoma and 87% of those with ACG. Bilateral blindness will be present in 4.5 million people with OAG and 3.9 million people with ACG in 2010, rising to 5.9 and 5.3 million people in 2020, respectively. The early diagnosis of glaucoma and early detection of its progression are twin challenges the present generation ophthalmologists face [3].

Since glaucomatous damage is irreversible, prevention of this injury before it occurs is the strategy available to those treating the disease. POAG is characterized by chronic progressive optic neuropathy developing in the presence of open angles with characteristic visual field defects and raised intra ocular pressure. In glaucoma the essential pathologic process is the loss of retinal gan-

glion cells and their axons. Studies have shown that glaucomatous damage to the retinal nerve fiber layer precedes functional loss by as much as 5 years [4,5].

The size and anatomical distribution of retinal ganglion cells varies throughout the posterior pole. Approximately 50% of retinal ganglion cells are located in the macular region 4 - 5 mm from the center of the fovea, with the peak density occurring 750 - 1100 micrometer from the foveal center where the cell density may be 4 - 6 cell bodies thick. Although cell diameter distribution is variable a skewed distribution towards layer cell diameter (14 - 16 micrometer) exists in the normal retina and such cells have been shown to be selectively lost in human and experimental models of glaucoma. Glaucomatous cupping of the optic disc is subject to variation in interpretation and is not sensitive for identifying small changes [6].

Drawings and photography of the optic nerve head depend on the subjective interpretation of the examiner and are subject to variability in interpretation. Quigley and co-workers showed that significant axonal loss may precede the development of visual field defects and identifiable cupping [7-9]. Zeimer., *et al*. reported a significant correlation between glaucomatous visual field defects and reductions in macular thickness using a retinal topographer (retinal thickness analyzer) based on the principles of slit lamp biomicroscopy.

Aims and Objectives

1. To analyze and establish the structure functional relationship between OCT macular volume/thickness parameters in patients with POAG suspects and POAG patients.
2. To correlate macular thickness and RNFL thickness in primary open angle glaucoma suspects and primary open angle glaucoma patients using stratus optical coherence tomography (OCT).

Materials and Methods

A prospective study was undertaken in the department of glaucoma services, Aravind Eye Hospital, Madurai between November 2004 and September 2005, a total of 290 eyes of 146 patients were studied and analyzed.

Inclusion criteria

1. Patients in the age group of 14 -75 years.
2. Patients with suspected POAG and patients with POAG diagnosed at the time of study or previously diagnosed as POAG patient.
3. Open angles on gonioscopy using modified shaffer's grading system.
4. Patients with refractive errors-myopia less than 5 diopters, hypermetropia less than 3.5 diopters and astigmatism less than 2 diopters.

Exclusion criteria

1. All types of glaucoma other than POAG.
2. All gross media opacities which interfere with the OCT imaging.
3. Patients with retinal and macular diseases.

Classification criteria

POAG suspect

1. No history of glaucoma
2. BCVA 20/40 OR better.
3. IOP ≤ 21 mm Hg.
4. HFA normal/subtle defects.
5. Abnormal/Asymmetrical cupping of the optic nerve head.

POAG

1. Incomplete NRR loss in any 1 quadrant quadrantic NRR loss.
2. Visual field loss one side of the horizontal meridian by HFA/Visual field loss above and below the horizontal meridian.
3. IOP > 21 mm Hg.

OCT macular neurosensory retinal thickness maps were used to calculate macular volume/thickness for comparison to humphrey visual field testing, intraocular pressure (IOP) measurements, optic nerve head damage and nerve fibre layer thickness.

Area under the receiver operator characteristics (AROC) curves for the association between macular retinal thickness and peripapillary NFL thickness and visual field findings were calculated in a sub group of eyes without visual field defect and eyes with visual field defect confined to one hemifield.

Statistical analysis

The data were analyzed using strata 8.1 software (STATA Corporation, College Station, Texas, USA). Mann Whitney U test were calculated for non-parametric data and area under receiver operator characteristic (AROC) curves were calculated for the association between visual field defects confined to a single hemifield and macular and peripapillary hemi-retinal OCT measurements.

Results

	POAG Suspect (N=142) Mean ± SD	POAG (N=148) Mean ± SD	p-value
IOP	18.3 ± 4.4	18.2 ± 4.7	0.585
Mean	-2.6 ± 5.3	-7.4 ± 7.9	< 0.001
Pattern Standard Deviation	3.8 ± 2.3	4.6 ± 3.1	0.171
Foveal Minimum	167.5 ± 36.1	160.6 ± 22.7	0.194
Total Macular Volume	6.8 ± 0.5	6.3 ± 0.4	< 0.001
Average Retinal Thickness	94.5 ± 14.5	81.5 ± 20.1	< 0.001
SMAX	146.0 ± 24.0	123.9 ± 29.7	< 0.001
IMAX	153.7 ± 27.8	126.2 ± 33.5	< 0.001
Fovea	197.4 ± 34.4	187.4 ± 20.8	0.007
Temporal Inner Macula	256.5 ± 21.1	240.7 ± 23.4	< 0.001
Superior Inner Macula	267.3 ± 21.4	254.0 ± 21.0	< 0.001
Nasal Inner Macula	273.0 ± 33.9	253.9 ± 24.2	< 0.001
Inferior Inner Macula	273.4 ± 31.7	253.5 ± 22.4	< 0.001
Temporal Outer Macula	220.0 ± 19.3	201.9 ± 18.2	< 0.001
Superior Outer Macula	235.7 ± 16.4	221.7 ± 20.5	< 0.001
Nasal Outer Macula	257.3 ± 30.4	238.3 ± 23.6	< 0.001
Inferior Outer Macula	227.4 ± 28.7	209.0 ± 20.2	< 0.001
Inner Ring	267.6 ± 24.3	250.5 ± 20.7	< 0.001
Outer Ring	235.1 ± 20.4	217.7 ± 17.6	< 0.001
Center + Inner	232.5 ± 27.6	219.0 ± 18.0	< 0.001
CD Ratio	0.6 ± 0.1	0.6 ± 0.1	< 0.001

Table 1

VF Defect Location	N	Mean ± SD	p-value
SUPINF			
None	121	0.52 ± 25.74	0.087
Superior	68	5.30 ± 12.50	
SUPINF			
None	121	0.52 ± 25.74	0.439
Inferior	57	4.40 ± 11.78	
SUPINF			
None	121	0.52 ± 25.74	0.059
Both	44	10.32 ± 23.15	
SMAXIMAX			
None	121	-8.34 ± 28.12	0.400
Superior	68	-4.06 ± 22.97	
SMAXIMAX			
None	121	-8.34 ± 28.12	0.322
Inferior	57	-4.63 ± 26.17	
SMAXIMAX			
None	121	-8.34 ± 28.12	0.026
Both	44	3.02 ± 26.78	

Table 2

	No VF Defect	Single Hemifield VF Defect	Both Hemifield VF Defect	ANOVA
Eyes	121	125	44	NA
Age (yr)	46.40 ± 12.2	52.29 ± 11.8	51.26 ± 13.3	0.028
MD (dB)	-1.93 ± 4.72	-5.15 ± 4.41	-13.66 ± 11.26	0.000
PSD (dB)	3.52 ± 2.11	4.25 ± 2.46	6.19 ± 4.30	0.000

Table 3

ANOVA: Analysis of Variance; MD: Mean Deviations; PSD: Pattern Standard Deviation; VF: Visual Field; NA: Not Applicable; NFL: Nerve Fiber Layer; Sup: Superior; Inf: Inferior; VF: Visual Field.

	Macular Retinal Thickness µm (SD)			Peripapillary NFL Thickness µm (SD)		
VF Defect Location	**Superior**	**Inferior**	**p-value**	**Superior**	**Inferior**	**p-value**
None (N = 121)	251.2 (15.2)	250.7 (31.6)	NA	148.1 (21.9)	156.5 (27.1)	NA
Superior (N = 68)	245.6 (18.7)	240.3 (15.3)	0.087	132.1 (23.7)	136.2 (26.3)	0.400
Inferior (N = 57)	244.4 (15.0)	240.0 (14.2)	0.439	135.9 (27.8)	140.6 (26.8)	0.322
Both (N = 44)	224.7 (21.7)	214.3 (18.7)	0.059	100.5 (28.1)	97.4 (30.6)	0.026

Table 4

	OCT Region	AROC superior	AROC Inferior	p-value
Sup. VF defect	Macula	0.66	0.72	0.006
(N = 112)	Peripapillary NFL	0.74	0.75	0.621
Inf. VF defect	Macula	0.69	0.73	0.116
(N = 101)	Peripapillary NFL	0.70	0.71	0.660

Table 5

Group	No. of eyes	Mean age (Years)	Mean IOP (mmHg)	Total macular volume (Cubic mm)	Average retinal thickness (Microns)	Mean macular thickness (Microns)
POAG Suspects	142	46.68 ± 12.24	18.36 ± 4.43	6.83 ± 0.58	94.55 ± 14.5	240.39 ± 14.04
POAG	148	52.66 ± 12.12	18.22 ± 4.74	6.35 ± 0.49	81.58 ± 20.13	224.23 ± 17.55

Diagnosis		N	Minimum	Maximum	Mean	Std. Deviation
POAG Suspect	Mean Macular thickness	142	211.40	300.00	240.39	14.0439
POAG	Mean Macular thickness	148	161.68	265.53	224.23	17.5551

Table 6

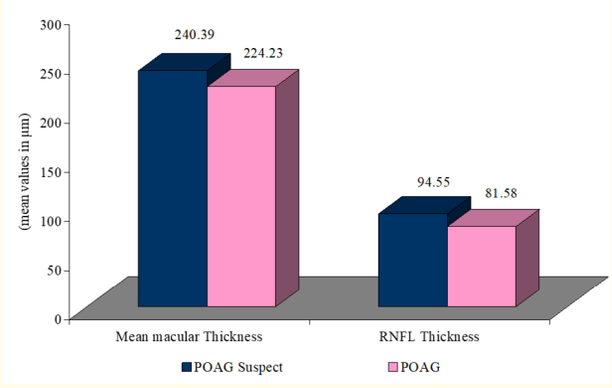

Figure 1

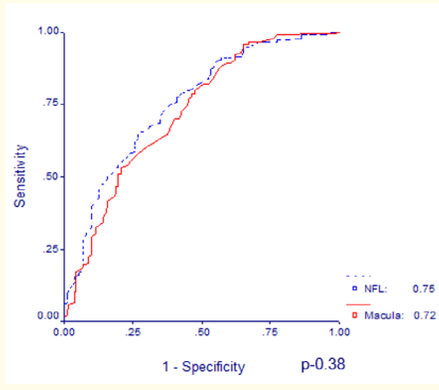

Figure 2

AROC curves

To evaluate the association between macular retinal and peripapillary NFL thickness with VF defect, AROC curves were calculated.

Area under the receiver operating characteristic (AROC) curves for optical coherence tomography inferior macular retinal and peripapillary (NFL) measurements for eyes with visual defects confined to the superior hemifield.

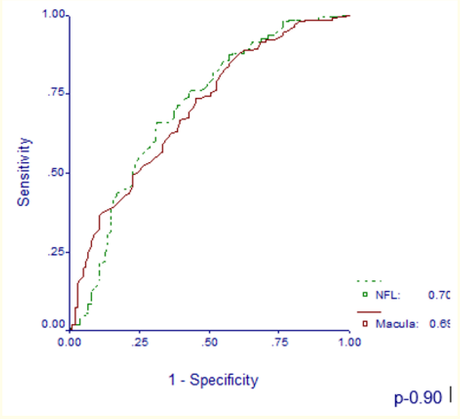

Figure 3

Area under the receiver operating characteristic (AROC) curves for optical coherence tomography superior macular retinal and peripapillary (NFL) measurements for eyes with visual defects confined to the inferior hemifield.

Discussion

This study is designed with the objective of analyzing the macular thickness and volume parameters in POAG Suspects and POAG patients to establish the structure functional relationship between OCT macular volume/thickness parameters in POAG Suspects and POAG patients.

The study compared the macular thickness with RNFL thickness in its association with the disease and found a positive correlation, hence this represent a surrogate indicator of retinal ganglion cell loss.

Areas under the receiver operator characteristics for macular thickness and peripapillary NFL thickness were studied and were found to be higher in areas corresponding to the VF defect location than the non-corresponding locations. Higher AROC values were found for areas that correspond to the location of the VF defect.

In our study, eyes with superior VF defects, the AROC values were significantly higher in the inferior retina than the superior for both macular retinal and peripapillary NFL measurements. Eyes with inferior VF defects, the difference in AROC's for corresponding and non-corresponding locations was not significant for macular retinal measurements but marginally significant for peripapillary NFL measurements. Comparing AROC's of macular and peripapillary NFL measurements at the same locations, the AROC for inferior peripapillary NFL was significantly higher compared to the inferior macular retinal measurements in patients with superior VF defects.

The RNFL thickness showed a slightly stronger relationship with the disease compared to the macular retinal thickness. But this finding may be due to under sampling of the tissue at risk, because only approximately 50% of the retinal ganglion cells are present in the macula, yet nearly 100% of the retinal ganglion cells are assessed in a peripapillary OCT NFL scan. Since glaucoma is a diffuse disease, the ability to measure the damage done by glaucoma in the entire eye may give peripapillary NFL assessment a distinct advantage over macular thickness evaluation in detecting glaucoma.

Another major advantage of the RNFL measurement over macular thickness measurement is the confounding of macular thickness measures by non-glaucomatous macular disease like diabetes and macular degenerations, directly affecting macular thickness and could obscure or exaggerate the abnormalities seen with glaucoma. These are not significant issues in peripapillary NFL assessment. This is not to say that macular thickness measurement may not be a useful parameter in the evaluation of glaucoma. It is significantly associated with the disease, and there may be fewer technical challenges in its measurement than in the quantification of peripapillary NFL thickness.

We found in this study that the OUTER RING macular thickness with our prototype OCT provided better correlation than did the INNER RING macular thickness in both the study groups. Thus, more peripheral areas of the macula showed a stronger association with glaucoma than did the more central macula. The study also showed that the inferior NFL was the parameter most strongly associated with glaucoma status. It is a well-known fact that optic nerve defects associated with glaucoma often occur initially at the inferior pole and that VF defects associated with glaucoma frequently manifest first in the superior VF, corresponding to the inferior pole defects.

Limitation of the Study

The limitation of the study is the lack of age matched controls from the normal population. It compares the pre-existing normative database of the machine in the presenting population of the clinic. So, a similar study with inclusion of normal population as age matched controls would possibly make the results more specific, classification of glaucoma suspects further into categories like ocular hypertension, glaucoma suspects and early glaucoma in subsequent trials in glaucoma diagnosis would make the use of OCT much more useful and rewarding for the present day ophthalmologists in treating the disease.

Conclusion

Macular retinal thickness as measured by OCT was capable of detecting glaucomatous damage and corresponded with peripapil-

lary NFL thickness. Glaucoma is a complex multifactorial disorder characterized by a typical pattern of optic nerve damage and visual field loss that is usually but not always associated with elevated IOP. Accepted parameters for monitoring glaucoma include descriptions and photography of the optic disc appearance, measurement of IOP, periodic threshold perimetry. Advances in posterior segment imaging technology provides a means for generating structural data useful in monitoring eyes with glaucomatous optic nerve damage. Objective, quantitative measurements of optic nerve and surrounding RNFL generated with these technologies correlate with known characteristics of optic disc function and visual function. Based on the findings we do not recommend the routine use of OCT macular scanning alone for glaucoma detection unless there are ocular pathologies that prevent scanning of the peripapillary region. Conversely, because macular retinal thickness corresponds well with peripapillary NFL thickness, macular scanning can provide a confirmation of abnormalities detected by peripapillary OCT scans, especially in subtle cases, particularly those with minimal or no perimetric findings, macular and peripapillary scans may reinforce each other in confirming the presence of early abnormalities.

The result of this report suggest that macular thickness measurements generated with OCT represent a neglected structural end point for glaucoma. Although glaucoma is an optic nerve disorder, the fundamental defining abnormality is localized at the level of the retinal ganglion cell. Glaucoma is known to cause loss of ganglion cells and their axons leading to a reduction in thickness of retinal ganglion cell thickness and could prove to have clinical value for glaucoma diagnosis and detection of change. Our results support this hypothesis and illustrate a significant correlation between macular thickness and two established indicators of glaucomatous damage- RNFL loss and visual field loss. We have found significant differences in mean macular thickness between POAG suspects and patients with established POAG using OCT. Furthermore, macular thickness and RNFL thickness assessments were strongly correlated with visual field global indices.

The study results support Zeimer., *et al*'s hypothesis that macular thickness is reduced in glaucoma. Conversely, we found that peripapillary NFL thickness is a more sensitive indicator of the presence or absence of glaucoma than was macular thickness. Nevertheless, macular thickness assessment clearly may have a role in the assessment and diagnosis of glaucoma.

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