

Correlation Of Visual Acuity With Macular Thickness In Early And Advanced Stages Of Primary Open Angle Glaucoma

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Abstract

Purpose: To evaluate association between visual acuity (VA) and macular thickness (MT) measured by Cirrus Optical Coherence Tomography (OCT) in patients of early and advanced stages of primary open angle glaucoma (POAG).

Material Method: A cross section observational study was conducted between 2016-2019. All POAG patients aged >40 years attending our hospital were study population. Uncorrected visual acuity (UCVA) and Best corrected Visual acuity (BCVA) was noted. Anterior and posterior segment assessment was done. Cirrus OCT was used to measure MT. POAG was grouped as early and advanced. P values < 0.05 was considered statistically significant.

Results: 155 patients were examined. 72 (46.5%) of them were in early POAG stage and rest 83 (53.5%) belonged to advanced stage. The mean age was 63.46 ± 8.5 years and Male patients were 91 (58.7%). Association of BCVA with stages of POAG was found to be statistically significant ($P < 0.001$) and it was worst in advance POAG. Association of mean MT with stages of POAG was statistically significant ($P < 0.001$) and it was less in advanced POAG. Range of mean deviation (MD) with stage of POAG was found to be statistically significant ($P < 0.001$). Association of MT with BCVA among overall study was reported to be statistically significant ($P = 0.006$). Association of MD with BCVA among overall study was statistically significant ($P < 0.001$).

Conclusion: Among POAG patients enrolled in the study an inverse correlation between BCVA & MT and BCVA & MD was observed. Level of correlation was mild and strong for MT and MD respectively. Correlation was found to be statistically significant.

Delhi J Ophthalmol 2021;31; 37-42; Doi <http://dx.doi.org/10.7869/djo.621>

Keywords : Primary open angle glaucoma; Visual acuity; Macular thickness; Optical coherence tomography.

Introduction

Glaucoma is the leading cause of irreversible blindness affecting 70 million people world wide.¹ It's grossly undiagnosed with only 50% to 90% people being aware of their condition.² As the population continues to age and average life expectancies increase, the prevalence of this debilitating disease will grow. Glaucoma is the most common cause of permanent vision loss in persons older than 40 years of age, after age-related macular degeneration.³

Glaucoma is a multifactorial, chronic progressive optic neuropathy characterized by loss of retinal ganglion cells (RGC), which leads to structural damage to the optic nerve head (ONH), retinal nerve fiber layer (RNFL), and consequent visual field defects.³ It can be broadly classified as open angle glaucoma and angle closure glaucoma. Open angle usually dominate with 86% of cases whereas angle Closure responsible for disproportionate number of cases with severe vision loss.⁴ Both open angle and angle closure can be primary or secondary due to other cause.⁵

Clinically glaucoma diagnosis is made by observing optic disc changes and by measurement of visual function with perimetry. Perimetry changes appear when nearly 40% RNFL is damaged.⁶ To detect pre-perimetric cases we have to focus on evaluation of RNFL and RGC changes. Peripapillary RNFL analysis is the most commonly used to diagnose glaucoma but suffer certain drawbacks related to

inter-patient variability in ONH morphology. To overcome some of these disadvantages, the macular thickness has been proposed as a means of glaucoma detection. Since 50% of RGCs are located in the macula, studying the thickness of macula and correlating it with visual acuity becomes important.⁷

Optical Coherence Tomography is a non-invasive, non-contact imaging modality that provides high-resolution cross-sectional imaging of ocular tissues. It uses Low coherence infrared light. OCT is highly reproducible, and is thus widely used as an adjunct in routine glaucoma patient management.⁸ Spectral-domain (SD) OCT (Cirrus Zeiss) allows for measurement of specific retinal layers implicated in the pathogenesis of glaucoma, namely: nerve fiber layer (RNFL), ganglion cell layer with inner plexiform layer (GCIPL), and ganglion cell complex (GCC) (composed of mNFL and GCIPL). Segmented analysis is purported to have better diagnostic ability for glaucoma than total retinal thickness, and may be comparable to RNFL thickness.

Macular Thickness does not change over time in healthy subjects and presence of reduced macular thickness suggests a strong possibility of pathology. Thus macular region is ideal for comparison with normative database. The structural and functional involvement of macula in all the stages of glaucoma has already been reported. Several studies indicate that there is decrease in MT and volume

among glaucomatous eyes. This is due to loss of RGCs and the finding correlates with RNFL thickness and visual field defect. VA assessment is important component of macular function test (MFT). Correlation between MT and VA plays important role in glaucoma monitoring and to achieve good quality of life.^{9,10}

Our study is an attempt to find association between VA and MT measured by Cirrus OCT in patients of early and late stages of POAG.

Materials And Methods

A cross section observational study was conducted in the department of Ophthalmology which is a tertiary care centre. The study was approved by ethical and academic research committee of our hospital. It adhered to the guidelines of the Declaration of Helsinki. The study was conducted between 2016 and 2019. The study population was glaucoma patients attending our ophthalmology department. Inclusion criteria was patients with early and advanced stages of POAG above the age of 40 years. Exclusion criteria was patients with any other ocular or systemic disease which could affect the retinal vasculature, media haze hindering visualization of fundus, high refractive error ($>\pm 6.00$ diopters [D] of spherical and $>\pm 3.00$ D of cylindrical error), macular pathology, previous incisional or laser surgery, pregnant or lactating woman, any other condition that could affect the accuracy of OCT or signal strength less than 8/10. A written and informed consent was taken. Participants were divided into two groups. Group-1 with early stage POAG in worse eye and Group-2 with advanced stage of POAG in worse eye.

Sample Size Calculation

The study conducted by Agrawal et al (2013) reported the prevalence of BCVA > 1.00 to be 0.04%.¹⁰ To achieve 95% confidence interval (CI), 80% power, 5% significance level and 10% margin of error we need a sample size of 154 participants. Therefore 155 subjects were proposed for this study.

The demographics information including, age, gender and residence were noted. The participants were asked about past history, personal history, medical and surgical history. A family history of glaucoma was also recorded. The visual status was recorded using a LogMAR chart held in a light

Table 1: Association of BCVA (LogMAR Scale) with Stage of POAG

SN	BCVA	Group-1 (Early POAG) (n=72)		Group 2 (Advance POAG) (n=83)		Total (n=155)	
		No	%	No	%	No	%
1	0-0.2	36	50.0	3	3.6	39	25.2
2	0.3-0.4	21	29.2	4	4.8	25	16.1
3	0.5-0.6	14	19.4	32	38.6	46	29.7
4	0.7-0.8	1	1.4	17	20.5	18	11.6
5	>0.8	0	0	27	32.5	27	17.4
		X ² =93.150 (df=3); p<0.001					

box at 6-meter distance from the participant. Presenting uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) was recorded for each eye in LogMAR notation. The anterior segment of the eye was assessed with slit lamp biomicroscopy (Topcon Corp., Tokyo, Japan). Applanation tonometry was used to measure intraocular pressure (IOP). The anterior chamber angle was evaluated using a two-mirror gonio lens (Volk Optical, Inc., Mentor, OH, USA). The central retina and other components of the posterior segment were evaluated using +90 D lens (Volk Optical, Inc., Mentor, OH, USA). Perimetry was conducted (SITA standard 30-2) by Humphrey Visual Field Analyser (Zeiss Model- 720i, Dublin, CA, USA). Pachymetry was also done by Oculus Pentacam (Model-70700, Wetzlar, Germany). SD-OCT (Cirrus Zeiss Meditec, Dublin, CA, USA) macular cube of 512 × 128 in 9 quadrants for each patient performed. An average of 9 readings were taken as the MT.

POAG patients were divided in early and advanced stages as per Hodapp-Parrish-Anderson (HPA) Glaucoma grading scale.^{11,12} Visual acuity was recorded as per WHO classification on Log MAR scale.

Statistical Analysis

Data was collected on pretested data collection form and then transferred to the spread sheet of Microsoft excel.[®] The data was exported to Statistical Package for Social Sciences (SPSS 21) (IBM, NY, USA) for further analysis. For qualitative variables, frequencies and percentage proportions were calculated. For quantitative variables, distribution curves were plotted. If the curves were normal, the mean and standard deviations were calculated. If the data were not normally distributed, the median and 25% quartiles were calculated. The 95% CI of the prevalence rate was calculated. For more than two independent variables in the subgroups, chi-square values, Student 't' test and ANOVA were used. P values less than 0.05 were considered statistically significant.

Results

One hundred fifty five patients were included in study. Seventy two (46.5%) of them were in early stage of POAG and rest 83(53.5%) belonged to advanced stage. The mean

Table 2: Macular Thickness and Mean Deviation with Stage of POAG

	Macular Thickness with Stage of POAG			Mean Deviation with Stage of POAG		
	Group-1	Group-2	Total	Group-1	Group-2	Total
Number	72	83	155	72	83	155
Min	221	215	215	-5.93	-27.57	-27.57
Max	294	289	294	-3.39	-12.21	-3.39
Median	273.00	243.00	263.00	-4.95	-20.73	-14.53
Mean	268.18	249.30	258.07	-5.00	-20.68	-13.40
S.D.	16.74	21.95	21.79	0.66	3.87	8.35
			't'=5.949; p<0.001			't'=33.912; p<0.001

age was 63.46 ± 8.5 years and male patients were 91 (58.7%). Male to female ratio was 1.42. Association of gender in both groups (early POAG & advanced POAG) was not found to be significant ($P=0.223$). Right eye involvement was more among both groups but it was not significant ($P=0.725$).

Association of BCVA with stages of POAG was found to be highly significant ($P<0.001$) and it was worst in advance POAG (Table-1). Association of mean MT with stages of POAG was statistically significant ($P<0.001$) but it was less in advanced POAG (Table-2). Difference of mean deviation (MD) with stage of POAG was found to be statistically significant ($P<0.001$) (Table-2). Association of MT with BCVA among overall study was reported to be statistically

significant ($P=0.006$) (Table-3). Association of MD with BCVA among overall study was statistically significant ($P<0.001$) (Table-3). Association of MT with different BCVA among early POAG ($P=0.543$) and advance POAG ($P=0.571$) was not significant (Table-4,5). Association of MD with different BCVA among early stage POAG patients was not found to be statistically significant ($P=0.419$) but among advanced stage POAG patients was found to be statistically significant ($P=0.027$).

Among overall POAG patients enrolled in the study an inverse correlation between BCVA & MT and BCVA & MD was observed. Level of correlation was mild and strong

Table 3: Macular thickness and Mean Deviation with BCVA among overall study population

BCVA LogMAR	Macular thickness with BCVA among overall study population					Mean Deviation with BCVA among overall study population				
	No	Min	Max	Mean	S.D.	No	Min	Max	Mean	S.D.
0-0.2	39	221	294	266.74	18.84	39	-22.25	-4.14	-5.95	3.45
0.3-0.4	25	225	286	264.16	17.87	25	-21.6	-3.39	-6.87	4.87
0.5-0.6	46	219	289	253.43	20.72	46	-26.27	-3.73	-16.05	7.81
0.7-0.8	18	215	289	253.33	27.92	18	-25.57	-5.78	-18.78	4.97
>0.8	27	217	288	250.96	22.18	27	-27.57	-12.34	-22.11	4.09
Total	155	215	294	258.07	21.79	155	-27.57	-3.39	-13.40	8.35
	'F'=3.730; p=0.006					'F'=49.678; p<0.001				

Table 4: Macular thickness and Mean Deviation with BCVA among early POAG (Group-1) patients

BCVA LogMAR	Macular thickness with BCVA among early POAG (Group-1) patients					Mean Deviation with BCVA among early POAG (Group-1) Patients				
	No	Min	Max	Mean	S.D.	No	Min	Max	Mean	S.D.
0-0.2	3	221	294	267.36	19.20	36	-5.93	-4.14	-5.03	0.63
0.3-0.4	21	225	286	266.00	17.15	21	-5.89	-3.39	-4.85	0.68
0.5-0.6	14	265	289	273.93	6.17	14	-5.72	-3.73	-5.10	0.69
0.7-0.8	1	263	263	263.00	.	1	-5.78	-5.78	-5.78	.
>0.8	0	0
Total	72	221	294	268.18	16.74	72	-5.93	-3.39	-5.00	0.66
	'F'=0.721; p=0.543					'F'=0.956; p=0.419				

Table 5: Macular thickness and Mean Deviation with BCVA among advance POAG (Group-2) patients

BCVA LogMAR	Macular thickness with BCVA among advance POAG (Group-2) patients					Mean Deviation with BCVA among advance POAG (Group-2) Patients				
	No	Min	Max	Mean	S.D.	No	Min	Max	Mean	S.D.
0-0.2	3	243	270	259.33	14.36	3	-22.25	-14.24	-17.01	4.54
0.3-0.4	4	237	281	254.50	21.11	4	-21.6	-14.57	-17.46	2.96
0.5-0.6	32	219	286	244.47	18.30	32	-26.27	-14.39	-20.83	3.25
0.7-0.8	17	215	289	252.76	28.67	17	-25.57	-12.21	-19.55	3.88
>0.8	27	217	288	250.96	22.18	27	-27.57	-12.34	-22.11	4.09
Total	83	215	289	249.30	21.95	83	-27.57	-12.21	-20.68	3.87
	'F'=0.735; p=0.571					'F'=2.910; p=0.027				

Table 6: Correlation of Macular Thickness and Mean Deviation with BCVA (LogMAR)

Variable	Pearson's Correlation Coefficient (r)	Level of Correlation	P value	Significance
Overall				
Macular Thickness	-0.30	Mild	<0.001	Very High
Mean Deviation	-0.75	Strong	<0.001	Very High
Early Stage POAG (Group-1)				
Macular Thickness	0.018	Weak/NO	0.881	Not Significant
Mean Deviation	-0.088	Weak/NO	0.461	Not Significant
Advanced Stage POAG (Group-2)				
Macular Thickness	0.038	Weak/NO	0.732	Not Significant
Mean Deviation	-0.252	Weak/NO	0.022	Significant

$$F = \frac{\text{Mean Of Sum of Between Differences}}{\text{Mean of Sum Of Within Group Differences}}$$

for MT and MD respectively. Correlation was found to be highly significant statistically. (Table-6)

On exploring the correlation separately in early stage POAG and advanced POAG patients, correlation was weak and statistically non-significant.

Discussion

This was a hospital based cross section observational study among >40 year old glaucoma patients. More than half of POAG patients were in advanced stage. Males were found to be more associated with POAG than females but it was not significant statistically. Laterality was more for right than for left among POAG but statistically insignificant. Among overall POAG patients enrolled in the study an inverse correlation between BCVA & MT and BCVA & MD was observed. Level of correlation was mild and strong for MT and MD respectively. Correlation was found to be highly significant statistically. On exploring the correlation separately in early stage POAG and advanced POAG patients, correlation were weak and statistically non-significant

The majority of cases in our study were in advanced stage of POAG (53.5%). Giovannini et al.¹³ also found higher advanced stages of POAG while Guedes et al.¹⁴ and Kim et al.¹⁵ reported more early stages. One reason for higher numbers of advanced stage glaucoma cases in present study could be lack of awareness and poor primary healthcare facilities owing to which most of the patients came to us in advanced stage of disease. The mean age reported in our study was 63.46 ± 8.5 year, quite similar to that reported by Arun et al.¹⁶ in hospital based study (64.14 year) while Vijaya et al.¹⁷ found less (59.85 year) in community based study.

It can be explained as many cases remain undiagnosed is reflected by younger age of patient in community based study while in general the age profile in present study was close to the affected population visiting a healthcare facility.

The current study found Male dominance (58.7%) but association of gender with both groups was not found to be significant. No gender predisposition to POAG has been reported in epidemiological studies. However some other reported male gender to be significantly associated with higher risk of glaucoma.^{18,19} In hospital based study male predominance is reported.²⁰ The gender profile of patients in present study was similar to that reported in hospital based study by Arun et al. (68.96%) male. The higher prevalence of male in present study not only indicates a higher prevalence of glaucoma among male but it could also be due to gender related differences in healthcare services utilization.

As far as side (right/left) is concerned, the present study found right eye to be more associated with glaucoma (52.9%) than left eye. As such there is no report suggesting higher risk of glaucoma to a particular side. We need more study to confirm this.

In present study the proportion of those having LogMAR value ≤ 0.6 was significantly higher in early stage POAG (98.6%) as compared to that in advanced stage POAG (47%). Visual impairment is an inherent character of glaucoma and is marked by advancement of glaucoma too. When we see overall range of visual acuity values in early and advanced stages of glaucoma, we found it to be quite diversified with adequate representation of different LogMAR value in our study. Compare to this, in a study of Agarwal et al. three BCVA categories were planned and in topmost category (LogMAR >1.0) there were only 4 (8%) cases while majority of patients had BCVA in a range of LogMAR 0.00-0.48. Compared to this, the distribution of LogMAR value in present study was quite balanced.

Average MT ranged from 215 μ to 294 μ (mean 258 μ) in our study. Mean MT of early POAG was significantly higher (268 μ) as compared to advanced stage of POAG (249 μ). These findings are in agreement with the observation made by Giovannini et al. in volumetric assessment of MT. Rao et al. and Karmout et al.²² also reported similar trend. The finding of present study also indicates that with advancement of glaucoma severity, there is significant decline in MT.

The range of MD with stage of POAG was statistically significant. The MD values were significantly higher (-20.68) in advanced stage POAG as compared to early stage POAG (-5.00). This relationship was obvious as the classification of severity of glaucoma was based on Visual Field MD value itself.

The MT was declining with increasing LogMAR BCVA value and it was statistically significant in present study. Mean MT with LogMAR BCVA 0-0.2 was 266.74μ, 0.5-0.6 was 253.43 μ and >0.8 was 250.96 μ. Similar trend was also reported by Agarwal et al. However the present study had more diverse range of LogMAR values, as we used five visual

acuity categories compared to three in Agarwal et al. and we had at least 18 cases in a single category thus was able to study the relationship in more diversified manner. Kim et al. found similar relation with declining in RNFL thickness and ganglion cell thickness with increasing LogMAR values. The present study showed a significant relationship between LogMAR BCVA and Visual Field (VF) MD. It was seen that with increasing BCVA the negative MD value increases significantly and this change was significant for almost all between visual acuity category comparisons. Similar result reported by Wilensky and Hawkins.²³ with contrast sensitivity and visual acuity. In our study with the help of MT measurement we also want to convey that ganglion cell damage in the macular layer is correlated with structural and functional changes in the form of visual field and visual acuity etc.

In present study we did not find a significant association between Visual field MD & BCVA LogMAR value and MT & BCVA LogMAR values when evaluated in a narrow range of BCVA between early stage and advanced stage. There could be two reasons for that, first while doing so, the range of BCVA categories became too narrow, secondly, the findings did not indicate a straight line correlation but indicate a curvilinear pattern, thus indicating that despite existence of a relationship between VF and structural changes, there is difference in time of manifestation of these changes. Kim et al. reported a curvilinear relationship between SD-OCT parameters and BCVA in open angle glaucoma. Our study reported mild linear correlation between BCVA and MT while evaluating the entire study groups. However on evaluating the same in early and advanced glaucoma separately, we failed to get significant correlation. Contrary to this Kim et al. found a curvilinear relationship between BCVA and SD-OCT parameters for severe glaucoma only. We need further study to explore it.

The relationship between MD and BCVA was significant as a whole but when we evaluated the same in early and advanced stages of glaucoma separately, we found it to be significant only in advanced stage of glaucoma. Wilensky and Howkins reported mild significant correlation between LogMAR BCVA and MD, however they did not explore this into different stages of glaucoma. Nevertheless, the trends in different studies indicate a significant relationship between various functional and structural parameters.

Conclusions

The study found that LogMAR BCVA, MD and MT depict a structural and functional relationship. LogMAR BCVA values show an association with both MD and MT. Similarly early and advanced stages of glaucoma were seen to be correlated with MD and MT, showing structural and functional deterioration with advancement of POAG. The findings of the study are interesting and corroborate the findings of some previous pilot study, However further studies in large and different groups of population are needed to strengthen the findings of our study.

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Cite This Article as: R.K. Chaurasia, Vidushi Kapil, Ziaul H Yasir Correlation Of Visual Acuity With Macular Thickness In Early And Advanced Stages Of Primary Open Angle Glaucoma *Delhi Journal Ophthalmology* 2020; 31 (3) 37-42

Acknowledgments: Nil

Conflict of interest: None declared

Source of Funding: None

Date of Submission: 30th August 2019

Date of acceptance: 22nd May 2020

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