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Original Research Article

Evaluation of Optic Nerve Head (ONH), Retinal Nerve Fibre (RNFL) Thickness and Ganglion Cell Complex (GCC) By Using OPTICAL COHERENCE TOMOGRAPHY (OCT) in Primary Open Angle Glaucoma, Glaucoma Suspects and Control Group

Dr. Anand Reddi¹, Dr. M.D. Priyanka², Dr. Manasa Bharanikana³, Dr. Raja Rajeswari Malladi⁴, Dr. Bhagavatula Venkata Sujatha Ratna Kumari⁵

 ¹Associate Professor, Department of Ophthalmology, NRIIMS, Sangivalasa, Visakhapatnam, Andhra Pradesh, India.
 ²Senior Resident, Department of Ophthalmology, S.V. Medical College, Tirupathi, Andhra Pradesh, India.
 ³Assistant Professor, Department of Ophthalmology, NRIIMS, Sangivalasa, Visakhapatnam, Andhra Pradesh, India.
 ⁴Professor, Department of Ophthalmology, NRIIMS, Sangivalasa, Visakhapatnam, Andhra Pradesh, India.
 ⁵Professor, Department of Ophthalmology, NRIIMS, Sangivalasa, Visakhapatnam, Andhra Pradesh, India.

Corresponding Author

Dr. M.D. Priyanka, Senior Resident, Department of Ophthalmology, S.V. Medical College, Tirupathi, Andhra Pradesh, India.

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ABSTRACT

Background

To evaluate and correlate the optic nerve head (ONH), retinal nerve fibre layer (RNFL) thickness and ganglion cell complex (GCC) by using OCT in Primary open angle glaucoma, glaucoma suspects and control group.

Methods

This was a prospective, non- randomized hospital based case control study which includes 90 patients who attended department of ophthalmology OPD, NRIIMS, Visakhapatnam. Among these subjects, 30 patients were diagnosed with POAG (primary open angle glaucoma), 30 patients were considered as glaucoma suspects and 30 control group patients were evaluated over a period of 18 months from January 2022 to June 2023 after obtaining clearance from institutional ethics committee and written informed consent from the study participants.

Result

The average age of POAG was 58.43 ± 9.34 , in glaucoma suspects was 55.43 ± 8.89 and control group in this study was 54.37 ± 9.06 . In POAG, 40.0% were females and 60.0% were males. In Glaucoma suspects, 46.7% were females and 53.3% were males. Control

group includes 50.0% females and 50.0% males. The optic disc parameters like cup area, rim area, C: D ratio between Control group, Suspect group and POAG group were statistically significant. The RNFL thickness in all quadrants and average RNFL thickness between Control group, Suspect group and POAG group were statistically significant. The GCC (Ganglion cell complex) which includes GCL++ and GCL+ between Control group, Suspect group and POAG were statistically significant. In Control group, the Optic nerve head and RNFL thickness was moderately correlated. In Suspects, the Optic nerve head and RNFL thickness shows small correlation. In POAG, the Optic nerve head and RNFL thickness in Control group, Suspect group and POAG were not statistically significant.

Conclusion

This study concludes that OCT can serve as a useful guideline in diagnosis, management, prognostication and research in glaucoma. Ganglion cell complex (GCC) is a promising factor to detect early structural changes in glaucoma suspects and to monitor the progression.

Keywords: optical coherence tomography, retinal nerve fibre layer, primary open angle glaucoma, ganglion cell complex, optic nerve head

INTRODUCTION

Glaucoma ranks as the second most prevalent cause of blindness worldwide¹, with primary open angle glaucoma's (POAG) comprising the majority of cases^{2,3}. POAG is characterized by progressive damage to retinal ganglion cells and their axons, resulting in neuroretinal rim thinning and visual field loss alongside an open iridocorneal angle⁴.

Glaucoma encompasses a spectrum of diseases marked by optic neuropathy and loss of retinal ganglion cells, leading to distinct alterations in the optic nerve and corresponding visual field (VF) defects on standard automated perimetry (SAP). Vision loss in glaucoma is typically irreversible and progressive, emphasizing the importance of early diagnosis and treatment in preserving visual function and preventing further deterioration. However, early diagnosis of glaucoma can be challenging as structural damage may precede detectable changes on SAP⁵. To address this challenge, various technologies such as optical coherence tomography (OCT), scanning laser topography, and scanning laser polarimetry have been utilized to provide objective and quantitative measurements of the retina, aiming to enhance diagnostic accuracy and reproducibility. Recent reviews have explored their applications in the diagnosis and management of glaucoma patients.⁶⁻⁸

Proper screening and effective treatment play crucial roles in early detection of glaucoma, mitigating significant visual impairment. Optic nerve head damage primarily attributed to reduce aqueous outflow rather than over production, is pivotal in glaucoma pathogenesis⁹. The loss of retinal nerve fiber layer and optic nerve head damage often correlates with visual field defects indicating the onset of open angle glaucoma. Notably, a substantial decline in ganglion cell number, up to 25 - 30% occurs prior to the manifestation of significant field defects underscoring the concept of pre-perimetric glaucoma.^{10,11,12}

The development of glaucoma primarily results from irreversible ganglion cell loss, distributed across three retinal layers: inner plexiform layer (IPL), ganglion cell

layer (GCL) and retinal nerve fibre layer (RNFL). These layers undergo characteristic alterations accompanying typical visual field defects^{13,14}. Optical Coherence Tomography serves as a non-invasive, non-contact tool for measuring RNFL and choroid thickness, facilitating early detection and monitoring of nerve fiber layer loss while quantifying RNFL thickness. A detailed assessment of the optic nerve head and RNFL thickness plays a pivotal role in identifying glaucoma and providing insights into the location and severity of visual field defects. OCT emerges as a cornerstone in glaucoma screening, particularly among high risk groups, aiding in timely identification and monitoring of progression.^{10,13,15}

AIMS AND OBJECTIVES

Aim

To evaluate and correlate the optic nerve head(ONH), retinal nerve fibre layer (RNFL) thickness and ganglion cell complex (GCC) by using OCT in Primary open angle glaucoma, glaucoma suspects and control group.

Objectives

- 1. Evaluation and association of optic nerve head, retinal nerve fiber layer thickness and ganglion cell complex among control group, glaucoma suspects and primary open angle glaucoma by using OCT.
- 2. Identification of early structural changes in glaucoma suspects.
- 3. Monitoring the advancement of glaucoma in early stages of POAG.

MATERIALS AND METHODS

This was a prospective, non- randomized hospital based case control study which includes 90 patients who were attending ophthalmology opd, NRI Institute of medical sciences, Sangivalasa, Visakhapatnam. Among these subjects, 30 patients were diagnosed with POAG (primary open angle glaucoma), 30 patients are considered as glaucoma suspects and 30 control group patients were evaluated over a period of 18 months.

All the patients who attended ophthalmology OPD underwent a detailed ocular examination which includes: (1). Snellen's visual acuity testing. (2). Refraction. (3). Evaluation of IOP by Goldmann's applanation tonometry. (4). Slit lamp examination of anterior segment. (5). Gonioscopy using 4 mirror gonio lens. (6). Direct ophthalmoscope, 78D, 90Dlens, Indirect ophthalmoscope. (7). Fundus photography. (8). 3D OCT (Optical coherence tomography) for detailed examination.

Inclusion criteria

Study subjects who are diagnosed with POAG, glaucoma suspects along with control group above the age of 40 years.

Exclusion criteria

a. Normotensive glaucoma. b. Angle closure glaucoma c. Secondary glaucoma's d. other Retinal pathologies e. Patients without compliance and not co-operative for the study.

All OCT scans were done after pupil dilatation. Protocols for scanning used in this study includes Fast optic disc and Fast RNFL Thickness.

Statistical methods

Descriptive statistical analysis has been done out in the current study. Results on continuous estimations are introduced on Mean \pm Standard deviation and results on categorical estimations are introduced in percentage (%).

RESULTS

The study and analysis of 90 patients taken in to consideration is as follows:

Table 1: Grouping of subjects based on age							
Age(in years)	POAG		GS		Control		
	Count	%	count	%	Count	%	
40 - 49	8	26.7%	11	36.7%	12	40.0%	
50 - 59	5	16.7%	10	33.3%	8	26.7%	
>/=60	17	56.7%	9	30.05	10	33.3%	
total	30	100%	30	100%	30	100%	
Mean +/- SD	58.43 ±	9.34	55.43 ± 8.89		$54.37~\pm~9.06$		
P value - 0.226							

In the current study, the mean age of POAG was 58.43 ± 9.34 , glaucoma suspects was 55.43 ± 8.89 and Controls was 54.37 ± 9.06 .

Table 2: Grouping of subjects based on gender						
CENDED	POAG		(GS	CONTROL	
GENDER	Count	%	Count	%	Count	%
FEMALE	12	40%	14	46.7%	15	50%
MALE	18	60%	16	53.3%	15	50%
TOTAL	30	100%	30	100%	30	100%
P VALUE – 0.731						

In POAG, 40.0% were females and 60.0% were males. In Glaucoma suspects, 46.7% were females and 53.3% were males. Control group includes 50.0% females and 50.0% males.

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Table 03: Differentiation of optic nerve head in control group, suspects and POAG							
	POAG		GS		CONTROL		P-VALUE
ODP	MEAN	SD	MEAN	SD	MEAN	SD	
$DA(mm^2)$	2.42	0.52	2.46	0.73	2.43	0.44	0.953
$CA (mm^2)$	1.88	0.71	1.46	0.83	1.17	0.51	0.001*
$RA (mm^2)$	0.54	0.44	1.00	0.28	1.20	0.43	0.000*
C/D RATIO	0.76	0.22	0.56	0.18	0.47	0.17	0.000*
CD RATIO	0.96	0.14	0.74	0.12	0.67	0.17	0.000*
HORIZONTAL	0.80	0.14	0.74	0.15	0.07	0.17	0.000
CD RATIO	0.86	0.16	0.72	0.13	0.65	0.16	0.000*
VERTICAL	0.80	0.10	0.72	0.15	0.05	0.10	0.000

The cup area, rim area, C:D ratio, C:D Horizontal and Vertical parameters are statistically significant to differentiate between POAG, suspects and control group.

Table 04: Differentiation of RNFL thickness among POAG, suspects and control							
group							
RNFL	POA	AG	GS		Con	D Value	
thickness	Mean	SD	Mean	SD	Mean	SD	r-value
Superior RNFL	78.70	31.63	104.07	29.69	128.47	16.75	0.000*
Inferior RNFL	71.97	34.37	111.73	26.24	133.70	17.07	0.000*
Temporal RNFL	48.53	17.02	57.50	11.22	67.90	12.14	0.000*
Nasal RNFL	60.43	21.95	77.47	14.98	83.13	14.16	0.000*
Average RNFL	65.50	18.37	87.67	13.95	103.27	9.73	0.000*

The thickness of RNFL was statistically significant in differentiating the progression of glaucoma in POAG, glaucoma suspects and control group. RNFL thickness also helps in differentiating between POAG and suspects and assessing the progression of disease

 Table 05: Comparison of GCL+ among POAG, suspects and control group

	Table v5: Comparison of GCL+ among POAG, suspects and control group								
GCL+ POAG GS Control	Control								
Count%Count%Count	%								
0 sector loss 2 6.7% 12 40% 28 9	3.3%								
1 sector loss 1 3.3% 5 16.7% 2 6	5.7%								
2 sector loss 0 0.0% 5 16.7% 0 0).0%								
3 sector loss 5 16.7% 2 6.7% 0 0).0%								
4 sector loss 3 10% 3 10% 0 0).0%								
5 sector loss 3 10% 2 6.7% 0 0).0%								
6 sector loss 16 53.3% 1 3.3% 0 0	0.0%								
Total 30 100% 30 100% 30 1	00%								
P - value = 0.000*									

About 93.3% of control group shows nil sector loss and 6.7% shows single sector loss. In suspect group, about 40.0% of patients shows nil sector loss. 33.4% of patients shows single and 2 sector loss. About 13.4% shows 3 and 5 sector loss.10.0% of patients shows 4 sector loss. Only a small proportion (3.3%) shows total sectoral loss. The sectoral loss in different quadrants has not progressed within 2years duration. In POAG group, about 53.3% shows 6 sector loss. 20% of patients shows 4 and 5 sector loss. 16.7% shows 3 sector loss. Only a small amount of population(10%)shows nil and single sector loss . The GCL+ shows statistical significance (P <0.05%) to differentiate between POAG, suspects and Controls group.

DISCUSSION

Glaucoma stands as a significant cause of irreversible and preventable visual impairment. Precise recognition of damage and timely treatment administration are crucial to prevent the onset of visual defects. Recent investigations employing optical imaging systems have highlighted the potential utility of RNFL thickness in the early diagnosis of glaucoma¹⁶. The loss of RNFL serves as a robust indicator of glaucomatous damage, occurring before quantifiable optic nerve head (ONH) and viaual field (VF) damage, sometimes up to six years before noticeable VF loss. Therefore, the utilization of OCT enhances the likelihood of detecting these abnormalities in regions of physiological reduced visibility. The diagnosis and monitoring of optic neuropathy due to glaucoma rely on the detection of disc and RNFL loss and their progression using precise and objective methos¹⁷.

The present study aims to evaluate optic nerve head, retinal nerve fiber layer thickness and ganglion cell complex among POAG, glaucoma suspects and control group using OCT. This examination involved assessing 90 patients based on various parameters and resulting outcomes.

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AGE GROUP

In the current study, there are 3 groups which include POAG, glaucoma suspects and control group. Among the POAG group, the majority (56.7%) were aged over 60 years, followed by 26.7% in the 40-49 age group and 16.7% in the 50-59 age group. In the glaucoma suspects group, the highest proportion (36.7%) fell in the 40-49 age range, followed by 50-59 years, with the smallest percentage (30%) being over 60 years old. Within the control group, most subjects were aged 40-49 years (40.0%) followed by those over 60 years (33.3%), and then 50-59 years (26.7%). The average age was 58.43 \pm 9.34 years in the POAG group, 55.43 \pm 8.89 years in the glaucoma suspects group, and 54.37 \pm 9.06 years in the control group.

Table no. 6: Association of average age with other studies							
Name of the study	Mean age						
	POAG	GS	CONTROLS				
CURRENT STUDY	58.43 ± 9.34	55.43 ± 8.89	54.37 ± 9.06				
Bharadwaj R et al ¹⁸		56.83 ± 4.76	55.43 ± 5.80				
Khan SF et al ¹⁹	61.09 ± 8.15		55.46 ± 8.51				
Myung Geun Choi et al ²⁰	54.4 ± 11.8		41.7 ± 6.5				

The mean age of POAG group in our study was similar to Myung Geun et al²⁰, the mean age of suspect group in our study was similar to Bharadwaj R^{18} study and the mean age in Khan SF^{19} study is higher when compared to the current study.

Gender distribution

The current study shows that the distributions of patients in POAG was 60.0% males and 40.0% females. In Glaucoma suspect group, 53.3% were males and 46.7% were females. In control group, 50.0% were males and 50.0% were females.

In the current study, there is male preponderance compared to females which was similar to other studies like Bharadwaj R¹⁸ and Khan SF¹⁹. The prevalence of POAG was more in male population compared to females. The reason for male preponderance in the current study was due to more attendance of males in opd in our hospital. Females attending opd was less due to lack of awareness. But in Myung Geun Choi²⁰ study, there is female preponderance compared to males.

Optic nerve head parameters

In the current study, among the optic nerve head parameters, the rim area in POAG group was 0.54 ± 0.44 (P value 0.000°), in suspects was 1.00 ± 0.28 , in control group was 1.20 ± 0.43 . The cup area in POAG was 1.88 ± 0.71 (P value 0.001°), in suspects was 1.46 ± 0.83 , in control group was 1.17 ± 0.51 . The CDR in POAG was 0.76 ± 0.22 , in suspect group was 0.56 ± 0.18 , in control group was 0.47 ± 0.17 . The Vertical C:D ratio was 0.86 ± 0.16 in POAG group, 0.72 ± 0.13 in suspect group and 0.65 ± 0.16 in control group. In Bharadwaj R et al study¹⁸, the vertical C: D ratio was 0.60 ± 0.11 in suspect group and 0.42 ± 0.04 in control group.

Myung Geun Choi et al²⁰ study shows that C: D ratio was 0.69 ± 0.18 in POAG and 0.29 ± 0.21 in control group.

Cup area in POAG and control group were 1.97 ± 0.67 and 0.76 ± 0.60 . Rim area was 0.81 ± 0.46 in POAG group and in control group was 1.72 ± 0.51 . The disc area was 2.78 ± 0.60 in POAG and 2.47 ± 0.41 in controls.

In Khan SF et al study¹⁹, the average CDR in suspects and in POAG was 0.38 ± 0.06 and 0.75 ± 0.09 .

Praveen kumar GS et al²¹ shows that disc area in POAG and suspect group was 2.82 ± 0.33 and 2.91 ± 0.43 . Rim area was 0.89 ± 0.29 in POAG and 1.27 ± 0.25 in suspects. The cup area was 1.92 ± 0.50 and 1.87 ± 0.51 , C: D ratio was 0.72 ± 0.12 and 0.62 ± 0.10 in POAG and suspect group.

Jakub J. Kaluzny et al²² shows that the disc area in controls, suspects and POAG group was 1.71, 1.73 and 1.70. The rim area was 1.19, 0.42 and 0.66. The cup area was 0.52, 0.55 and 1.03. The C: D ratio was 0.29, 0.39 and 0.60.

In the present study, the optic nerve head parameter like rim area (RA) among control group, POAG and suspects was lower when compared with other studies like Myung Geun Choi²⁰ and Praveen Kumar GS²¹. The cup area (CA) in POAG group in the current study was lower when compared to other studies mentioned above. The C:D ratio of controls and suspects in the present study was higher when compared with Myung Geun Choi²⁰ and Khan SF study¹⁹. The distribution of C:D ratio and the C:D ratio Horizontal among the three groups in the current study was slightly higher when compared to the other studies.

Retinal nerve fibre layer thickness

In the current study, the Superior RNFL thickness of POAG was lower when compared with Khan SF¹⁹ and higher in Myung Geun study²⁰. In controls and suspects, it is of lower value compared with others.

The inferior RNFL thickness distribution among the three groups in the present study was similar to other studies. But in Khan SF¹⁹, the values were lower compared to present study.

The distribution of Nasal RNFL thickness was higher in the present study when compared with other studies.

The Temporal RNFL thickness among three groups in the present study was similar with other studies, except in Myung Geun Choi et al²⁰ in which the temporal thickness was higher.

In MyungGeun Choi et al²⁰ study, the mean RNFL thickness among control and POAG group was 104.3 ± 10.7 and 101.4 ± 8.6 .

In Bharadwaj R et al¹⁸ study, the average RNFL thickness among suspect and control group was 84.13 ± 7.42 and 103.85 ± 8.95 .

Khan SF et al study¹⁹ shows that the mean RNFL thickness among control and POAG group was 91.91 ± 6.85 and 58.14 ± 15.76 .

In the present study, the distribution of mean RNFL thickness in POAG group in the current study was different compared to other studies. In suspects, the distribution was similar with the other studies. The mean RNFL thickness in control group was similar with other studies except in Khan SF et al¹⁹ study which shows a lower value.. This is mainly due to ethnic differences in study population and the size of study subjects which was larger in other studies compared to the present study. The duration of presentation differs among the present study with other studies.

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GCL+ Distribution

Out of total study population, about 53.3% of POAG group shows 6 sector (Total sectoral loss). 20% of study subjects shows 4 and 5 sector loss. 16.7% shows 3 sector loss. 6.7% show nil sector loss. Only a small amount of population (3.3%) shows single sector loss. In control group, there is nil sector loss in 93.3% of study subjects. About 6.7% shows single(1) sector loss This indicates that only a small amount. In glaucoma suspect group, about 40% shows nil sector loss. About 33.4% shows single and 2 sector loss. 13.4% shows 3 and 5 sector loss.10% of study subjects shows 4 sector loss. Only a small proportion of population (3.3%) shows 6 sector (Total sectoral) loss. This shows that the majority of subjects shows nil and single sector loss. Early detection of glaucoma can be possible with GCL+ assessment which is statistically significant in this study. Majority of population showed progression of GCL+ sector loss because in the present study regular follow up of suspect population was not done within the duration of study. Present study shows that GCL ++ (GCL +IPL+ mRNFL) and GCL+ (GCL+IPL) was a promising parameter to detect the early structural and functional loss in suspect and control population before RNFL changes. These parameters were found to be statistically significant (P<0.05) to compare between POAG, suspects and controls

In our study, the association of RNFL thickness with GCC sector loss was analysed under four categories in glaucoma suspect group.

Out of 30 glaucoma suspects, 13.4% shows normal GCL++ and GCL+ with normal retinal nerve fibre layer thickness.

16.6% shows abnormal GCL++ and GCL+ with abnormal retinal nerve fibre layer thickness which indicates that suspects had already progressed into glaucoma who needs vigorous treatment and initiation of neuroprotective agents.

56.6% shows abnormal GCL++ and GCL+ with normal RNFL thickness which indicates that all these patients needs regular follow-up to monitor the progression of disease.

13.4% shows normal GCL++ and GCL+ with abnormal RNFL thickness which indicates that risk factors like myopia associated with RNFL thinning in about 6.7% patients.

Mwanza et al²³ study shows that GCIPL diagnostic possibilities are between 0.918 and 0.956, and their values are comparable with the best diagnostic parameters—RNFL (between 0.933 and 0.939) and ONH parameters (0.910 and 0.962) without statistically significant difference between them.

Azusa A et al²⁴ study shows that GCL++ and GCC+ are statistically significant indicators to detect any early changes before RNFL changes.

Miftahul Akhyar L11 et al study shows that GCL++ Average in Controls and POAG was 107.23 ± 8.6 and 85.04 ± 15.05 (P value<0.0001) and GCL+ Average was 70.19 ± 5.56 and 58.63 ± 7.7 (P value<0.0001) which shows statistical significance similar to the present study.

Bhagat PR et al²⁵ shows that the mean macular GCC in POAG was 82.48 ± 13.21 , 79.80 ± 12.88 . In controls was 102.70 ± 7.19 , 101.82 ± 7.42 . This study detects pre-perimetric glaucoma and may show progression earlier than pRNFL in pre-perimetric glaucoma.

The present study shows that GCL++ and GCL+ are reliable and statistically significant indicators to detect any early changes in suspects before RNFL changes.

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Optic nerve head, RNFL thickness and GCL+

In Control group, the correlation between the inferior RNFL thickness and GCL+ was moderately significant (P=0.032). In suspects, the correlation between the inferior, average RNFL thickness and GCL+ was highly significant (P=0.000) The superior RNFL thickness and GCL+ was moderately significant (P=0.038). In POAG group, the correlation between the temporal RNFL thickness and GCL+ was highly significant (P=0.001). In the present study, the optic nerve head parameters association with retinal nerve fibre layer thickness and ganglion cell complex analysis shows that the GCC has reliable sensitivity to detect early changes. Rest of the parameters were not significantly correlated because of the small study population and the regular follow up of the study subjects was not done. Jin Wook J et al²⁶ study shows that the best parameter from the GCIPL generally had a higher sensitivity than those of the RNFL and ONH parameters with comparable specificity (P < 0.05.) Francesco O et al study45 shows that the RNFL parameters are still preferable to macular parameters for diagnosing manifest glaucoma, but the differences are small. The case control study suffers from limitation due to over estimation of accuracy. There are variations in the association of optic nerve head parameters, retinal nerve fibre layer thickness and ganglion cell complex in the present study compared with other studies 71 like Bharadwaj R¹⁸, Khan SF¹⁹, Jin Wook J²⁶ and Francesco O study²⁷ because of smaller study population, lack of consideration of risk factors, short duration of study and lack of regular follow up of study subjects.

LIMITATIONS OF THE STUDY

- The current study was limited to small cohort comprising primary open angle glaucoma, glaucoma suspects, and a control group.
- Being a single- centre study, the generalizability of the findings to the broader population is constrained.
- Larger randomized control trials and multicentre studies are warranted to validate the results.
- Lack of regular patient follow-up was a limitation in this study.
- Continuous patient monitoring is essential to track glaucoma progression and detect early glaucomatous changes.
- The study duration was relatively short compared to other studies.
- Prolonged study duration is necessary for comprehensive assessment and monitoring of disease progression.

CONCLUSION

This study underscores the critical importance of early detection and treatment of glaucoma, considering its prevalence, potential for early identification through proper screening, irreversible damage and a significant portion of patients presenting with advanced damage due to disease's silent nature.

In the evaluation of glaucoma, ganglion cell complex (GCC) analysis emerges as the most sensitive examination in the early stages, surpassing pRNFL statistically. In mild and moderate glaucoma stages, GCC and RNFL exhibit comparable performance in disease detection, with thinning thickness of pRNFL and GCC strongly correlating with glaucoma severity. Consequently, GCC and pRNFL are excellent parameters for monitoring glaucoma progression during these stages, highlighting OCT's pivotal role in

detecting glaucoma changes over time, aiding in management, prognostication and research endeavors.

Ultimately, OCT stands as a crucial tool for assessing glaucoma or other optic nerve affecting conditions, with GCC and RNFL correlations demonstrating superior efficacy in monitoring glaucoma progression and distinguishing it from othe optic nerve affecting diseases. The GCC emerges as a promising factor for early etection of structural changes in glaucoma suspects and for monitoring disease progression.

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