Original Article

Retinal nerve fiber layer and ganglion cell complex thickness analysis in patients having relative afferent pupillary defect

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Purpose: To determine the retinal nerve fiber layer (RNFL) thickness and ganglion cell complex (GCC) thickness in patients having relative afferent pupillary defect (RAPD) measured by optical coherence tomography (OCT). **Methods:** This cross-sectional study was conducted on 30 patients with posterior segment disease and glaucoma presenting with RAPD. The control group comprised 30 patients with the aforementioned diseases without RAPD. RAPD was graded using neutral density filters placed over the unaffected eye. Peripapillary RNFL thickness and macular GCC were measured using the Cirrus HD-OCT machine. **Results:** There were 45 males and 15 females. There was a statistically significant ($P < 0.05$) difference in the mean of average RNFL thickness in patients having RAPD (64.73 ± 15.16 µm in the affected eyes) as compared to sick control (82.73 ± 11.33 µm in the affected eyes). It was further observed that there was a decrease in RNFL thickness with advancing grades of RAPD. There was a statistically significant ($P < 0.05$) difference in the mean of average GCC thickness in patients having RAPD (51.57 ± 14.96 µm in the affected eyes) as compared to sick control (76.36 ± 8.06 µm in the affected eyes). **Conclusion:** Our study suggests that there is a significant reduction in RNFL thickness and GCC thickness in RAPD patients as compared to the sick control group.

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A relative afferent pupillary defect (RAPD) is a key sign of asymmetric or unilateral lesions of the anterior visual pathway. It can be observed in cases of asymmetrical retinal or optic nerve damage[1] and helps to quantify the loss of neuronal function.[2]

OCT provides high-resolution images of the retinal nerve fiber layer (RNFL), macular ganglion cell layer (GCL), and optic nerve head.[3] It enables imaging of the structural layers of the retina with an axial resolution of 10 µm.[4]

The aim of this study was to determine the RNFL thickness and GCC thickness in patients having RAPD as measured by OCT.

Methods

This cross-sectional hospital-based study was conducted during September 2019–December 2021 in 60 patients at a tertiary eye care center. The research obeyed the tenets of the Declaration of Helsinki. A well-informed written consent for conducting various tests was obtained from eligible patients participating in the study. Participants of age more than 18 years of age with good visual acuity were included in the study. Patients with any media opacity in which OCT cannot be done (dense corneal opacity, dense cataract, vitreous hemorrhage), very young or uncooperative patients, blind eye or very low visual acuity, and previous ocular surgery (especially of the posterior segment) were excluded from the study. The approval from institutional ethical committee of Jawaharlal Nehru Medical college was obtained on 21.12.2019.

Detailed history taking and ophthalmic evaluation were done. Best-corrected visual acuity was measured at a distance of 4 m by using standard ETDRS charts; intraocular pressure measurement was also done. All patients underwent meticulous slit-lamp and fundus examination by direct and indirect ophthalmoscopy and slit-lamp biomicroscopy by 90D lens.

They also underwent pupillary examination, and RAPD was quantified by performing swinging flashlight test by keeping neutral density (ND) filters before the less affected/normal eye according to previous reports.[4-7] It was performed in a dimly lit room. The swinging flashlight test was done and then RAPD was graded by placing the ND bar with increasing density in front of the normal/less affected eye and performing the swinging light test. The density of the ND filters was increased in a 0.3-log-unit stepwise manner until RAPD was undetectable.

OCT was performed using the Cirrus HD-OCT 5000 machine after pupillary dilatation. The procedure was explained to the

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patient beforehand. The average RNFL thickness of the entire circumference of the optic disc and quadrant-wise thicknesses were obtained and recorded. Macular GCC thickness was measured quadrant-wise. Scans that had signal strength less than 7 or had low analysis confidence were repeated until three optimal scans were obtained.

All tests, except OCT and indirect ophthalmoscopy, were performed on undilated pupils, and all tests were performed on the same day.

The patients were divided into two groups based on the presence or absence of relative afferent pupillary defect. The study group comprised 30 patients with glaucoma, optic nerve diseases, retinal vascular diseases (e.g., ischemic central retinal vein occlusion and branch retinal vein occlusion) presenting with RAPD. Although glaucoma is a bilateral disease, the eye having RAPD was taken as the affected eye and the eye without RAPD was taken as the fellow eye. The sick control group comprised 30 patients with glaucoma, retinal vascular diseases (e.g., non-ischemic central retinal vein occlusion, and Branch retinal vein occlusion) presenting without RAPD. In bilateral cases of glaucoma, the more affected eye presenting without RAPD was taken as the affected eye and the other eye not having RAPD was taken as the fellow eye. In the case of retinal diseases, the eye having the disease without RAPD was taken as the affected eye and the other eye not having RAPD was taken as the fellow eye.

Statistical analysis

Statistical analysis was performed using SPSS 21 (Statistical Package for the Social Sciences version 21) for Windows software (SPSS Inc., Chicago, Illinois, USA). Values were presented as mean ± SD for continuous variables and as numbers (percentages) for categorical variables. Independent sample *t* test was used for analyzing statistical significance of changes in variables within the groups and between the groups. Bivariate correlation was applied for analyzing the statistical significance of changes in RNFL thickness with grades of RAPD. ROC curves were used to assess the accuracy of the average RNFL and GCC thickness as a predictor of RAPD. $P < 0.05$ was taken as significant.

Results

A total of 60 patients were enrolled in this study. The mean age of the 30 RAPD patients (49.33 years; SD = 10.76) was similar to the mean age of 30 sick control subjects (52.43 years; SD = 10.32). There were 45 males (75%) and 15 female (25%) patients. There was no significant difference between any group with regard to age and gender distribution and thus were age- and gender-matched.

Out of the 30 patients in the study group, there were 13 patients with bilateral glaucoma (43.3%), eight patients with branch retinal vein occlusion (26.7%), five patients with ischemic central retinal vein occlusion (16.7%), three cases of optic neuritis (10%), and one case of pituitary tumor (3.3%).

Out of 30 patients included in the sick control group, there were 24 bilateral glaucoma patients (80%), four patients of branch retinal vein occlusion (13%), and two patients of non-ischemic central retinal vein occlusion (7%).

The RAPD range was between 0.3 and 1.2 log units, with a mean of 0.76 log units. Nine patients had a 0.3-log-unit RAPD, 10 patients had a 0.6-log-unit RAPD, and 11 patients had a 1.2-log-unit RAPD.

In the study group with RAPD, RNFL thickness of the affected eye was the least in the temporal quadrant, followed by nasal, inferior, and superior quadrants, and in the fellow eye, the RNFL thickness of the fellow eye was the least in the temporal quadrant, followed by nasal, superior, and inferior quadrants. This difference was found to be statistically significant in all quadrants except in the temporal quadrant, as shown in Table 1.

In sick control without RAPD, the RNFL thickness of the affected eye was the least in the temporal quadrant, followed by nasal, superior, and inferior quadrants, and in the fellow eye, RNFL thickness of the fellow eye was the least in the temporal quadrant, followed by nasal, inferior, and superior quadrants. RNFL thickness was slightly less in the affected eye as compared to the fellow eye, and this difference was found to be statistically insignificant, as shown in Table 2.

The mean of average RNFL thickness was 82.73 ± 11.33 μm in the affected eyes of the sick control group without RAPD and 64.73 ± 15.16 μm in the affected eyes of the study group with RAPD. On comparing RNFL thickness between the affected eye in the study group with RAPD and the sick control group without RAPD, it was observed that the thickness was markedly

Table 1: Statistical analysis of comparison of RNFL thickness in both the eyes of the study group with RAPD

Variables	Affected eye (μm)	Fellow eye (μm)	Difference (μm)	*P*
Average RNFL thickness	64.73±15.16	84.53±12.27	19.80	<0.001
Superior quadrant	74.37±26.90	104.46±18.08	30.09	<0.001
Inferior quadrant	74.10±26.90	106.93±18.30	32.83	<0.001
Temporal quadrant	53.50±18.81	59.06±8.74	5.56	0.167
Nasal quadrant	56.63±13.94	66.03±10.88	9.40	0.003

Table 2: Statistical analysis of comparison of RNFL thickness in both eyes of the sick control group without RAPD

Variables	Affected eye (μm)	Fellow eye (μm)	Difference (μm)	*P*
Average RNFL thickness	82.73±11.33	83.53±10.64	0.80	0.779
Superior quadrant	101.53±15.15	106.53±13.75	5.0	0.186
Inferior quadrant	103.43±22.49	103.36±21.32	0.07	0.991
Temporal quadrant	58.23±8.58	56.83±9.41	1.40	0.549
Nasal quadrant	67.90±10.80	67.53±10.70	0.37	0.895

reduced in all quadrants in the study group. The difference was maximum in the inferior quadrant, followed by superior, nasal, and temporal quadrants in descending order, and this difference was found to be statistically significant ($P < 0.001$), as shown in Table 3.

Association between grades of RAPD and RNFL thickness

- Bivariate correlation was applied between the various grades of RAPD and the average RNFL thickness difference between affected and fellow eye in study group with RAPD. A weak positive but statistically insignificant correlation was found between RAPD grades and RNFL thickness difference interpretation (Pearson's correlation coefficient = 0.239; $P = 0.203$). It was found that an increase in RNFL thickness difference between affected and fellow eye was associated with higher grades of RAPD.
- Bivariate correlation was applied between the various grades of RAPD and the average RNFL thickness ratio between affected and fellow eye in study group with RAPD. A weak negative but statistically insignificant correlation was found between RAPD grades and RNFL thickness ratio interpretation (Pearson's correlation coefficient = −0.191; $P = 0.311$). It was found that a decrease in RNFL thickness ratio between affected and fellow eye was associated with higher grades of RAPD.

ROC curves were used to assess the accuracy of the average RNFL thickness as a predictor of RAPD. Significant values for the area under the ROC (AUROC) curve were 0.86 (95% confidence interval: 0.761–0.956, $P < 0.001$) [Fig. 1]. When RNFL thickness was reduced to 79.5 µm, the sensitivity and specificity of the presence of RAPD were 83.3% and 80%, respectively.

In the study group with RAPD, the GCC thickness of the affected eye was the least in the inferior quadrant, followed by inferonasal, superotemporal, inferotemporal, superonasal, and superior quadrants, and in the fellow eye, the GCC thickness was the least in the inferotemporal quadrant, followed by superonasal, superior, superotemporal, inferior, and inferonasal quadrants. This difference was found to be statistically significant as shown in Table 4.

In the sick control group without RAPD, the GCC thickness of the affected eye was the least in the inferotemporal quadrant, followed by inferior, superotemporal, inferonasal, superior, and superonasal quadrants, and in the fellow eye, the GCC thickness of the fellow eye was the least in the inferotemporal quadrant, followed by superotemporal, inferior, superior, inferonasal, and superonasal quadrants. GCC thickness was slightly less in the affected eye as compared to the fellow eye, and this difference was found to be statistically insignificant, as shown in Table 5.

The mean of the average GCC thickness was 76.36 ± 8.06 µm in the affected eyes of the sick control group without RAPD and 51.57 ± 14.96 µm in the affected eyes of the study group with RAPD. On comparing GCC thickness between the affected eye in the study group with RAPD and the sick control group without RAPD, it was observed that the thickness was markedly reduced in all quadrants in the study group. The difference was the highest in the inferonasal quadrant followed by superonasal, inferior, superotemporal, superior, and inferotemporal quadrants in descending order. This difference was found to be statistically significant ($P < 0.001$), as shown in Table 6.

ROC curves were used to assess the accuracy of the average GCC thickness as a predictor of RAPD. Significant values for the area under the ROC (AUROC) curve were 0.90 (95% confidence interval: 0.823–0.980, $P < 0.001$) [Fig. 2]. When GCC thickness was reduced to 68.5 µm, the sensitivity and specificity of the presence of RAPD were 83.3% and 76.7%, respectively.

Discussion

RAPD represents the relative asymmetry of afferent input to the pupillomotor center of the brain. It is an important parameter

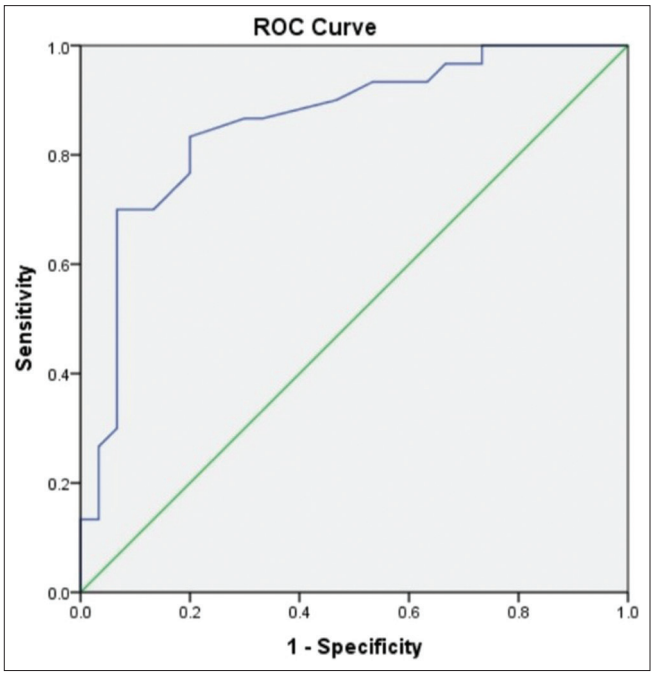

Figure 1: ROC curve for average RNFL thickness for study group with RAPD

Table 3: Statistical analysis of comparison of RNFL thickness between the affected eyes of the study group with RAPD and sick control group without RAPD

Variables	Affected eye of the study group (µm)	Affected eye of the sick control group (µm)	Difference (µm)	*P*
Average RNFL thickness	64.73±15.16	82.73±11.33	18.00	<0.001
Superior quadrant	74.37±26.9	101.53±15.15	27.16	<0.001
Inferior quadrant	74.10±26.90	103.43±22.49	29.33	<0.001
Temporal quadrant	53.50±18.81	58.23±8.57	4.73	<0.001
Nasal quadrant	56.63±13.94	67.90±10.80	11.27	<0.001

Table 4: Statistical analysis of comparison of GCC thickness in the affected and fellow eyes of the study group with RAPD

Variables	Affected eye of the study group (μm)	Fellow eye of the study group (μm)	Difference (μm)	*P*
Average GCC thickness	51.57±14.96	73.20±8.29	21.63	<0.001
Superior quadrant	55.30±19.28	72.97±11.21	17.67	<0.001
Superotemporal quadrant	51.13±16.98	73.10±11.69	21.97	<0.001
Superonasal quadrant	52.67±20.13	72.33±11.02	19.66	<0.001
Inferior quadrant	47.40±19.24	73.90±8.56	26.50	<0.001
Inferotemporal quadrant	52.57±17.45	72.10±15.11	19.53	<0.001
Inferonasal quadrant	50.03±18.10	74.50±8.64	24.20	<0.001

Table 5: Statistical analysis of comparison of GCC thickness in both eyes of the sick control group without RAPD

Variables	Affected eye (μm)	Fellow eye (μm)	Difference (μm)	*P*
Average GCC thickness	76.36±8.06	79.54±4.649	3.18	0.068
Superior quadrant	78.03±7.52	79.03±5.301	1.00	0.554
Superotemporal quadrant	76.26±6.49	78.47±4.804	2.21	0.142
Superonasal quadrant	79.30±9.06	80.43±5.799	1.13	0.567
Inferior quadrant	73.93±11.66	78.63±5.702	4.70	0.054
Inferotemporal quadrant	73.90±11.03	78.17±5.433	4.27	0.064
Inferonasal quadrant	76.93±8.96	79.96±5.99	6.04	0.130

for quantifying the loss of neuronal function in an asymmetric optic nerve disease.

In our study, it was found that the mean of the average RNFL thickness was 82.73 ± 11.33 μm in the affected eyes of the sick control group without RAPD and 64.73 ± 15.16 μm in the affected eyes of the study group with RAPD. On comparing RNFL thickness between the affected eye in the study group with RAPD and the sick control group without RAPD, it was observed that the thickness was markedly reduced in all quadrants in the study group with RAPD. The difference was the highest in the inferior quadrant, followed by superior, nasal, and temporal quadrants in descending order, and this difference was found to be statistically significant ($P < 0.001$).

In the study group with RAPD, it was found that the RNFL thickness of the affected eye was least in the temporal quadrant, followed by nasal, inferior, and superior quadrants, and in the fellow eye, it was the least in the temporal quadrant, followed by nasal, superior, and inferior quadrants.

In the present study, the RNFL thickness in the affected eyes was found to be less when compared to the fellow eye in average thickness and in all the four quadrants in the study group with RAPD, and this difference was found to be statistically significant in all quadrants except in the temporal quadrant.

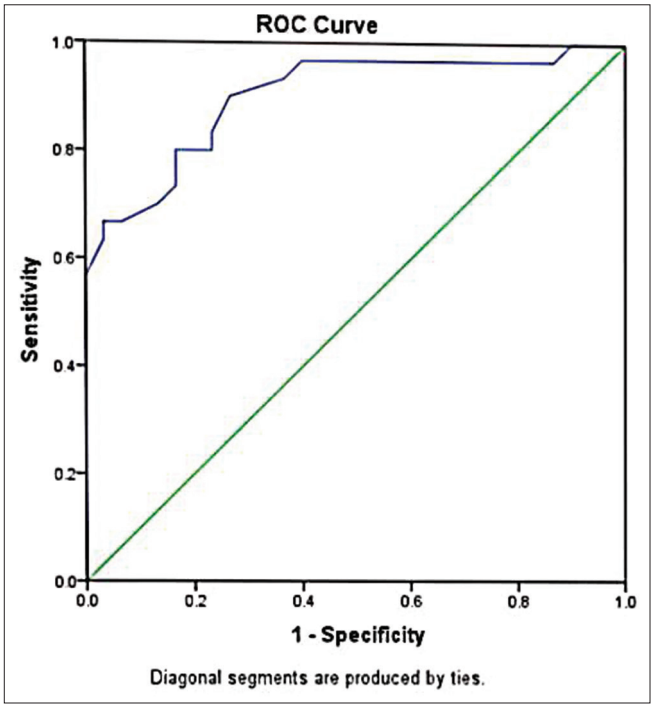

Figure 2: ROC curve for average GCC thickness for study group with RAPD

In the sick control group without RAPD, the RNFL thickness in the affected eye was found to be the least in the temporal quadrant, followed by nasal, superior, and inferior quadrants, and in the fellow eye, it was the least in the temporal quadrant, followed by nasal, inferior, and superior quadrants.

In the present study, RNFL thickness was slightly less in the affected eye as compared to the fellow eye in average thickness and in all the four quadrants in the sick control group without RAPD, and this difference was found to be statistically insignificant.

Chew *et al*.[8] conducted a study on 50 glaucoma patients, out of which 25 were having RAPD and 25 without RAPD, to assess the RNFL thickness reduction necessary for RAPD to manifest in patients of glaucoma. They reported that the mean RNFL thickness in both eyes in the RAPD group (67.8 ± 10.7 μm) was significantly lower than that in the control group (92.3 ± 15.3 μm). Significant differences in RNFL thickness ($P < 0.0001$) were found between control and RAPD patients. The study reported that a decrease in RNFL thickness

Table 6: Statistical analysis of comparison of GCC thickness between affected eyes of the study group with RAPD and sick control group without RAPD

Variables	Affected eye of group A (μm)	Affected eye of group B (μm)	Difference (μm)	*P*
Average GCC thickness	51.57±14.96	76.36±8.06	24.79	<0.001
Superior quadrant	55.30±19.28	78.03±7.52	22.73	<0.001
Superotemporal quadrant	51.13±16.98	76.26±6.49	25.13	<0.001
Superonasal quadrant	52.67±20.13	79.30±9.06	26.63	<0.001
Inferior quadrant	47.40±19.24	73.93±11.66	26.53	<0.001
Inferotemporal quadrant	52.57±17.45	73.90±11.03	21.33	<0.001
Inferonasal quadrant	50.03±18.10	76.93±8.96	26.90	<0.001

to 83% of that in the other eye, which equates to a 17% loss in RNFL thickness, produced an RAPD in the thinner eye that was detectable by using the swinging-flashlight test.

Greenfield *et al*.[9] conducted a study to correlate macular thickness and retinal nerve fiber layer thickness in normal and glaucomatous eyes using OCT. They took 59 patients, out of which 29 were normal and 30 had glaucoma. All eyes having glaucoma had associated visual field loss. The mean RNFL thickness in the affected quadrant (89 ± 53 μm) was significantly lower ($P = 0.009$) than in the unaffected quadrant (121 ± 39 μm). They concluded that macular thickness changes correlate with changes in visual function and RNFL thickness in glaucoma and this is a surrogate marker of retinal ganglion cell loss.

In our study, a weak positive but statistically insignificant correlation was found between RAPD grades and RNFL thickness difference between affected and fellow eyes in the study group with RAPD (Pearson's correlation coefficient = 0.239; $P = 0.203$). It was found that an increase in RNFL thickness difference between affected and fellow eyes was associated with higher grades of RAPD. A weak negative but statistically insignificant correlation existed between RAPD grades and RNFL thickness ratio between affected and fellow eyes in the study group with RAPD (Pearson's correlation coefficient = −0.191; $P = 0.311$). It was found that a decrease in RNFL thickness ratio between affected and fellow eyes was associated with higher grades of RAPD.

Nakanishi *et al*.[4] conducted a study to find out the correlation between the amount of RNFL thickness reduction and the depth of a clinically detectable RAPD in patients with unilateral optic atrophy. They took 20 eyes of 20 patients (ten male and ten female) with unilateral optic atrophy of various etiologies. They used linear regression analysis to find the correlation between RAPD and the ratio of affected to unaffected average RNFL thickness which revealed a correlation coefficient $R^2 = 0.48$ ($P = 0.0007$). They reported that RAPD was not clinically detected until at least approximately 25% of the retinal nerve fibers were lost when compared with the unaffected eyes.

Younis and Eggenberger[10] conducted a study to evaluate the relationship between RAPD and RNFL thickness assessed by OCT in patients with unilateral or asymmetric demyelinating optic neuropathy. They took 72 patients with this disease and concluded that the size of RAPD correlated with both the difference in RNFL thickness and the ratio of the RNFL thickness in the fellow eyes to the more affected eyes and in all quadrants.

Tatsumi *et al*.[11] conducted a study on 29 consecutive glaucoma patients to estimate the relationship between the depth of clinically detectable RAPD and the reduction ratio of retinal nerve fiber layer thickness in the more advanced eyes relative to that in the contralateral less advanced eyes in patients having asymmetrical glaucomatous optic neuropathy. They concluded that when RAPD was clinically detected, the RNFL thickness in the more advanced eyes decreased to approximately 73% of that in the less advanced. Besada *et al*.[12] conducted a study to investigate the correlation between the RAPD and RNFL thickness loss in patients with asymmetric optic neuropathy. They included 33 subjects with glaucoma and eight subjects with optic neuropathy. They obtained significant correlations ($P < 0.02$) for the RAPD and the percentage difference loss of the RNFL thickness parameter. At a 0.6-log-unit RAPD, the average mean percentage difference loss was 23% for the circumpapillary RNFL thickness. They reported that significant correlations exist between RNFL thickness loss for circumpapillary RNFL thickness and peripheral circumpapillary RNFL thickness and RAPD.

In our study, it was found that the mean of the average GCC thickness was 76.36 ± 8.06 μm in the affected eyes of the sick control group without RAPD and 51.57 ± 14.96 μm in the affected eyes of the study group with RAPD.

On comparing GCC thickness between the affected eyes in the study group with RAPD and sick control group without RAPD, it was observed that the thickness was markedly reduced in all quadrants in the study group with RAPD. The difference was the highest in the inferonasal quadrant, followed by superonasal, inferior, superotemporal, superior, and inferotemporal quadrants in descending order. This difference was found to be statistically significant ($P < 0.001$).

In the sick control group without RAPD, it was found that the GCC thickness of the affected eye was the least in the inferotemporal quadrant, followed by inferior, superotemporal, inferonasal, superior, and superonasal quadrants, and the in the fellow eye, it was the least in the inferotemporal quadrant, followed by superotemporal, inferior, superior, inferonasal, and superonasal quadrants. This difference was found to be statistically insignificant.

Bhagat *et al*.[13] conducted a study to determine the importance of ganglion cell complex (GCC) analysis as a parameter for early diagnosis of glaucoma and for following glaucoma progression and to compare glaucoma progression with conventional visual field analysis using OCT. They

reported that the average GCC thickness was the highest in the normal study group with RAPD, and the thickness decreased as the severity of glaucoma increased.

Gracitelli *et al*.[14] conducted a study to examine the relationship between RAPD and macular structural damage measured by macular ganglion cell inner plexiform layer thickness. They observed a correlation between the RAPD score and asymmetric macular structural damage ($P < 0.001$).

Besada *et al*.[12] conducted a study to investigate and compare the correlation of the RAPD with GCC in contrast to RNFL thickness parameters in patients with asymmetric optic neuropathy. They included 33 subjects with glaucoma and eight subjects with optic neuropathy. They obtained significant correlations ($P < 0.02$) for the RAPD and the percentage difference loss of the GCC and RNFLT parameters. The grouped mean percentage difference loss for RNFLT was significantly different from that of the GCC ($P < 0.001$). They reported that significant correlations exist between GCC and RAPD.

There are some limitations to our study: the sample size was small, a disease-specific relationship between RAPD and RNFL thickness reduction should be carried out to find the exact correlation, and this should be a large-scale community-based study rather than a hospital-based study to involve more number of participants and validate the findings.

Conclusion

In conclusion, our study suggests that there is a significant reduction in RNFL and GCC thickness in RAPD patients as compared to the sick control group not having RAPD. RNFL thickness decreased with the advancing grades of RAPD.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Kalaboukhova L, Fridhammar V, Lindblom B. Relative afferent pupillary defect in glaucoma: A pupillometric study. Acta Ophthalmol Scand 2007;85:519-25.
2. Lagreze WD, Kardon RH. Correlation of relative afferent pupillary defect and estimated retinal ganglion cell loss. Graefes Arch Clin Exp Ophthalmol 1998;236:401-4.
3. Rebolleda G, Diez-Alvarez L, Casado A, Sánchez-Sánchez C, de Dompablo E, González-López JJ, *et al*. OCT: New perspectives in neuro-ophthalmology. Saudi J Ophthalmol 2015;29:9-25.
4. Nakanishi Y, Nakamura M, Tatsumi Y, Nagai-Kusuhara A, Negi A. Quantification of retinal nerve fibre layer thickness reduction associated with a relative afferent pupillary defect. Graefes Arch Clin Exp Ophthalmol 2006;244:1480-4.
5. Digre KB. Principles and techniques of examination of the pupils, accommodation, and lacrimation. In: Miller NR, Newman NJ, editors. Walsh and Hoyt's Clinical Neuro-Ophthalmology. 6th ed. Baltimore: Lippincott Williams & Wilkins; 2005. p. 715-37.
6. Kaback MB, Burde RM, Becker B. Relative afferent pupillary defect in glaucoma. Am J Ophthalmol 1976;81:462-8.
7. Brown RH, Zilis JD, Lynch MG, Sanborn GE. The afferent pupillary defect in asymmetric glaucoma. Arch Ophthalmol 1987;105:1540-3.
8. Chew SS, Cunnningham WJ, Gamble GD, Danesh-Meyer HV. Retinal nerve fibre layer loss in glaucoma patients with a relative afferent pupillary defect. Invest Ophthalmol Vis Sci 2010;51:5049-53.
9. Greenfield DS, Bagga H, Knighton RW. Macular thickness changes in glaucomatous optic neuropathy detected using optical coherence tomography. Invest Ophthalmol Vis Sci 2002;43:931.
10. Younis AA, Eggenberger ER. Correlation of relative afferent pupillary defect and retinal nerve fibre layer loss in unilateral or asymmetric demyelinating optic neuropathy. Invest Ophthalmol Vis Sci 2010;51:4013-6.
11. Tatsumi Y, Nakamura M, Fujioka M, Nakanishi Y, Kusuhara A, Maeda H, *et al*. Quantification of retinal nerve fibre layer thickness reduction associated with a relative afferent pupillary defect in asymmetric glaucoma. Br J Ophthalmol 2007;91:633-7.
12. Besada E, Frauens BJ, Makhlouf R, Shechtman D, Rodman J, Demeritt M, *et al*. More sensitive correlation of afferent pupillary defect with ganglion cell complex. J Optom 2018;11:75-85.
13. Bhagat PR, Deshpande KV, Natu B. Utility of ganglion cell complex analysis in early diagnosis and monitoring of glaucoma using a different spectral domain optical coherence tomography. J Curr Glaucoma Pract 2014;8:101-6.
14. . Gracitelli CP, Tatham AJ, Zangwill LM, Weinreb RN, Abe RY, Diniz-Filho A, *et al*. Asymmetric macular structural damage is associated with relative afferent pupillary defects in patients with glaucoma. Invest Ophthalmol Vis Sci 2016;57:1738-46.