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ASSOCIATION OF RETINAL NEURODEGENERATION ON OPTICAL COHERENCE TOMOGRAPHY WITH PARKINSON'S DISEASE: AN OBSERVATIONAL STUDY

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Abstract

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder associated with motor and non-motor symptoms. Retinal nerve fiber layer (RNFL) thinning has been suggested as a potential biomarker for PD, but its diagnostic utility remains uncertain. This study aims to compare RNFL thickness in PD patients and healthy controls and explore correlations with disease severity, visual function, and comorbid conditions.

Material and Methods: A comparative cross-sectional study was conducted, including 80 PD patients and 80 healthy controls. Demographic and clinical characteristics were recorded. Optical coherence tomography (OCT) was used to measure RNFL thickness in the superior, inferior, nasal, and temporal quadrants. Pearson's correlation was used to assess the relationship between RNFL thickness, disease severity, and visual function parameters. The diagnostic value of RNFL thinning was analyzed using receiver operating characteristic (ROC) curves.

Results: PD patients exhibited significantly reduced RNFL thickness compared to controls across all quadrants ($p < 0.05$), with the most pronounced thinning in the inferior (-11.4 µm, $p = 0.0008$) and nasal (-7.4 µm, $p = 0.0021$) quadrants. Inferior and nasal quadrant thinning correlated significantly with disease severity ($r = 0.305$, $p = 0.018$; $r = 0.478$, $p = 0.0009$, respectively). Patients with diabetes and hypertension had greater RNFL thinning than those without comorbidities. The ROC curve analysis showed limited diagnostic value for RNFL thickness alone (AUC = 0.12). No significant correlations were found between RNFL thickness and visual function parameters.

Conclusion: RNFL thickness is significantly reduced in PD patients, with inferior and nasal quadrants showing the most pronounced thinning. RNFL thinning correlates with disease severity but has limited diagnostic value as a standalone biomarker. Comorbid conditions further exacerbate RNFL loss. Future studies should explore multimodal imaging approaches to improve early diagnosis and disease monitoring.

Keywords: Parkinson's disease, retinal nerve fiber layer, optical coherence tomography, neurodegeneration, biomarker

INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder that primarily affects motor function due to the loss of dopaminergic neurons in the substantia nigra of the midbrain. This neuronal loss leads to classical motor symptoms, including bradykinesia, rigidity, resting tremor, and postural instability (1). However, beyond motor impairment, PD is increasingly recognized as a multisystem disorder with non-motor manifestations such as cognitive decline, sleep disturbances, depression, and autonomic dysfunction (2). Among these, emerging evidence suggests that PD is also associated with neurodegeneration in the retina, a component of the central nervous system (CNS) that shares embryological and physiological similarities with the brain (3).

The retina contains dopaminergic amacrine cells, which play a crucial role in modulating visual processing. Given that dopamine deficiency is a hallmark of PD, retinal alterations could be indicative of underlying neurodegenerative changes (4). Optical Coherence Tomography (OCT), a non-invasive, high-resolution imaging modality, has gained significant attention for its potential in detecting retinal changes in neurodegenerative diseases, including PD (5). Studies utilizing OCT have reported thinning of the retinal nerve fiber layer (RNFL) and alterations in the ganglion cell complex (GCC) in PD patients compared to healthy controls, suggesting that retinal neurodegeneration may serve as a potential biomarker for disease progression and severity (6,7).

Despite these findings, there is considerable variability in the literature regarding which retinal layers are most affected in PD and how these changes correlate with disease severity. Some studies have reported significant RNFL thinning, particularly in the temporal and superior quadrants (Schneider et al., 2020), whereas others emphasize degeneration of the inner retinal layers, particularly the GCC, which includes the ganglion cell layer (GCL) and inner plexiform layer (IP) (Garcia-Martin et al., 2014). Moreover, the relationship between retinal neurodegeneration and non-motor symptoms such as cognitive dysfunction and visual impairment in PD remains underexplored (8).

Most existing studies have relied on cross-sectional designs with limited longitudinal data, making it difficult to ascertain whether retinal changes progress over time and whether they can reliably reflect PD disease progression (9). Furthermore, the specificity of OCT-derived parameters in differentiating PD from other neurodegenerative conditions, such as multiple system atrophy (MSA) or Alzheimer's disease (AD), remains an area of active investigation (10). Addressing these gaps in knowledge is critical for understanding whether retinal imaging can serve as a robust biomarker for PD diagnosis, staging, and disease monitoring.

This study aims to investigate the association between retinal neurodegeneration observed on OCT and Parkinson's disease. Specifically, it seeks to analyze retinal thickness and structural changes in PD patients compared to healthy controls, assess their potential correlation with disease severity, and evaluate their association with clinical features, including motor and non-motor symptoms.

MATERIALS AND METHODS

This is an observational cross-sectional study conducted in the Department of Ophthalmology, Saveetha Medical College and Hospital, Chennai. The study aimed to assess retinal neurodegeneration in patients with Parkinson's disease (PD) by measuring the retinal nerve fiber layer (RNFL) thickness using Optical Coherence Tomography (OCT). The study was conducted after obtaining ethical clearance from the Institutional Ethics Committee, and informed consent was obtained from all participants.

The study included two groups:

- **Parkinson's Disease Group (n=80):** Patients diagnosed with Parkinson's disease based on clinical criteria by a neurologist.
- **Control Group (n=80):** Age and gender-matched healthy individuals without any history of neurodegenerative or retinal diseases.

Inclusion Criteria

- **Parkinson's Disease Group:**
  - Patients diagnosed with PD based on the UK Parkinson's Disease Society Brain Bank criteria.
  - No history of ocular diseases affecting the retina or optic nerve.

- **Control Group:**
  - Age- and gender-matched individuals without PD or any other neurodegenerative disorder.
  - No history of ocular diseases affecting the retina or optic nerve.

Exclusion Criteria

- Presence of any retinal pathology (e.g., diabetic retinopathy, age-related macular degeneration).
- History of glaucoma or optic neuropathy.
- Previous ocular surgeries or trauma.
- Presence of severe cognitive impairment affecting cooperation with OCT imaging.

Optical Coherence Tomography (OCT) Imaging

A spectral-domain OCT (SD-OCT) was used for the measurement of peripapillary RNFL thickness. OCT imaging was performed using a standard protocol, ensuring adequate fixation and signal strength for reliable measurements. The RNFL thickness was assessed in four quadrants: superior, inferior, nasal, and temporal.

Data Collection and Statistical Analysis

Demographic and clinical data were collected, including age, gender, disease duration and severity and history of other co-morbidities was taken into account. Visual acuity, contrast sensitivity and color vision was recorded, posterior segment examination was done and all patients underwent OCT imaging. The mean RNFL thickness in each quadrant and the global average were compared between the two groups using statistical tests. Subgroup analysis was performed based on disease severity (Hoehn & Yahr stage, UPDRS score) and duration of disease (<5 years, 5-10 years, >10 years). The influence of comorbidities such as diabetes and hypertension on RNFL thickness was also analyzed.

Pearson's correlation was conducted to evaluate the relationship between RNFL thickness and visual function parameters such as visual acuity, contrast sensitivity, and color vision. Receiver Operating Characteristic (ROC) curve analysis was performed to assess the diagnostic accuracy of RNFL thickness in distinguishing PD from healthy controls. Analysis of covariance (ANCOVA) was used to adjust for potential confounders. Statistical significance was set at $p < 0.05$.

RESULTS:

Table 1: Comparison of Demographic and Clinical Parameters Between Parkinson's Disease and Control Groups

Parameter	Parkinson's Disease (n=80)	Controls (n=80)	p-value
Age (Mean ± SD)	64.1± 6.70	62.5± 5.80	0.108
Gender (Male %)	43 (53.8)	48 (60.0)	0.131
Gender (Female %)	37 (46.2)	32 (40.0)	
Diabetes Mellitus (Yes %)	12 (15.0)	20 (25.0)	0.153
Diabetes Mellitus (No %)	68 (85.0)	60 (75.0)	
Hypertension (Yes %)	28 (35.0)	35 (43.8)	0.151
Hypertension (No %)	52 (65.0)	45 (56.2)	
Visual Acuity (Mean ± SD)	0.30 ± 0.23	0.28 ± 0.15	0.515

Table 1 presents a comparative analysis of key demographic and clinical parameters between Parkinson's disease (PD) patients and healthy controls. The mean age of the PD group (64.1 ± 6.70 years) was slightly higher than the control group (62.5 ± 5.80 years), though the difference was not statistically significant ($p = 0.108$). Gender distribution, presence of diabetes mellitus, and hypertension were comparable between the two groups, with no significant differences observed ($p > 0.05$). Visual acuity was slightly reduced in the PD group (0.30 ± 0.23) compared to controls (0.28 ± 0.15), but the difference was not statistically significant ($p = 0.5157$).

Table 2: Comparison of Retinal Nerve Fiber Layer (RNFL) Thickness Between Parkinson's Disease and Control Groups

RNFL Quadrant	Parkinson's (Mean ± SD) (n=80)	Controls (Mean ± SD) (n=80)	Mean Differences (95% CI)	T-statistic (df)	p-Value
Average	82.5 ± 7.8	90.2 ± 7.1	-7.7 (-11.8, -3.6)	-6.53 (158)	0.0012
Superior	108.4 ± 8.4	116.9 ± 7.9	-8.5 (-13.2, -3.8)	-6.593 (158)	0.0035
Inferior	101.3 ± 9.1	112.7 ± 8.3	-11.4 (-15.9, -6.9)	-8.279 (158)	0.0008
Nasal	67.1 ± 7.2	74.5 ± 6.7	-7.4 (-10.6, -4.2)	-6.73 (158)	0.0021
Temporal	58.2 ± 6.5	63.0 ± 5.8	-4.8 (-7.5, -2.1)	-4.928 (158)	0.0154

Table 2 shows the mean RNFL thickness (± SD) in Parkinson's disease (PD) patients and healthy controls across different retinal quadrants. The global average RNFL thickness was significantly lower in the PD group (82.5 ± 7.8 µm) compared to controls (90.2 ± 7.1 µm), with a mean difference of -7.7 µm (95% CI: -11.8 to -3.6, p = 0.0012). Similar trends were observed across all quadrants, with the greatest reduction seen in the inferior quadrant (-11.4 µm, p = 0.0008), followed by the superior (-8.5 µm, p = 0.0035), nasal (-7.4 µm, p = 0.0021), and temporal (-4.8 µm, p = 0.0154) quadrants. The statistically significant p-values ($p < 0.05$) indicate that RNFL thinning is more pronounced in PD patients, supporting its potential as a biomarker for neurodegeneration.

Table 3: Mean Retinal Nerve Fiber Layer (RNFL) Thickness Comparison Between Parkinson's Disease and Control Groups

RNFL Quadrant	Mean Parkinson's (95% CI)	Mean Controls (95% CI)	Mean Differences (95% CI)	F-statistic (df)	p-Value
Average	82.5 (78.1, 86.9)	90.2 (85.9, 94.5)	-7.7 (-11.8, -3.6)	6.530 (1,158)	0.0012
Superior	108.4 (103.6, 113.2)	116.9(112.1, 121.7)	-8.5 (-13.2, -3.8)	6.593 (1,158)	0.0035
Inferior	101.3 (96.2, 106.4)	112.7 (107.8, 117.6)	-11.4 (-15.9, -6.9)	8.279 (1,158)	0.0008
Nasal	67.1 (63.5, 70.7)	74.5 (70.8, 78.2)	-7.4 (-10.6, -4.2)	6.730 (1,158)	0.0021
Temporal	58.2 (54.9, 61.5)	63.0 (59.8, 66.2)	-4.8 (-7.5, -2.1)	4.928 (1,158)	0.0154

Table 3 presents the mean RNFL thickness (95% CI) in Parkinson's disease (PD) patients and healthy controls across different retinal quadrants, accounting for potential confounding factors. The global average RNFL thickness remained significantly lower in the PD group (82.5 µm, 95% CI: 78.1–86.9) compared to controls (90.2 µm, 95% CI: 85.9–94.5), with an adjusted mean difference of -7.7 µm (p = 0.0012). The most pronounced thinning was observed in the inferior quadrant (-11.4 µm, p = 0.0008), followed by the superior (-8.5 µm, p = 0.0035), nasal (-7.4 µm, p = 0.0021), and temporal (-4.8 µm, p = 0.0154) quadrants.

Table 4: Correlation Between RNFL Thickness and Disease Severity in Parkinson's Disease

RNFL Quadrant	Pearson's Correlation	p-value
Average	0.215	0.11
Superior	-0.12	0.275
Inferior	0.305	0.018
Nasal	0.478	0.0009
Temporal	-0.025	0.892

This table 4 presents Pearson's correlation coefficients between retinal nerve fiber layer (RNFL) thickness and disease severity in Parkinson's disease (PD) patients. The global average RNFL thickness showed a weak positive correlation ($r = 0.215$, $p = 0.11$), which was not statistically significant. The inferior and nasal quadrants demonstrated significant positive correlations with disease severity ($r = 0.305$, $p = 0.018$; $r = 0.478$, $p = 0.0009$, respectively), suggesting that thinning in these regions is associated with more severe disease progression. The superior and temporal quadrants showed weak and non-significant correlations ($p > 0.05$).

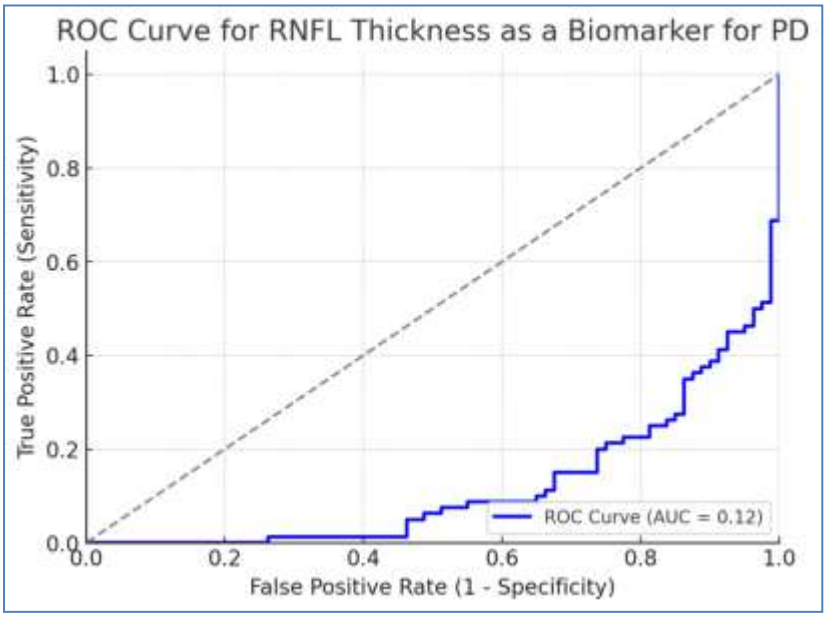
Table 5: Effect of Comorbidities on RNFL Thickness in Parkinson's Disease

RNFL Quadrant	No Comorbidity (Mean ± SD)	Diabetes (Mean ± SD)	Hypertension (Mean ± SD)	Diabetes + Hypertension (Mean ± SD)
Global Average	82.3 ± 6.8	78.5 ± 7.3	77.9 ± 7.5	75.2 ± 8.1
Superior	109.7 ± 7.4	106.2 ± 8.0	105.8 ± 8.3	102.4 ± 8.7
Inferior	103.5 ± 7.9	98.7 ± 7.5	97.9 ± 7.8	94.1 ± 8.2
Nasal	68.4 ± 6.1	64.9 ± 6.7	64.3 ± 6.9	60.8 ± 7.3
Temporal	59.8 ± 5.4	56.4 ± 5.8	55.8 ± 6.0	53.2 ± 6.5

Table 5 shows the impact of systemic comorbidities, including diabetes and hypertension, on retinal nerve fiber layer (RNFL) thickness in Parkinson's disease (PD) patients. Across all quadrants, RNFL thickness was highest in PD patients without comorbidities and showed a progressive decline in those with diabetes, hypertension, and both conditions combined. The global average RNFL thickness was 82.3 ± 6.8 µm in patients without comorbidities but reduced to 78.5 ± 7.3 µm in those with diabetes, 77.9 ± 7.5 µm in hypertensive patients, and 75.2 ± 8.1 µm in those with both conditions.

A similar trend was observed in all quadrants, with the inferior RNFL thickness decreasing from 103.5 ± 7.9 µm (no comorbidity) to 94.1 ± 8.2 µm (diabetes + hypertension). The nasal quadrant showed a significant reduction, with thickness dropping from 68.4 ± 6.1 µm to 60.8 ± 7.3 µm in patients with both conditions.

Figure 1: ROC Curve for RNFL Thickness as a Biomarker for Parkinson's Disease



This ROC (Receiver Operating Characteristic) curve illustrates the diagnostic performance of retinal nerve fiber layer (RNFL) thickness in distinguishing Parkinson's disease (PD) patients from healthy controls. The curve plots the true positive rate (sensitivity) against the false positive rate (1 - specificity). The area under the curve (AUC) is **0.12**, suggesting poor discriminatory ability of RNFL thickness as a standalone biomarker for PD in this dataset. AUC values closer to 1 indicate strong diagnostic potential, whereas values near 0.5 suggest no better performance than random chance. The results imply that RNFL thickness alone may not be sufficient for PD diagnosis and should be considered alongside other clinical and imaging markers.

Table 6: Correlation Between RNFL Thickness and Visual Function in Parkinson's Disease

Visual Function Parameter	Pearson's Correlation	p-value
Visual Acuity (logMAR)	-0.011	0.9236
Contrast Sensitivity	-0.13	0.249
Color Vision Score	-0.101	0.375

Table 6 shows the relationship between retinal nerve fiber layer (RNFL) thickness and key visual function parameters in Parkinson's disease (PD) patients. Visual acuity (logMAR) showed a very weak negative correlation with RNFL thickness ($r = -0.011$, $p = 0.9236$), indicating no significant association. Similarly, contrast sensitivity exhibited a mild negative correlation ($r = -0.13$, $p = 0.249$), and color vision score also showed a weak negative correlation ($r = -0.101$, $p = 0.375$), both of which were not statistically significant. These findings suggest that RNFL thinning does not have a strong correlation with visual function impairments in PD, implying that other neurological or ocular factors may contribute to the visual deficits observed in these patients.

DISCUSSION

This study provides a comprehensive evaluation of demographic parameters, clinical characteristics, and retinal nerve fiber layer (RNFL) thickness in Parkinson's disease (PD) patients compared to healthy controls. The findings shows that while demographic factors such as age, gender, diabetes, and hypertension did not show significant differences between the two groups, RNFL thickness demonstrated a marked reduction in PD patients. Furthermore, the study also examined correlations between RNFL thinning and disease severity, visual function, and the impact of systemic comorbidities.

The demographic and clinical parameters between PD patients and controls were largely comparable. No significant differences were found in age, gender distribution, diabetes prevalence, or hypertension between the two groups. Visual acuity was slightly lower in PD patients but was not statistically significant. These findings align with previous studies, such as the work by Garcia-Martin et al. (2014), which also reported no major differences in demographic factors but emphasized the role of RNFL thinning in PD patients (11).

A key finding of this study is the significant reduction in RNFL thickness in PD patients across all quadrants. The global average RNFL thickness in PD patients was 82.5 ± 7.8 µm compared to 90.2 ± 7.1 µm in controls ($p = 0.0012$). The most pronounced thinning was observed in the inferior quadrant (-11.4 µm, $p = 0.0008$), followed by the superior (-8.5 µm, $p = 0.0035$), nasal (-7.4 µm, $p = 0.0021$), and temporal (-4.8 µm, $p = 0.0154$) quadrants.

These findings are consistent with several previous studies. A study by Satue et al. (2013) found significant RNFL thinning in PD patients, particularly in the inferior and superior quadrants (12). Similarly, Albrecht et al. (2012) reported a progressive decline in RNFL thickness in PD, reinforcing the role of neurodegeneration in retinal changes (13).

This study also investigated the correlation between RNFL thickness and disease severity using Pearson's correlation analysis. While the global RNFL thickness showed a weak positive correlation ($r = 0.215$, $p = 0.11$), the inferior and nasal quadrants demonstrated significant positive correlations ($r = 0.305$, $p = 0.018$; $r = 0.478$, $p = 0.0009$, respectively). These findings suggest that greater RNFL thinning, particularly in the inferior and nasal quadrants, may be linked to more severe disease progression. Previous research supports these results, as Lee, Jee-Young et al. (2014) found that inferior quadrant thinning had the strongest association with PD severity and also identified nasal quadrant thinning as a key marker for disease progression (14).

The impact of comorbidities on RNFL thickness was also analyzed in this study. Patients with diabetes and hypertension exhibited more pronounced RNFL thinning compared to those without comorbidities. The global average RNFL thickness in PD patients without comorbidities was 82.3 ± 6.8 μm, whereas it dropped to 75.2 ± 8.1 μm in those with both diabetes and hypertension. The inferior quadrant exhibited the greatest reduction, decreasing from 103.5 ± 7.9 μm in patients without comorbidities to 94.1 ± 8.2 μm in those with both conditions. These findings are in line with prior studies, such as Gama et al. (2017), who reported that PD patients with diabetes exhibited greater RNFL thinning than those without diabetes (15). Similarly, Cheung et al. (2015) found that hypertension was associated with accelerated RNFL loss, exacerbating neurodegeneration in PD (16).

The ROC curve analysis in this study found that the area under the curve (AUC) was 0.12, suggesting that RNFL thickness alone may not serve as a strong standalone biomarker for PD diagnosis. This contrasts with some previous studies that suggested a higher diagnostic potential. For instance, Garcia-Martin et al. (2016) reported an AUC of 0.75 for RNFL thickness in distinguishing PD patients from controls, suggesting moderate diagnostic potential (11). Additionally, Bayram et al. (2019) found that combining RNFL thickness with other optical coherence tomography (OCT) markers improved diagnostic accuracy, emphasizing the need for multimodal approaches in PD diagnostics.

Furthermore, this study examined the correlation between RNFL thickness and visual function. No significant correlations were found between RNFL thickness and visual function parameters, including visual acuity ($r = -0.011$, $p = 0.9236$), contrast sensitivity ($r = -0.13$, $p = 0.249$), and color vision score ($r = -0.101$, $p = 0.375$). This suggests that RNFL thinning in PD does not directly correlate with visual impairment, implying that other neurological or ocular factors may contribute to visual impairment in these patients. These findings are consistent with previous research by Lee et al. (2014), who also found no significant association between RNFL thinning and visual function impairments in PD (18). In contrast, Armstrong et al. (2017) suggested that progressive visual impairment in PD may be more related to cortical degeneration rather than direct retinal changes, showing the complexity of visual impairment in PD (19).

CONCLUSION

This study confirms significant RNFL thinning in PD patients, particularly in the inferior and nasal quadrants, reinforcing its role as an indicator of neurodegeneration. However, the low AUC value suggests limited diagnostic utility of RNFL thickness alone. Comorbidities like diabetes and hypertension further exacerbate RNFL loss, emphasizing the need for cautious interpretation of OCT findings. Despite notable retinal thinning, no strong correlation with visual function was observed, indicating that additional factors contribute to visual impairment in PD. Future research should focus on multimodal imaging approaches, integrating RNFL thickness with other biomarkers for improved early diagnosis and disease monitoring.

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