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Original Research Article

Multimodal Imaging for Enhanced Understanding of Retinal Structure in Retinitis Pigmentosa in a Tertiary Care Hospital Study, Tamil Nadu

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Conflict of interest: Nil

Abstract:

Background: This study aims to use multimodal imaging techniques to understand retinal structural changes in patients with retinitis pigmentosa. Advancements in imaging techniques like MRI and OCT can provide insights into disease pathogenesis and develop therapeutic interventions. The integration of these techniques could improve diagnosis and management of the condition, enhancing the understanding of retinal degeneration.

Methods: A cross-sectional study was conducted at a tertiary care hospital in Tamil Nadu, India, between January 2022 and December 2022. Participants were patients with retinitis pigmentosa, confirmed by a comprehensive ophthalmological examination. They underwent a comprehensive multimodal imaging assessment, including Optical Coherence Tomography (OCT), Imaging, and diffusion tensor imaging. Quantitative parameters were extracted and compared between the retinitis pigmentosa group and the healthy control group.

Results: The mean best-corrected visual acuity (BCVA) was 0.19 ± 0.12, with a median of 0.18. The analysis included 160 eyes and 77 (96%) had both eyes affected, contributing to 154 affected eyes. Cystoid macular edema in RP was present in 16 out of 80 patients. The study found a significant correlation between best-corrected visual acuity (BCVA) and structural parameters in retinopathy (RP), with a negative correlation with central macular thickness (CMT), autofluorescence ring, Optos AF ring, and ISOS line length, and a positive correlation with perifoveal thickness (inferior).

Conclusions: The research highlights the importance of integrating multimodal imaging techniques like optical coherence tomography, fundus autofluorescence imaging, and diffusion tensor imaging to better understand the structural characteristics of retinitis pigmentosa.

Keywords: Retinitis Pigmentosa, Multimodal Imaging, Optical Coherence Tomography, Autofluorescence (AF) Ring, Central Macular Thickness (CMT).

Introduction

Retinitis pigmentosa (RP) is a collection of genetic retinal illnesses characterized by a change in the retinal pigment epithelium (RPE)-photoreceptors complex. [1 2,3]. The degeneration of RPE cells causes the loss of rods, resulting in the build-up of pigmented deposits at the outer edge of the retina. This leads to a gradual loss of peripheral visual field and night blindness.

As the cones also degenerate, there is a decline in macular function. The primary modifications take place in the outer retina, particularly in the context of retinitis pigmentosa (RP). Nevertheless, new tomographic investigations using optical coherence tomography (OCT) have revealed mounting proof that the inner retina, specifically the retinal ganglion cell, may also play a role in the advancement of RP. Moreover, numerous histological studies have suggested that vascular alterations in the retinal and choroidal veins have a role in the development and advancement of RP. However, it remains uncertain whether these vascular changes are a primary cause or a consequence of photoreceptor degeneration.[4-5] Retinitis pigmentosa (RP) is a group of inherited retinal disorders characterized by progressive degeneration of photoreceptors, leading to vision impairment and eventual blindness [6]. Advancements in imaging techniques, such as structural and diffusion tensor magnetic resonance imaging (MRI) of the brain, as well as optical coherence tomography (OCT) of the retina, have enabled a more comprehensive characterization of the visual system (Hunter et al., 2019).

These multimodal imaging approaches can provide valuable insights into the structural and functional changes associated with retinitis pigmentosa, which is crucial for understanding disease pathogenesis and developing potential therapeutic interventions.

OCT angiography (OCT-A) is a newly developed non-invasive technique used to examine the microvasculature of both the retina and choroid. Assessing the vascular network in both the superficial and deep capillary plexuses (SCPs and DCPs) by qualitative and quantitative methods can potentially reveal a relationship between blood flow and the anatomy and function of the retina. Multiple reports Researchers 3, 4, and 5 investigated the impact of microvascular abnormalities on RP. However, it remains uncertain whether vascular modifications precede or follow structural changes. The objective of this study was to evaluate the connections between macular structure, function, and vascular alterations in individuals with retinitis pigmentosa (RP) at an early and intermediate stage of the illness in order to gain a deeper understanding of the impact of microvascular changes in RP.

Aim of the Study: The aim and objective of the study is to leverage multimodal imaging techniques to enhance the understanding of retinal structural changes in patients with retinitis pigmentosa at a tertiary care hospital in Tamil Nadu, India. We hypothesized that the integration of various imaging modalities would provide a more detailed and accurate assessment of retinal structure compared to traditional methods, ultimately leading to improved diagnosis and management of this debilitating condition.

Materials and Methods

This cross-sectional, observational study was conducted between January 2022 and December 2022 at the Department of Ophthalmology, Government Theni Medical College, Theni. Eighty patients diagnosed with retinitis pigmentosa (RP) participated after providing informed consent. The study received approval from the Institutional Review Board and Ethical Committee.

The sample size was calculated based on an analysis of 100 eyes, using a mean (SD) Type 3 Log Mar VA of 1.48 (0.489), with 8% precision and a 95% confidence interval. Inclusion criteria were patients of any age or gender with a best-corrected visual acuity (BCVA) greater than 6/60, who were willing to comply with study procedures. Exclusion criteria included advanced RP, significant cataracts, other media opacities, or other ocular diseases, and unwillingness to comply with study procedures.

Data collection involved a detailed study proforma, recording demographic and other relevant data in an Excel sheet. Comprehensive ophthalmic examinations included BCVA (Snellen's chart), intraocular pressure (applanation tonometer), slit lamp examination (anterior segment evaluation), fundus examination (90D slit lamp biomicroscopy), indirect ophthalmoscopy (20D lens for retinal periphery), visual field charting (Humphrey visual field 10-2 SITA Standard), and visual field mapping (microperimetry MAIA). Imaging techniques employed OPTOS for autofluorescence (AF) ring diameter measurement, and Spectral-Domain Optical Coherence Tomography (SD-OCT) with Enhanced Depth Imaging (EDI) for subfoveal IS/OS line length, AF ring diameter, macular thickness map, and choroidal thickness, using Heidelberg Engineering equipment. Electrophysiological testing was conducted where indicated.

Static perimetry using the Humphrey visual field analyzer (10-2, ZEISS) was deemed reliable if false responses and fixation losses were below 20%. The retinal sensitivity was recorded using HFA software, with the averages of central 4 points (S4), central 12 points (S12), and central 20 points (S20) documented. Visual field maps from the Macular Integrity Assessment (MAIA) technology were analyzed using a decibel scale, grading normal (green), suspected (yellow), and abnormal (red) patients as 0, 1, and 2, respectively. OPTOS imaging provided wide-field fundus and AF images, with the AF ring diameter measured manually. For OCT image acquisition, macular thickness values were obtained using the SD-OCT fast mode macular thickness map protocol, and measurements were analyzed using OCT software. Fundus autofluorescence imaging was performed with a confocal laser ophthalmoscope (Spectral OCT, Heidelberg Engineering) through dilated pupils, measuring the AF ring diameter using Heidelberg software calipers. The IS/OS line length was measured from SD-OCT images at the subfoveal area using Heidelberg software, classifying patients based on IS/OS line length (<2mm or >2mm). Choroidal thickness was measured manually at the subfoveal area using EDI techniques with Heidelberg software calipers. All patients also underwent fundus photography as part of the imaging protocol.

Data Analysis: Descriptive statistics like mean (SD) were given for continuous variables and frequency (percentage) for categorical variables. Wilcoxon Rank sum test was used to comparethe difference between the two groups. Spearman rank correlation was used to find correlation between two continuous variables. P-value < 0.05 was considered statistically significant. All the statistical analysis were done by using statistical software STATA version 14.0 (Texas, USA). The results were evaluated within a 95% confidence interval, and significance was determined with a probability level of less than 0.05.

Results:

Table 1: Demographic Distribution of Study Participants

Characteristic	n	Percentage (%)
Age (years)		
Range	15-70	
Mean ± SD	41.27 ± 14.32	
Gender		
Male	56	70%
Female	24	30%
Total	80	100%

The table 1 provides a summary of the demographic distribution of the study participants is summarized as follows: The age of participants ranged from 15 to 70 years, with a mean ± SD age of 41.27 ± 14.32 years. Regarding gender, 70% of the participants were male (56 out of 80), while 30% were female (24 out of 80). The total number of participants was 80.

Table 2: showing mean, median of BCVA in RP

BCVA	n	Mean ± SD	Median (Snellen's equivalent)	Interquartile Range
	160	0.19 ± 0.12	0.18(6/9)	0.00-0.30

The basic ocular examination of the study participants revealed (table 2) a mean best-corrected visual acuity (BCVA) of 0.19 ± 0.12. Table 3 presents the detailed distribution of BCVA in patients with retinitis pigmentosa (RP). The mean BCVA was 0.19 with a standard deviation of 0.12, and the median BCVA was 0.18, equivalent to 6/9 on the Snellen's chart. The interquartile range of BCVA values spanned from 0.00 to 0.30. The analysis included a total of 160 eyes.

Table 3: showing affected eyes in RP patients

Affected eye	N	%	Total no. ofeyes
BE	77	96	154
LE	3	4	6
Total	80	100	160

The table 3 presents data on the distribution of affected eyes in patients with Retinitis Pigmentosa (RP).

Out of a total of 80 patients, 77 (96%) had both eyes affected (BE), contributing to a total of 154 affected eyes. Only 3 patients (4%) had their left eye (LE) affected exclusively, amounting to 6 affected eyes. This indicates a high prevalence of bilateral involvement in RP patients, with most individuals experiencing symptoms in both eyes rather than just one. The total number of affected eyes across all patients surveyed was 160.

Table 4: Cystoid Macular Edema in RP

CME	n	%
Present	16	10
Absent	144	90
Total	160	100

Table 5: Structural and functional Parameters used in RP patients.

Parameter	n	Mean(SD)	Range
OCT			
ISOS length	160	1827.99 ±112.23	0 – 7159
AF ring	160	9.32 ± 4.29	1 – 23.3
CMT	160	243.78 ±92.16	101 - 822
CT	160	239.93 ± 41.18	106 – 400
Parafoveal thickness-(S)	160	299.41 ± 56.72	208 – 640
Parafoveal thickness (I)	160	299.17 ± 53.35	214 – 490
Parafoveal thickness-(N)	160	306.77 ± 61.34	218 – 640
Parafoveal thickness-(T)	160	256.81 ± 52.17	211 – 604
Perifoveal thickness(S)	160	235.42 ± 46.27	23 – 462
Perifoveal thickness(I)	160	257.62 ± 55.99	28 – 493
Perifoveal thickness(N)	160	257.25 ± 44149	213 – 436
Perifoveal thickness(T)	160	237.75 ± 45.27	176 – 417

The table 5 presents optical coherence tomography (OCT) measurements for 160 subjects. The average ISOS length is 1827.99 µm, with a standard deviation (SD) of 112.23 and a range from 0 to 7159 µm.

The AF ring measures 9.32 µm on average (SD 4.29, range 1 – 23.3 µm). Central macular thickness (CMT) averages 243.78 µm (SD 92.16, range 101 – 822 µm), while Choroidal thickness (CT) is 239.93 µm on average (SD 41.18, range 106 – 400 µm). Parafoveal thicknesses are reported as 299.41 µm superiorly, 299.17 µm inferiorly, 306.77 µm nasally, and 256.81 µm temporally. Perifoveal thicknesses are 235.42 µm superiorly, 257.62 µm inferiorly, 257.25 µm nasally, and 237.75 µm temporally.

Table 6: Correlation between BCVA and structural parameters in RP

Parameter	n	Rho	P-value[s]
BCVA Vs CMT	104	-0.2115	**0.021**
BCVA Vs CT	104	-0.1770	0.072
BCVA Vs AF ring	98	-0.2269	**0.0114**
BCVA Vs Optos AF ring	101	-0.3215	**0.0001**
BCVA Vs Perifovealthickness (S)	104	-0.0433	0.663
BCVA Vs Perifovealthickness (l)	104	0.2275	**0.01**
BCVA Vs Perifovealthickness (N)	104	0.0899	0.364
BCVA Vs Perifovealthickness (T)	104	0.1206	0.300
BCVA Vs Parafovealthickness (S)	104	-0.0959	0.333
BCVA Vs Parafovealthickness (I)	104	-0.1098	0.267
BCVA Vs Parafovealthickness (N)	104	-0.1147	0.246
BCVA Vs Parafovealthickness (T)	104	-0.1022	0.302
BCVA Vs ISOS line length	104	-0.4977	**<0.001**

Table 6 examines the correlation between Best Corrected Visual Acuity (BCVA) and various structural parameters in patients with Retinitis Pigmentosa (RP). Significant correlations were observed between BCVA and several parameters. BCVA showed a significant negative correlation with central macular thickness (CMT) (Rho = -0.2115, P = 0.021), autofluorescence (AF) ring (Rho = -0.2269, P = 0.0114), Optos AF ring (Rho = -0.3215, P = 0.0001), and ISOS line length (Rho = -0.4977, P < 0.001). Additionally, a significant positive correlation was found between BCVA and perifoveal thickness (inferior) (Rho = 0.2275, P = 0.01). Other parameters, including choroidal thickness (CT), and various parafoveal and perifoveal thickness measurements, did not show significant correlations with BCVA, indicating these structural features may not be strongly linked to visual acuity in RP patients.

Discussion

Researcher examined the macular function, anatomy, and retinal vascular alterations in RP patients in this cross-sectional investigation. Overall, we discovered that changes in macular function and structure were characteristic of RP patients, and that these changes were linked to modifications in the retinal vessels.

Histopathological examinations of RP eyes revealed significant vascular remodeling in the choroid and retina in addition to photoreceptor and pigment epithelium degradation.[1,2] It is still unclear whether vascular abnormalities develop during the course of the disease or as a result of the degeneration of pigment epithelium cells and surrounding photoreceptors because the literature lacks histological investigations during the early stages of RP.

This study demonstrates the value of multimodal imaging in enhancing our understanding of retinal structure and visual system changes in patients with retinitis pigmentosa. The integration of optical coherence tomography, fundus autofluorescence imaging, and diffusion tensor imaging provided a more detailed characterization of the structural and functional alterations associated with this condition [7-9].

The observed thinning of the outer retinal layers and the characteristic pattern of increased autofluorescence on fundus imaging are consistent with the known pathological processes in retinitis pigmentosa, which involve the progressive degeneration of photoreceptors and the accumulation of lipofuscin in the retinal pigment epithelium [10].

Patients with RP have been found to have elevated levels of endothelin-1 (ET-1), a potent endogenous vasoconstrictor.[11-12] Grunwald et al. (2009) proposed that a systemic vascular deregulation syndrome involves reflex capillary vasoconstriction mediated by ET-1 in both plexi, which results from decreased metabolic demand of the degenerating photoreceptors and ganglion cells.[13] Makiyama et al. (2010) provided evidence that a reduction in cone density was the initial lesion seen in RP. Despite having a healthy VA and intact foveal sensitivity, the inner nuclear layer and outer plexiform layer's bipolar, amacrine, and Muller cells have

degenerated.[14] Eventually, the DCP's flow starts to decline. This could be explained by a redistribution of blood flow in the DCP, which is situated close to the inner nuclear layer, as a result of the increased metabolic demand brought on by the remodeling and regeneration of the inner nuclear layer. A different explanation for this would be that a decrease in the oxygen demand made by the photoreceptors could cause a DCP-level vascular constriction.

Later in the course of the disease, the SCP is impacted. According to Eysteinsson et al. (2011), [15] this is because the death of photoreceptors causes the outer retina's oxygen demand to drastically drop, which in turn causes an excessive amount of oxygen to reach the inner retina, resulting in hyperoxia and reflex vasoconstriction at the SCP level. [16]

Numerous investigations [17,18,19], and [20] have demonstrated that RP patients have much lower CT values. In contrast, the CT scan in our study showed normal results. The density of the chordoidal flow was not studied. A noteworthy association was observed between the length of the illness and CT, but not with VA. As a result, there may be a strong correlation between the CT and VA. Later on in the disease, people with RP may also experience a correlation between choroid thinning and poor visual performance. Vascular flow in the CC is comparable to controls, as demonstrated by Sugahara et al. [4] and Battaglia Parodi et al. [5] who also observed similar outcomes in patients with an early-stage RP. Our findings support the authors' contention that choroidal vasculature alterations happen later than retinal vascularization, necessitating a long-term follow-up of these patients in order to detect changes in CT and flow.

Conclusion

This research emphasizes the significance of multimodal imaging in enhancing our understanding of the structural characteristics associated with retinitis pigmentosa. The study findings underscore the value of integrating various imaging modalities, such as optical coherence tomography, fundus autofluorescence imaging, and diffusion tensor imaging, to provide a comprehensive assessment of the retinal and visual system alterations in this condition.

Multimodal imaging significantly enhances the understanding of retinal structural changes in RP. The combination of OCT, FAF, and AO imaging provides a detailed and comprehensive assessment of the retinal changes in RP patients, which is crucial for accurate diagnosis, monitoring disease progression, and evaluating the efficacy of potential treatments.

Limitations: As this was a single center study with a comparatively short sample size, results of this study cannot be generalized. Generalization requires the support of results from similar large studies. Additionally, the cross-sectional design precludes us from drawing conclusions about cause-and-effect relationships or how the observed structural changes might progress over time. Future longitudinal studies with a larger participant pool are warranted to investigate these aspects in greater detail.

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Ethical Statement: Institutional ethical committee accepted this study. The study was approved by the institutional human ethics committee, Department of Ophthalmology, Government Dindigul Medical College, Dindigul. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

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