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Edi Mod Spectral Domain Optical Coherence Tomography Evaluation of The Choroid in Retinitis Pigmentosa: A Case-Control Study

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ABSTRACT

Objective: The evaluation of choroidal thickness measurements became possible after the developments in optical coherence tomography (OCT) technology. This study aimed to evaluate choroidal features in Retinitis Pigmentosa subjects with EDI (Enhanced depth imaging) mode spectral domain optical coherence tomography (SD-OCT).

Material and Method: A hundred and three eyes of 54 RP subjects underwent scanning with EDI-OCT for central retinal and choroidal thickness measurements and were compared with 40 healthy controls. Submacular choroidal thickness measurements were obtained beneath the fovea and at 500 µm intervals for 2.5 mm nasal and temporal to the center of the fovea.

Results: Mean subfoveal choroidal thickness measurements were 253.2±74.9 µm in RP patients and 336.2±91.7 µm in control ($p<0.0001$). There was no correlation between subfoveal choroidal thickness and visual acuity in RP patients. The choroid had an irregular shape in 85 % of RP patients. The thickest point of the choroid was not subfoveal as in healthy eyes, and excessive nasal thinning of the choroid was observed in 93 % of RP patients.

Conclusion: Submacular choroidal thickness was significantly reduced but did not correlate with the visual acuity in RP patients.

Keywords: Enhanced depth imaging, Optical coherence tomography, Choroidal thickness, Central retinal thickness, Retinitis pigmentosa

INTRODUCTION

Retinitis pigmentosa (RP) is a heterogeneous group of retinal dystrophies characterized by progressive loss of rod and cone cells. There are 1.5 million affected individuals worldwide, with about one in 4000 people affected (1). Rod-cone dystrophy is the most common form of RP, characterized by night blindness, progressive peripheral field loss in daylight, and eventual blindness after several decades. In extreme cases, blindness may develop rapidly over about two decades or slowly over a period that does not result in blindness. When the patient has cone-rod dystrophy, the clinical presentation is decreased in visual acuity rather than visual field loss (1).

There are several approaches to diagnosing RP: Genetic counseling is always recommended as, in most cases, RP is non-syndromic but can also present in many syndromic forms. A molecular diagnosis may be possible for some genes. RP is typically diagnosed clinically based on the progressive signs of night blindness and peripheral visual field defects. Besides, there are fundus lesions and hypovolted electroretinograms (2).

RP presents with choroidal dystrophy. It is readily diagnosed by fluorescein angiography and shows atrophy of the choriocapillaris in all cases.

Most publications indicate a decrease in choroidal thickness (3-5). Nevertheless, previous studies measuring the choroidal thickness in patients with retinal degeneration could not clearly define the choroidal borders and complete choroidal thickness profile. The method known as enhanced depth imaging (EDI) Optical coherence tomography (OCT) is a transpupillary imaging diagnostic imaging method that can examine the retina cross-sectionally with 8-10 µm resolution (6).

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Currently, no treatment is available to slow the progression of the disease or restore vision. Thus, the prognosis for RP is poor. In terms of treatment, the therapeutic approach consists of slowing down the degenerative process through sunlight protection, vitamin therapy, and treating complications as they occur. Gene therapy, neuroprotection, and retinal prostheses are emerging as new therapeutic strategies. Retinal electronic and photovoltaic visual prosthesis research continues regarding partial visual rehabilitation in end-stage disease (1, 2).

A reliable measurement of choroidal thickness is essential for electrode design. This is why the choroidal thickness may be the final selection point regarding visual prostheses. Consequently, the choroid in diseased eyes requires further study. This study evaluated and compared the healthy choroidal thicknesses measured by the EDI technique.

MATERIALS AND METHODS

Recruitment and Data Collection

Fifty-four patients (103 eyes) diagnosed with RP and 40 (80) healthy volunteers were included in the study, who were unrelated to each other. The patients and the control group first underwent a comprehensive ophthalmological examination.

The following criteria were used to identify the RP disease phenotype: night blindness, perception of visual field changes, attenuated retinal vessels, electroretinogram abnormalities, and loss of visual field.

The following criteria were used as exclusion criteria of the study: patients who cannot adapt to OCT measurements (mental retard patients and pediatric patients), patients with nystagmus, cataracts, vitreous opacities, corneal opacity that will reduce vision, patients with myopia over -6 diopters, and over +4 diopters, glaucoma, any eye disorder other than the refractive error that would affect the measurements (keratoconus, diabetic retinopathy, hypertensive retinopathy, chorioretinitis, central serous chorioretinopathy), patients with a history of eye irritation or surgery, the pregnant. Three eyes could not be photographed due to nystagmus, one eye could not be photographed because it was absolute, and one eye that had a uveitis attack were not included in the study.

It appears to describe the various diagnostic tests that were performed on study participants, including the measurement of visual acuity using a Snellen chart, detailed biomicroscopy, keratometry, intraocular pressure measurement using Goldmann applanation tonometry, and fundus examination after pupil dilation. The sentence then goes on to specify that central macular and choroidal thicknesses were evaluated using SD-OCT in EDI mode.. Submacular choroidal thickness, 2.5 mm nasal and temporally choroidal thickness at 500 µm intervals, and central retinal thickness were measured. A single technician performed the imaging and qualified to acquire OCT images. Two independent, experienced OCTreaders conducted the measurements, and the results were compared.

The measurements were compared with the features and values of 40 healthy controls of similar age, gender, and spherical equivalent. Volunteer patients with similar age, gender, and spherical equivalent values with no systemic or ophthalmological disease other than refractive error were included as the control group.

Study design

Study approval has been received from the institutional review board for this prospective case-control study conducted in the department of ophthalmology of a tertiary care research and education hospital of Erciyes University, Turkey. A total of 40 patients were diagnosed with RP, and the 54 healthy volunteers who were admitted for controls in the outpatient clinics underwent an ophthalmologic examination. During the 2-month study period, RP patients who applied to the ophthalmology outpatient clinic and met the study criteria were collected sequentially. EDI-OCT scans were always performed in the morning-time clinics To standardize the measurements and prevent possible diurnal variations in choroidal alterations (7).

Ethical Issues

According to the World Medical Association Declaration of Helsinki, the regional scientific ethics committee approved this study. The ethical approval date is 04.07.2014, and the number is 2014/379. All subjects provided written informed consent.

Statistical Analysis

All analyses were performed on SPSS v21. Data are given mean ± standard deviation, median (25p-75p) for continuous variables, and frequency (percentage) for categorical variables. The utilization of Chi-square tests performed categorical comparisons. One-way analysis of variance (ANOVA), Kruskal-Wallis H test, and Wilcoxon t-tests were used for comparisons between groups. Multiple comparisons Siegel-Castellan was done with the test. $p<0.05$ values were defined as the significance level for all statistical analyses.

RESULTS

We recruited 54 patients diagnosed with RP and 40 healthy controls with an average of 31.38 (13 - 65) and 36.32 (14 - 70) years of age, respectively ($p>0.05$). In both groups, females were in the majority 32 female (59.3%) RP cases and 30 female (75%) healthy controls ($p>0.05$). The mean spherical equivalent (EQ) of the RP group and the control cases was -1.25 (Plan - (-5.00)) dioptres and -1.65 (Plan -(-4.25)) dioptres, respectively ($p>0.05$).

The mean subfoveal choroidal thickness was 253.2±74.9 µm in the RP group and 336.2±91.7 µm in the control group. Subfoveal Choroidal thickness was found to be significantly thinner in the RP group (please see figure 1) than in the control group (please see figure 2) ($p<0.0001$). Choroidal thickness in the RP group was significantly thinner than in the control group for each localization in measurements made at 500-micron intervals towards the 2.5 mm nasal and temporal aspects of the fovea ($p<0.01$). Choroid thickness measurements were obtained in both groups in the nasal found thinner than temporal. The mean choroidal thickness of 2.5 mm nasal of the fovea was 128 µm in the RP group and 242 µm in the control group ($p<0.001$). The mean choroidal thickness of 2.5 mm temporal to the fovea was 201 µm in the RP group and 302 µm in the control group ($p<0.001$). The baseline features of the EDI-OCT measurements are presented in Table 1 (please see **Table 1**).

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In the control group, choroidal thickness showed the thinnest curve in the nasal, thickest in the subfoveal, and tapering again temporally. The maximal choroidal thickness was on the subfoveal area in the control patients (counter to the RP ones). The nasal thinning in RP patients was excessive in 83% of cases.

Central retinal thickness was 199.4±69.4 µm in the RP group and 220.7±11.9 µm in the control group (p>0.05).

The RP group positively correlated with subfoveal choroidal and central retinal thickness.

Subfoveal choroidal and central retinal thickness did not correlate in the control group.

The RP group observed no correlation between subfoveal choroidal thickness and best-corrected visual acuity (BCVA).

The RP group found no correlation between subfoveal choroidal thickness and spherical equivalent values.

In the control group, the thickness of the subfoveal choroidal layers decreased as the spherical equivalent increased.

When the RP and control groups were considered together, men had significantly thinner subfoveal choroidal thickness than women (M= 275-micron, F= 306 micron).

There was no significant difference between men and women in the central retinal thickness (p>0.05).

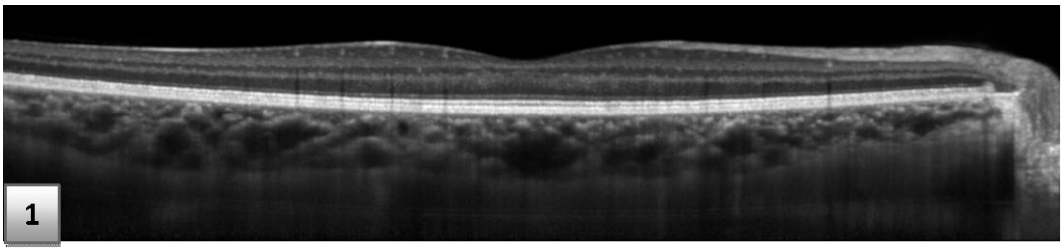

Figure 1. Optical coherence tomography image of a healthy eye with a normal thickness of the choroidal layer

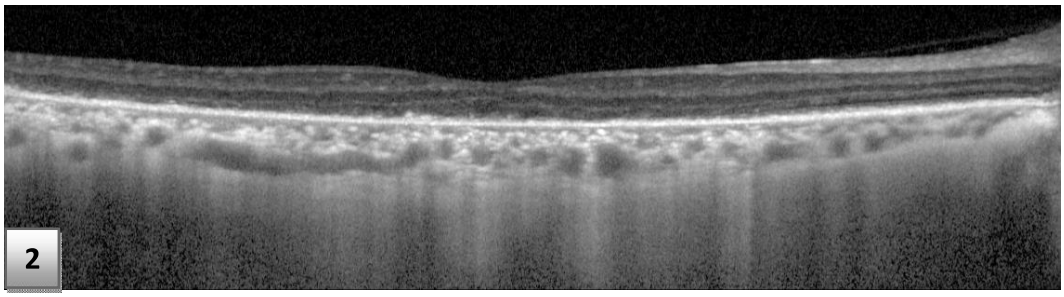

Figure 2. Enhanced depth imaging of choroidal thinning in retinitis pigmentosa patient.

Table 1. The mean choroidal thickness at the central and peripheral retina of healthy subjects and patients with retinitis pigmentosa

Choroidal thickness	RP (mean±sd)	Control (mean±sd)	P value
TEMPORAL(2.5mm)	201±73.42 µm	302±61.55 µm	(p<0.001)
FOVEA	253.2±74.9µm	336.2±91.7µm	(p<0.0001)
NAVAL(2.5mm)	128 ±58.42 µm	242±48.83 µm	(p<0.001)

DISCUSSION

We evaluated choroidal thickness in the present study's relatively large group of RP patients. Patients with RP exhibited a significantly thinner choroidal layer compared to controls with similar age and refractive error.

The average choroidal thickness in the RP series was significantly thinner compared to the control group for each localization in measurements. These data agree with those of a previous investigation, which reported decreased choroidal blood flow in the patient and animal models of RP (8, 9). According to some authors, the characteristic photoreceptor degeneration in RP may cause this choroidal thinning: RP-related genetic defects may cause photoreceptor atrophy causing blood flow reduction.

A reduction in photoreceptors would decrease oxygen demand and, consequently, a reduction in blood supply (8-10).Conversely, according to other group researchers, vascular dysfunction may be a primary cause of the disease (11, 12). We also suggest that the thin choroid in the RP group of our study can be attributed to this decreased blood flow.

Choroidal thickness was not significantly associated with visual acuity in our study series. Similar to our study, no correlation has already been found with visual acuity (3, 13). The reason may be that RP patients can still retain a relatively good central vision even in very advanced stages of the disease. Like our study, Yeoh et al. reported no correlation between choroidal thinness, visual acuity, and central retinal

thickness in patients with various inherited retinal disorders, including Stargardt disease and macular dystrophy (14). In their study, Parodi et al. evaluated the functional importance of the retinal layer changes in RP patients. with multivariate regression analysis; they revealed that retinal layers are associated with a BCVA decline (15).

We confirm that choroidal thickness is significantly reduced in females compared to males. A male-to-female comparison of choroidal thickness in healthy eyes found that men had thicker choroids than women (16).

While previous studies found choroidal thinness to be associated with the degree of disease (5, 17), genetic predisposition (18), and age (5), we could not analyze the relation of choroid structure with age and disease stage. We did not perform genetic analyses of the patients. Again, we did not take into account the symptomatic process of the disease in this study because it is tough to define the exact manifestation of symptoms due to the insidious onset of RP, and we could not obtain reliable information about the onset of the disease from the patients in the detailed anamnesis. The onset of symptoms also depends on the person's environment (a person living in the countryside may notice nyctalopia symptoms earlier than someone living in the city). The best solution to this problem would be to prospectively collect choroidal thickness data according to RP disease progression. To accomplish this, it is necessary to correlate the changes in the choroidal vessels with parameters such as genetic factors, the severity of the disease, and age in a population-based study with larger sample size. Correlation studies may be conducted in specific genetic subtypes of RP in the future to investigate which specific mutations could be correlated with choroidal alterations.

A strong positive correlation was found between choroidal thickness and central retinal thickness. These findings suggest that RP's retinal and choroidal degeneration begin simultaneously in eyes. In our study, choroidal thickness was irregular in the RP group; the nasal choroid layer showed focal thinning. A thinner nasal choroid layer has been reported in previous studies (18-20). Our study confirms a similar choroidal profile in the healthy participants: with the thickest area present subfoveal and thinner regions nasally and temporally

The loss of choriocapillaris may result in mild choroidal thinning in certain hereditary retinal diseases. Intensified and widespread choroidal tissue loss may lead to further thinning. Even though EDI OCT resolution cannot accurately discriminate choriocapillaris, it can measure approximately 10% of the total choroidal thickness. As a result, our ability determines whether the thinning described in our report has reached the choriocapillaris was limited.

Choroidal thickness measurement was possible even in the most severe cases. It is promising to know that even in advanced stages, a small choroidal layer remains, especially under the fovea. Continuous perfusion is essential for the viability of the remaining retinal cells. Therefore, long-term stimulation via implants may also be possible. Again, it is important to define the distance between the eye layers correctly. Because interfering with the prosthesis in the thin choroidal layers may cause perforations.

CONCLUSION

RP is a retinal degeneration characterized by altered blood flow of the retina and choroid layer. With the present study, EDI-ECT demonstrated significantly thinner choroids in RP patients compared to age-matched and refraction-matched controls. In this group of patients, visual acuity was not related to the thickness of the subfoveal choroidal layer. However, it was found that the central retinal and subfoveal choroidal thickness were positively correlated. The results of this study support previous findings indicating a decreased choroidal vascular thickness and volume in patients diagnosed RP. Studying the correlation between choroidal thickness and the stage of the disease is vital in Rp patients. In further studies, it may be worthwhile to conduct a long-term follow-up study on RP patients and their choroidal layer status.

Strengths and Limitations

Based on our knowledge, the current study is one the most comprehensive studies measuring the choroidal thickness in RP patients and comparing these parameters with visual function.

The main limitation of the present study is that the patients were diagnosed RP based on clinical signs and auxiliary diagnostic techniques. The patients were not subjected to diagnostic genetic testing.

Its cross-sectional design is another limitation of the study. An evaluation of choroidal thickness is needed in patients with RP on a prospective, longitudinal basis. The role of the choroid in RP will be further illuminated by investigating retinal architecture and correlating it with vision and disease stages.

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Ethical approval: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and/or with the Helsinki Declaration of 1964 and later versions. Informed consent or substitute for it was obtained from all patients for being included in the study. Written consent was obtained from each patient to use their hospital data.

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