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Original Article

Evaluation of Peripapillary Choroidal Thickness, Retinal Nerve Fiber Layer, and Optic Nerve Head Parameters in Patients with Multiple Sclerosis

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Abstract

Objectives: The objectives of the study are to assess the peripapillary choroidal thickness (PPCT), retinal nerve fiber layer (RNFL), and optic nerve head (ONH) parameters in multiple sclerosis (MS) patients compared to healthy subjects.

Methods: One hundred and twenty-eight eyes from 64 patients were included in this cross-sectional study. Eighty-two eyes of 41 MS patients and 46 eyes of 23 healthy subjects were examined. PPCT and RNFL were measured using spectral-domain optical coherence tomography (OCT). PPCT was measured from the four quadrants around the optic disc at a distance of 1 mm (PPCT-1) and 2 mm (PPCT-2) from the edge of the ONH and the beginning of the retinal pigment epithelium. ONH parameters were measured with Heidelberg retinal tomography (HRT-3). Disease duration, the number of episodes, MS subtypes, and Expanded Disability Status Scale (EDSS) scores were recorded.

Results: The RNFL measurements and the mean PPCT-1 and PPCT-2 were significantly lower in MS patients compared to healthy individuals. PPCT-1 and PPCT-2 were measured as the thickest in the temporal quadrant, followed by the superior, nasal, and inferior quadrants, respectively, in both groups. When the ONH parameters were evaluated, cup/disc area ratio, cup area, and cup volume values were significantly higher, whereas optic rim volume and rim area values were significantly lower in MS patients compared to healthy subjects ($p<0.05$). We observed significant changes in RNFL and ONH parameters of MS patients in parallel with disease severity determined by EDSS scores and the presence of optic neuritis.

Conclusion: There were significant changes in RNFL thickness, PPCT, and ONH parameters when MS patients were compared with healthy subjects. Assessment of RNFL and PPCT with OCT and ONH with HRT-3 may be useful in the follow-up of MS patients.

Keywords: Multiple sclerosis, optic nerve head, peripapillary choroidal thickness

Introduction

Multiple sclerosis (MS) is a neurodegenerative and autoimmune disease causing various neuro-ophthalmic disorders. Optic neuritis (ON), optic nerve atrophy, diplopia, blurred vision, nystagmus, and eye movement disorders occur when the visual pathways are affected during the disease. Various visual field defects may be observed even if the patient's visual acuity is normal (1,2).

The leading cause of neurological dysfunction in MS is axonal loss. Although axons are relatively well preserved in

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the early period of MS, irreversible axonal deterioration and functional disability may occur as the disease progresses, even in patients receiving therapy (3). Mainly non-myelinated axons form the retinal nerve fiber layer (RNFL). Therefore, it is possible to reveal axonal loss with measurements of RNFL thickness and provide information about axonal loss throughout the central nervous system as a biomarker of progression in patients with MS (3,4). Optical coherence tomography (OCT) allows the retinal layers and choroidal tissue to be assessed. The RNFL thickness and choroidal thickness have been shown to decrease in MS patients (5,6).

Vascular dysregulations are thought to be responsible for the etiopathogenesis of MS (7). However, the role and biological response of the choroidal tissue around the optic nerve head (ONH) in neurological diseases such as MS, which affect the ONH, have not been fully elucidated. Peripapillary choroidal thickness (PPCT) is a parameter that can be measured by OCT. It has been reported that PPCT measured at different zones decreases in diseases such as glaucoma and MS (8-10).

Heidelberg retinal tomography (HRT) can assess the ONH in three dimensions with confocal laser scanning ophthalmoscopy (11). It has been reported that HRT can detect significant changes in ONH parameters in MS patients (12). However, as far as we are aware, there has been no study of the changes in PPCT measured perpendicularly at distances of 1 mm and 2 mm from the edge of the ONH and ONH parameters of MS patients by dividing them into subgroups according to their history of ON and Expanded Disability Status Scale (EDSS) score, which is used to evaluate the intensity of the disease and track changes in disability level in patients with MS (13).

We assessed the significance of RNFL, PPCT, and ONH parameters in the follow-up of MS patients by distinguishing them according to their history of ON episodes and EDSS scores and compared these outcomes with healthy controls in this study.

Methods

The study design was performed in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all individual participants who fulfilled the study criteria. This study was approved by the Ethical Board of Fatih Sultan Mehmet Education and Research Hospital (No: 17073117-050.06).

Study Design

One hundred and twenty-eight eyes of 64 patients participated in this cross-sectional research. Eight-two eyes of 41 MS patients who were followed up in the neurology department (group 1) and 46 eyes of 23 healthy controls (group 2) were evaluated. Two neurologists diagnosed the patients with MS using the McDonald criteria (14). Patients aged 18–65 years with a definite diagnosis of MS formed the study group. Healthy volunteers without ophthalmological or neurological comorbidity aged between 18 and 65 years formed the control group. Patients with ophthalmologic diseases other than refractive errors, patients with a coexisting systemic disease affecting the visual pathways, patients who underwent ophthalmic surgery, patients with active MS attacks or ON episodes within 90 days before the examination, patients with a spherical power of more than ± 5D, and a cylindrical power of more than ± 4D were not included.

All patients had a comprehensive neuro-ophthalmological examination, including pupillary reflexes, ocular motility, anterior segment evaluation, and fundus examination. The best-corrected visual acuity values, refractive status, spherical equivalents of refractive errors, central corneal thickness (CCT), and intraocular pressures (IOP) measured with an automatic non-contact tonometer, disease duration, number of MS episodes, number of ON episodes, MS subtypes, and EDSS scores of MS patients were recorded.

MS patients were reanalyzed after dividing them into two subgroups according to their EDSS values. Patients with an EDSS score below 2.5 were designated as group 1a (n=42) and those with an EDSS score of 2.5 and above were designated as group 1b (n=40). The study group was also separated into two subgroups considering their ON status: patients who had an ON were designated as group 1c (n=36), and patients without a previous ON were designated as group 1d (n=40). Patients with a history of visual deterioration for more than 90 days and those with a pale ONH were also added to group 1c.

Imaging Protocols and Measurements

The same expert performed all OCT scans between 14:00 and 16:30 without dilating the pupils using a spectral domain OCT (Nidek RS-3000, Japan). Scans with a signal quality below seven were not included in the study. The integrated software parameters were used to determine the average, inferior, superior, and temporal RNFL thickness around the ONH.

The PPCT was measured manually in enhanced depth imaging (EDI) OCT mode. It was measured vertically from the superior, inferior, temporal, and nasal regions around the ONH at a distance of 1 mm (PPCT-1) and 2 mm (PPCT-2) from the edge of the ONH. The vertical distance between the innermost edge of the choroido-scleral junction and the outermost edge of the RPE was calculated with the caliper function of the device software. The measurements were made twice by the same specialist who was unaware of the diagnoses of the patients, and the mean of the two measurements was used in the study to reduce manual errors. Figure 1 illustrates the technique used to measure nasal PPCT-1

and superior PPCT-2. The mean of PPCT-1 measured in four quadrants (PPCT-1-M) and the mean of PPCT-2 values measured in four quadrants (PPCT-2-M) were also calculated.

ONH was assessed with (HRT-3, HRT Software III GmBH 2006, Germany). HRT-3 scans were obtained with a 50 µm reference plane and a 15 × 15° angle. Before the images were acquired, we corrected for magnification errors using the patients' keratometry values and refractive errors. The device created a topographic image with a resolution of 384 × 384 pixels by performing three consecutive scans. After imaging, the boundaries of the optic disc were marked at 6 points and its contours were drawn. A topographic assessment of the ONH was performed using the image analysis software. Two ophthalmologists performed the HRT-3 scans without pharmacologic pupil dilation. The images with topographic standard deviation (SD) <30 µm were selected for analysis. The ratio of cup/disc (C/D) area, linear C/D, optic rim volume (RV), rim area (RA), cup volume (CV), cup area (CA), mean cup depth (MCD), and mean RNFL thickness were recorded.

Statistical Analysis

IBM SPSS Statistics Version 22 (SPSS Inc., Chicago, IL) software was used for statistical analyses. The Shapiro–Wilks test was used to assess the normality of the data. Student's t-test or Mann–Whiney U-test was used for comparisons of study and control groups according to the distribution of data. One-way ANOVA test with post hoc analysis or Kruskal–Wallis test was used for the comparison of more than two groups according to the distribution of data. The descriptive analysis of continuous variables was expressed as mean±SD. A $p<0.05$ was considered statistically significant.

Results

The study was performed on 128 eyes of 64 subjects aged between 18 and 65 years (mean: 39.97±10.24). Eighty-two eyes of 41 MS patients formed the study group (group 1), 46 eyes of 23 healthy subjects formed the control group (group 2). The mean age of group 1 was 41.93±10.95 years, and that of group 2 was 36.48±7.80 years. The subtype of MS was relapsing-remitting in the majority of cases (92.7%). 4.9% of patients had primary progressive, and 2.4% had secondary progressive subtype of disease. No significant difference was detected between the groups in terms of spherical equivalent, CCT, and IOP values ($p<0.05$). Table 1 shows the general characteristics of the patients in each group.

Table 1. General characteristics and comparison of group 1 and group 2

	Group 1 MS Mean±SD	Group 2 Control Mean±SD	Total Mean±SD	p
Age	41.93±10.95	36.48±7.80	39.97±10.24	[1]0.004*
BCVA	0.92±0.17	1±0.00	0.95±0.14	[2]0.000*
Spherical equivalent	-0.22±1.21	-0.66±1.63	-0.38±1.38	[1]0.082
CCT	536.83±24.94	537.91±31.33	537.22±27.29	[1]0.830
IOP	15.1±2.9	15.09±2.12	15.09±2.64	[1]0.981
Disease duration (years)	8.54±7.23			
Number of MS attacks	5.90±11.29			
Number of ON attacks	0.78±1.12			
EDSS score	2.80±1.79			
	n (%)	**n (%)**	**n (%)**	
Gender				
Male	26 (31.7)	20 (43.5)	46 (35.9)	[3]0.183
Female	56 (68.3)	26 (56.5)	82 (64.1)	
History of ON attack				
Present	36 (43.9)			
Absent	46 (56.1)			

[1]Student's t-test; [2]Mann–Whitney U test, [3]Chi-square test, *p<0.05. BCVA: Best-corrected visual acuity; CCT: Central corneal thickness; IOP: Intraocular pressure; MS: Multiple sclerosis; ON: Optic neuritis; EDSS: Expanded Disability Status Scale.

RNFL and PPCT values and ONH parameters of the study group and the control group are compared in Table 2. Significant thinning of mean PPCT-1 and mean PPCT-2 was observed in group 1 compared to group 2. The PPCT-1 in the nasal, temporal, and superior quadrants was thinner and the PPCT-2 in the superior and temporal quadrants was thinner in group 1 compared to group 2 ($p<0.05$). The PPCT-1 and PPCT-2 were measured thickest in the temporal quadrant, followed by the superior, nasal, and inferior quadrants, respectively, in both group 1 and group 2. HRT-3 analysis of the ONH revealed significant changes. Optic disc C/D area ratio, linear C/D ratio, CA, and CV were significantly higher in group 1 than in group 2; RV, RA, and RNFL values were significantly lower in group 1 than those in group 2 ($p<0.05$).

MS patients who had an EDSS value of below 2.5 formed group 1a (n=42), and patients with an EDSS value of 2.5 and above constituted group 1b (n=40) for subgroup analysis. The analysis of the general characteristics, RNFL, PPCT, and ONH parameters of these groups is shown in Table 3. In addition to superior PPCT-1, temporal PPCT-1, and PPCT-1-M,

Table 2. Distribution of the RNFL, PPCT, and ONH parameters of group 1 and group 2

	Group 1 MS Mean±SD	Group 2 Control Mean±SD	p
OCT-RNFL			
Inferior	115.84±25.74	133.39±13.65	[1]0.000*
Superior	116.84±26.03	129.37±14.21	[1]0.001*
Nasal	66.98±16.57	75.72±16.29	[1]0.005*
Temporal	59.57±14.91	71.02±13.62	[1]0.000*
Average	89.82±17.41	102.33±8.15	[1]0.000*
OCT-PPCT-1			
Inferior	150.77±50.76	160.15±53.05	[1]0.325
Superior	184.88±47.95	208.41±58.86	[1]0.016*
Nasal	173.01±44.17	194±50.86	[1]0.016*
Temporal	185.15±48.63	210.2±53.32	[1]0.008*
Average	173.45±41.02	193.19±46.64	[1]0.014*
OCT-PPCT-2			
Inferior	160.54±51.4	177.52±55.66	[1]0.084
Superior	215.39±54.58	242±55.79	[1]0.010*
Nasal	207.61±58.63	227.72±58.37	[1]0.065
Temporal	230.91±50.52	257.33±48.32	[1]0.005*
Average	203.61±44.46	226.14±42.77	[1]0.006*
HRT			
C/D (area)	0.3±0.17	0.2±0.14	[1]0.001*
C/D (linear)	0.52±0.16	0.41±0.17	[1]0.000*
RA	1.43±0.39	1.68±0.45	[2]0.002*
RV	0.36±0.18	0.48±0.21	[2]0.002*
CA	0.67±0.53	0.45±0.37	[2]0.007*
CV	0.17±0.29	0.1±0.12	[2]0.023*
MCD	0.23±0.11	0.21±0.12	[2]0.154
RNFL	0.21±0.09	0.26±0.07	[1]0.002*

[1]Student t-Test, [2]Mann–Whitney U test, *P<0.05. MS: Multiple sclerosis, OCT: Optical coherence tomography, RNFL: Retinal nerve fiber layer, PPCT: Peripapillary choroidal thickness, PPCT-1: PPCT values measured from 1 mm, PPCT-2: PPCT values measured from 2 mm, HRT: Heidelberg retinal tomography, ONH: Optic nerve head, C/D: Cup/Disc, RA: Rim area, RV: Rim volume, CA: Cup area, CV: Cup volume, MCD: Mean cup depth.

Table 3. Evaluation of general characteristics, RNFL, PPCT, and ONH parameters of group 1a, group 1b, and group 2

	Group 1a (EDSS<2,5) (n=42) Mean±SD	Group 1b (EDSS≥2.5) (n=40) Mean±SD	Group 2 Control (n=46) Mean±SD	p
Age	39.76±12.47	44.2±8.68	36.48±7.8	[1]0.002*
BCVA	0.96±0.13	0.88±0.19	1±0	[2]0.000*
Spherical equivalent	-0.22±1.37	-0.22±1.02	-0.66±1.63	[1]0.222
CCT	535.24±30.62	538.5±17.33	537.91±31.33	[1]0.846
IOP	15.07±2.44	15.13±3.35	15.09±2.12	[1]0.996
Gender (Male/Female)	16/26	10/30	20/26	[3]0.192
OCT-RNFL				
Inferior	122.57±21.22	108.78±28.34	133.39±13.65	[1]0.000*
Superior	124.52±17.96	108.78±30.62	129.37±14.21	[1]0.000*
Nasal	70.29±14.03	63.5±18.41	75.72±16.29	[1]0.003*
Temporal	60.1±12.43	59.03±17.28	71.02±13.62	[1]0.000*
Average	94.36±13.47	85.05±19.83	102.33±8.15	[1]0.000*
OCT-PPCT-1				
Inferior	139.12±46.69	163±52.54	160.15±53.05	[1]0.067
Superior	179.52±45.16	190.5±50.68	208.41±58.86	[1]0.035*
Nasal	171.26±46.9	174.85±41.62	194±50.86	[1]0.055
Temporal	181.1±55.39	189.4±40.62	210.2±53.32	[1]0.023*
Average	167.75±40.63	179.44±41.09	193.19±46.64	[1]0.024
OCT-PPCT-2				
Inferior	147.38±47.27	174.35±52.5	177.52±55.66	[1]0.015*
Superior	198.88±51.3	232.73±53.09	242±55.79	[1]0.001*
Nasal	197.71±57.6	218±58.6	227.72±58.37	[1]0.056
Temporal	234.93±60.4	226.7±37.83	257.33±48.32	[1]0.014*
Average	194.73±43.97	212.94±43.57	226.14±42.77	[1]0.004
HRT				
C/D (area)	0.24±0.13	0.36±0.19	0.2±0.14	[1]0.000*
C/D (linear)	0.47±0.14	0.58±0.16	0.41±0.17	[1]0.000*
RA	1.5±0.38	1.35±0.39	1.68±0.45	[2]0.002*
RV	0.39±0.17	0.33±0.19	0.48±0.21	[2]0.003*
CA	0.5±0.35	0.84±0.62	0.45±0.37	[2]0.001*
CV	0.09±0.11	0.25±0.39	0.1±0.12	[2]0.000*
MCD	0.19±0.07	0.27±0.14	0.21±0.12	[2]0.012*
RNFL	0.23±0.08	0.2±0.1	0.26±0.07	[1]0.005*

[1]One-way ANOVA test; [2]Kruskal–Wallis test; [3]Chi-square test; *P<0.05, EDSS: Expanded disability status scale; BCVA: Best-corrected visual acuity; CCT: Central corneal thickness; IOP: Intraocular pressure; OCT: Optical coherence tomography; RNFL: Retinal nerve fiber layer; PPCT: Peripapillary choroidal thickness; PPCT-1: PPCT values measured from 1 mm; PPCT-2: PPCT values measured from 2 mm; HRT: Heidelberg retinal tomography; ONH: Optic nerve head; C/D: Cup/Disc; RA: Rim area; RV: Rim volume; CA: Cup area; CV: Cup volume; MCD: Mean cup depth.

the values of superior PPCT-2, inferior PPCT-2, and PPCT-2-M of group 1a were also significantly lower compared to group 2. The superior PPCT-2 of group 1a was thinner compared to group 1b ($p<0.05$). In addition, the temporal PPCT-2 of group 1b was thinner compared to the control group ($p<0.05$). The ratio of optical C/D areas, linear C/D ratio, CA, CV, and MCD values of group 1b were also significantly higher than those of group 1a and group 2 ($p<0.05$).

The MS patients were further separated into two subgroups according to whether they had an ON episode or not: those with a previous ON formed group 1c (n=36), and those without a previous ON episode formed group 1d (n=46). The evaluation of RNFL, PPCT, and ONH parameters of group 1c, group 1d, and group 2 are shown in Table 4. The superior, nasal, and temporal PPCT-1 were thinner in group 1c compared to group 2 ($p<0.05$). The superior and temporal PPCT-2 values of group 1c were also reduced compared to the control group ($p<0.05$). While no significant

Table 4. Evaluation of general characteristics, RNFL, PPCT, and ONH parameters of group 1c (ON+), group 1d (ON-), and group 2

	Group 1c (n=36) ON+ Mean±SD	Group 1d (n=46) ON- Mean±SD	Group 2 (n=46) Control Mean±SD	p
Age	44.81±9.19	39.67±11.76	36.48±7.8	[1]0.001*
BCVA	0.86±0.23	0.97±0.08	1±0	[2]0.000*
Spherical equivalent	-0.33±1.1	-0.14±1.29	-0.66±1.63	[1]0.183
CCT	537.5±20.48	536.3±28.16	537.91±31.33	[1]0.959
IOP	15.06±3.22	15.13±2.66	15.09±2.12	[1]0.992
Gender (Male/Female)	10/26	16/30	20/26	[3]0.332
OCT-RNFL				
Inferior	109.5±27.38	120.8±23.51	133.39±13.65	[1]0.000*
Superior	108.42±29.36	123.43±21.16	129.37±14.21	[1]0.000*
Nasal	62.78±16.74	70.26±15.84	75.72±16.29	[1]0.002*
Temporal	58.89±16.74	60.11±13.47	71.02±13.62	[1]0.000*
Average	84.86±18.89	93.7±15.26	102.33±8.15	[1]0.000*
OCT-PPCT-1				
Inferior	151.64±56.51	150.09±46.41	160.15±53.05	[1]0.612
Superior	177.22±55.82	190.87±40.4	208.41±58.86	[1]0.027*
Nasal	167.56±41.41	177.28±46.21	194±50.86	[1]0.036*
Temporal	180.47±44.9	188.8±51.55	210.2±53.32	[1]0.023*
Average	169.22±44.89	176.76±37.89	193.19±46.64	[1]0.037*
OCT-PPCT-2				
Inferior	160.72±55.35	160.39±48.71	177.52±55.66	[1]0.226
Superior	207.5±63.03	221.57±46.73	242±55.79	[1]0.019*
Nasal	202.94±59.45	211.26±58.37	227.72±58.37	[1]0.149
Temporal	222.42±43.76	237.57±54.79	257.33±48.32	[1]0.007*
Average	198.40±50.16	207.70±39.52	226.14±42.77	[1]0.015*
HRT				
C/D (area)	0.33±0.19	0.28±0.16	0.2±0.14	[1]0.002*
C/D (linear)	0.55±0.17	0.5±0.15	0.41±0.17	[1]0.001*
RA	1.33±0.30	1.51±0.43	1.68±0.45	[2]0.001*
RV	0.3±0.16	0.4±0.19	0.48±0.21	[2]0.000*
CA	0.75±0.58	0.6±0.48	0.45±0.37	[2]0.014*
CV	0.18±0.26	0.16±0.31	0.1±0.12	[2]0.040*
MCD	0.23±0.11	0.23±0.12	0.21±0.12	[2]0.354
RNFL	0.2±0.09	0.23±0.09	0.26±0.07	[1]0.004*

[1]One-way ANOVA test; [2]Kruskal–Wallis test; [3]Chi-square test; *P<0.05. ON: Optic neuritis; BCVA: Best-corrected visual acuity; CCT: Central corneal thickness; IOP: Intraocular pressure; OCT: Optical coherence tomography; RNFL: Retinal nerve fiber layer; PPCT: Peripapillary choroidal thickness; PPCT-1: PPCT values measured from 1 mm; PPCT-2: PPCT values measured from 2 mm; HRT: Heidelberg retinal tomography; ONH: Optic nerve head; C/D: Cup/Disc; RA: Rim area; RV: Rim volume; CA: Cup area; CV: Cup volume; MCD: Mean cup depth.

difference was observed between group 1c and group 1d in PPCT-1-M and PPCT-2-M measurements, the PPCT-1-M and PPCT-2-M values of group 1c were lower than those of group 2 ($p<0.05$). While the ratio of C/D area, linear C/D, CA, and CV were higher in group 1c than in group 2, only the linear C/D ratio of group 1d was higher compared to that of group 2 ($p<0.05$). RV and RNFL thickness was significantly reduced in group 1c compared to the control group; RV was also significantly lower in group 1c compared to group 1d ($p<0.05$).

Discussion

MS is a multifactorial systemic autoimmune disease causing axonal degeneration and vascular dysregulation (3,7). The role of the choroidal tissue around the ONH and the morphological changes of the optic disc in MS pathogenesis is not yet fully understood. As far as we know, this is the first study assessing the PPCT measured perpendicularly at a distance of 1 mm and 2 mm from the edge of the optic disc and the ONH characteristics of MS patients by distinguishing them considering the disease severity indicated by EDSS values and history of ON episodes.

It has been shown that progressive loss of optic axons in MS patients may be an important biomarker for monitoring disease progression, and RNFL attenuation has been shown to be associated with increased EDSS value, which is an indicator of progression in MS (15-17). We found that the RNFL was significantly thinner in all quadrants in MS patients who had a history of ON, and this thinning was associated with the EDSS score. In addition, the mean, inferior, and temporal RNFL was thinner in MS patients without a previous ON attack compared with healthy subjects.

We measured PPCT in MS patients in the four quadrants around the ONH perpendicularly at a distance of 1 mm and 2 mm from the optic disc and found that in addition to superior, nasal, and temporal PPCT-1, superior and temporal PPCT-2, mean PPCT-1, and mean PPCT-2 were significantly lower in MS patients. The PPCT-1 and PPCT-2 were measured thickest in the temporal quadrant in both MS patients and healthy participants, followed by the superior, nasal, and inferior quadrants, respectively. The reason why PPCT was measured thickest in the temporal quadrant may be a compensatory mechanism related to macular preservation. Moreover, Garcia et al. automatically calculated PPCT in MS patients using a swept-source OCT in four choroidal zones and showed that PPCT was significantly reduced in all zones in MS patients, with changes decreasing with increasing distance from the optic disc (9). PPCT was thicker in the superior division, followed by the temporal, nasal, and inferior divisions in their study in both control and MS patients.

Axonal damage in the RNFL due to neurodegeneration may lead to a decrease in blood flow to the neuroretina and consequently to a decrease in PPCT. As the choroidal tissue decreases, further RNFL damage may occur due to ischemia (5,16,18). The vascular elements involved in the inflammatory response may play a key role in reducing choroidal blood flow. Significant reductions in retrobulbar blood flow have been observed in patients with MS, and it has been suggested that this is possibly related to the blood levels of endothelin-1, which is a vasoconstrictor peptide (7,19). Spain et al. reported that the ONH flow index was lower in MS patients and MS impaired ONH blood flow (20). Esen et al. demonstrated that the choroidal thickness of the subfoveal region was not significantly different between MS patients who had ON and those without a previous ON (6). Similarly, we found that mean PPCT-1 and PPCT-2 measurements were not significantly different between MS eyes with or without previous episodes of ON. In addition, we found a significant decrease in mean PPCT-1 and PPCT-2 levels of MS eyes with previous ON compared to healthy subjects.

It was reported that the standard HRT could detect the ONH differences in 8 eyes of 23 MS patients using the normal database (12). It was highlighted that HRT-2 revealed a significant difference in RV, RNFL thickness, and optic disc cup shape measurement in patients with a previous single attack of ON (21). In our study, the ratio of the C/D areas, the linear C/D ratio, and the values CA and CV, measured by HRT-3, were significantly higher, and the RV, RA, and RNFL values were significantly lower in patients with MS than in healthy controls. Our results showed that C/D area ratio, linear C/D ratio, CA, CV, and MCD were significantly higher in patients with higher EDSS scores than those with lower EDSS scores and the control group, suggesting that HRT-3 is important for monitoring ONH changes in patients with MS during the follow-up of the disease. The finding that the duration of disease and the number of MS relapses were positively correlated with CA, CD, and MCD scores may be related to the fact that the vessels supplying the ONH are more exposed to vasoconstrictive agents with increasing disease duration and number of relapses (7).

This study has several limitations. It has been reported that refractive status, gender, age, IOP, ocular, and systemic diseases may affect the thickness of the choroid (22-26). In our study, gender distribution, IOP, and CCT values did not differ significantly between groups; however, small age differences between groups may have influenced the results. Besides, it has been reported that the choroidal thickness of the subfoveal region does not correlate with age in individuals under 60 years old (27). In addition, another study reported that no significant correlation was detected between PPCT and age (28). We did not evaluate the axial length of the patients; however, the refractive errors were not significantly different between the groups. One study found that

axial length and refractive status variables had a similar relation when measured with OCT (29). Although PPCT was measured manually using EDI-OCT, the technique has been shown to have high interobserver and intraobserver correlation and good reproducibility (25).

Conclusion

We observed a significant decrease in mean RNFL thickness and PPCT and demonstrated significant changes in ONH parameters in MS patients compared to healthy subjects. Our results showed that there were significant changes in RNFL thickness and ONH parameters in parallel with disease progression as determined by EDSS scores and the presence of ON. We believe that assessment of ONH parameters using HRT-3 as well as RNFL thickness may be useful in evaluating the progression of MS. Prospective, randomized, and long-term studies are needed to better understand the significance of PPCT, RNFL, and ONH changes in the clinical course and etiopathogenesis of MS.

Disclosures

Ethics Committee Approval: This study was approved by the Ethical Board of Fatih Sultan Mehmet Education and Research Hospital (No: 17073117-050.06).
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