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Retinal layers thickness and retinal vascular parameters in patients with multiple sclerosis

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多发性硬化症患者视网膜层厚度及血管参数研究

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摘要

目的:探究多发性硬化症(MS)患者视网膜血管性参数和视网膜层厚度变化。

方法:单中心病例对照研究。纳入 2020 年 3 月至 2021 年 3 月于伊朗大学神经内科及眼科就诊的 MS 患者作为 MS 组及年龄性别匹配的健康医院职工作为对照组。记录患者眼部参数,使用光学相干断层扫描评估各层视网膜厚度。

结果:本研究共纳入 85 例受试者,平均年龄为 40.44±11.52岁,其中女性共 61 例(72%)。对照组 43 例平均年龄为 39.49±11.07 岁,MS 组 42 例平均年龄为 41.40±12.01 岁。MS 组患者的平均病程为(8.45±6.04)a。MS 组患者右眼神经节细胞层厚度较对照组显著降低($P=0.034$)。此外,除左鼻侧外($P=0.106$),MS 组各检测方位视神经周围平均神经束值均显著低于对照组($P<0.05$)。MS 组双眼各区域深层及浅层毛细血管网的平均血流密度均低于对照组,其中所有浅层毛细血管网平均血流密度比较均具有统计学意义(除左眼鼻侧外,其余 $P<0.05$)。

结论:MS 患者视网膜厚度显著降低。光学相干断层扫描结果可作为评估 MS 患者疾病进展和预后的可靠工具。

关键词:多发性硬化症;光学相干断层扫描;视网膜;视网膜血管性疾病;视网膜层厚度

Abstract

• AIM: To investigate the changes of retinal vascular parameters and retinal layer thickness in patients with multiple sclerosis (MS).

• METHODS: This single-centered case-control study was performed on a MS group of 42 patients diagnosed with MS and a control group of 43 healthy hospital staff matched in terms of age and sex at Iran University, department of neurology and ophthalmology from March 2020 to March 2021. The ophthalmic parameters of each patient were recorded, and optical coherence tomography was used to evaluate the retinal thickness in the layers.

• RESULTS: This study enrolled a total of 85 participants, with a mean age of 40.44±11.52 years, including 61 females (72%). The control group consisted of 43 individuals with a mean age of 39.49±11.07 years, while the MS group comprised 42 participants with a mean age of 41.40±12.01 years. The mean disease duration in the MS group was 8.45±6.04 a. The thickness of the ganglion cell layer in the right eye was significantly lower in the MS group compared to the control group ($P=0.034$). In addition, except for the left nasal sector ($P=0.106$), the mean peripapillary neurofibrillation in all examined sectors were significantly lower in the MS group than in the control group ($P<0.05$). The average vessel density in both the deep and superficial capillary plexuses across all regions of both eyes was lower in the MS group than in the control group, with all comparisons for the superficial capillary plexus showing statistical significance ($P<0.05$ for all except the left nasal sector).

• CONCLUSION: The thickness of the retina of patients with MS is significantly reduced. Therefore, optical coherence tomography results can be used as a reliable tool to evaluate disease progression and prognosis in MS patients.

• KEYWORDS: multiple sclerosis; optical coherence tomography; retina; retinal vascular disorder; retinal layer thickness
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INTRODUCTION

Multiple sclerosis (MS) is a chronic progressive inflammatory and neurodegenerative disorder, leading to demyelination of the central nervous system (CNS). Increasing prevalence and incidence of MS and its economic and medical burdens pose the disease as one of the main causes of disability and mortality in the working age population. Signs and symptoms of MS vary individually, regarding the extent and location of degenerated nerve fibers. Different types of ocular involvement occur in approximately 80% of patients with MS, including vision impairment, visual haziness, dyschromatopsia, deficit of ocular movement, nystagmus and *etc*.[1-2]. Optic neuritis (ON), one of the most common manifestations of MS, is kind of optic neuropathy which induces visual impairment in young adults between the ages of 15-49[3]. It would emerge as a presenting symptom in 38% of patients with MS and can progress to MS within 15 years in 50% of patients[4-5]. Additionally, MS could induce several subclinical ophthalmic signs, containing retinal layer thinning and pathologic microvascular changes[6-7].

Considering new advanced noninvasive technologies, optical coherence tomography (OCT) and OCT angiography (OCTA) enable physicians to survey the retinal layers' segmentation and thickness, vessel density (VD) and microvascular patterns, respectively. Nerve fiber layer (NFL) and ganglion cell layer (GCL) are the most commonly affected retinal layers among patients with MS, regardless of experiencing ON or not, and could be readily obtained through OCT[7-8]. OCTA could capture high-resolution three-dimensional images of retinal and choriocapillary vasculatures and monitor the changes in MS eyes[6].

Several studies have demonstrated that the changes in retinal layer thickness and vascular density, as a marker of neural loss, contribute to the probable disability of MS[9]. Hence, these evaluations would predict the MS prognosis. In the present study, we aimed to determine the total retinal layers and peripapillary retinal nerve fiber layer (RNFL) thickness and microvasculature density of superficial and deep capillary plexuses of MS eyes with and without a history of ON compared with healthy control (HC) eyes using OCT and OCTA respectively, among Iranian population.

PARTICIPANTS AND METHODS

Ethical Approval The ethics committee of the Iran University of Medical Sciences (IUMS) approved the study design (No.3-273), and informed consent was obtained from all participants. The tenets of the Declaration of Helsinki were followed as well.

Participants Our case-control, comparative, and single-centered study was conducted at Iran University, department of neurology and ophthalmology from March 2020 to March 2021. A total of 42 healthy (as a control group) and 43 individuals with MS were recruited in the study. We used the McDonald 2017 criteria to diagnose MS and all mandatory antibodies and viral markers were checked [antinuclear antibodies (ANA; Titers), double stranded DNA (DsDNA; Titers), B2Glycoprotein (U/mL), Lupus anticoagulant (GPL unit), anti cardiolipine antibody (GPL U/mL), antineutrophil cytoplasmic antibody (CANCA; Titers), perinuclear anti-neutrophil cytoplasmic antibody (PANCA; Titers), anti phospholipid antibody (MPL units/mL) and human immunodeficiency virus (HIV) antibody (Titers), hepatitis B surface (HBS) antigen (mIU/mL), hepatitis C virus (HCV) antibody (IU/mL)]. Additionally, all patients underwent brain, cervical and thoracic magnetic resonance imaging (MRI)[10]. The Expanded Disability Status Scale (EDSS) score cutoffs were used to define disease severity[11]. The ophthalmic parameters of each patient were recorded. Best-corrected visual acuity (BCVA) and refractive errors of participants were measured precisely. Intraocular pressure (IOP) was measured by Goldmann applanation tonometer (GAT) twice and the mean was considered as IOP level. Patients with IOP>21 mmHg, glaucoma, pathologic myopic with refractive error ≥6 D, history of ocular surgery, retinal vascular disorders, and any corneal or vitreous opacities which prevent to capture of OCT and OCTA images were excluded. Subjects who could not cooperate in the imaging acquisition were also excluded.

OCTA images were obtained using the OptovueRTVue XR Avanti (Software version 2017.1.0.15, Optovue, Inc. Fremont, CA). Regarding Optovue, images with a quality score of <5 were excluded, and imaging was repeated until acceptable quality was achieved. The superficial capillary plexus (SCP) en face image was segmented automatically with an inner boundary set at the internal limiting membrane (ILM) and an outer boundary set 9 μm above the inner plexiform layer (IPL). The deep capillary plexus (DCP) en face image was segmented with an inner boundary 9 μm above the IPL and an outer boundary at 9 μm below the outer plexiform layer (OPL). Each set of optic disc scans comprised of 4.5 mm×4.5 mm images, centered on the disc, while foveal ones comprised of both 3 mm×3 mm and 6 mm×6 mm images, centered on the fovea. We used the Heidelberg Spectralis OCT instrument (Heidelberg Engineering, Inc., Heidelberg, Germany) to measure various retinal layers thickness including RNFL, GCL and other layers. Peripapillary optical coherence tomography of healthy person and patient with severe MS were shown in Figures 1 and 2, respectively.

The foveal avascular zone (FAZ), the central vessel-free area of the macula was evaluated automatically by OCTA.VD, which was defined as the percentage of the area occupied by blood vessels, in the SCP and DCP of the fovea cite (central 1 mm of the ETDRS grid), parafovea area (500-1500 mm from the foveal center), and the whole image, automatically was evaluated. Foveal VD was also measured automatically for VD of a ring limited by the FAZ outline and a parallel outer boundary 300 mm from the FAZ area (FD-300). Retinal layer thickness, in particular, RNFL and radial peripapillary capillary (RPC) density (whole, inside disc, and peripapillary density) were measured by OCTA automatically.

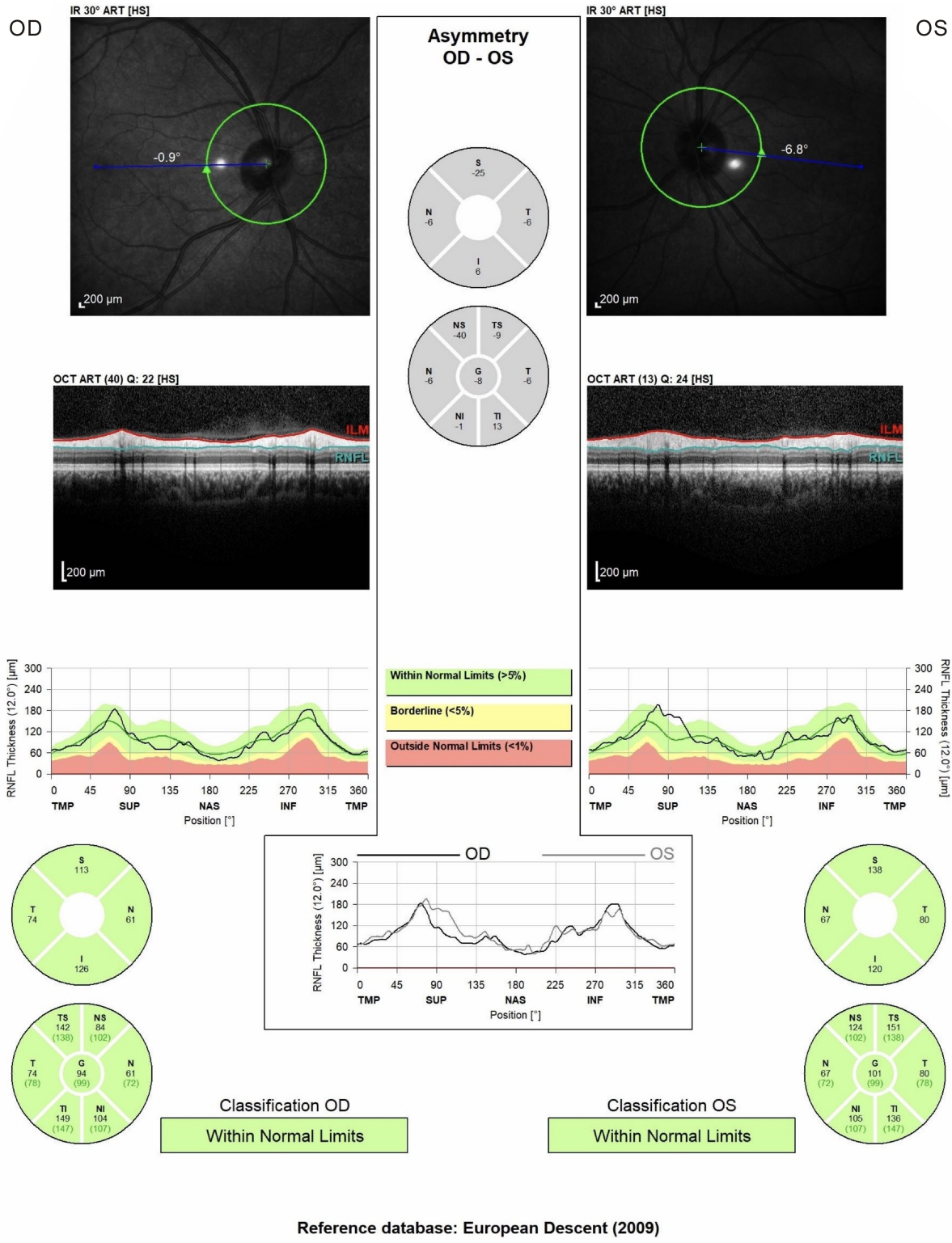

Figure 1 Peripapillary optical coherence tomography of healthy person. OCT: Optical coherence tomography; ILM: Internal limiting membrane; RNFL: Retinal nerve fiber layer.

Statistical Analysis Baseline characteristics of the study population are described as the mean ± SD values for continuous variables, and as frequencies (%) for categorical variables. To assess the homogeneity of two groups regarding demographics and clinical items, Chi-square and independent t-test were used. All of the analyses were done by SPSS 26 and $P<0.05$ was defined as a significant level.

RESULTS

The study population consisted of 42 healthy (as a control group) and 43 individuals with MS, with a mean age of 39.49±11.07 years and 41.40±12.01 years, respectively (the mean age of total participants was 40.44 ± 11.52 years). A total of 61(72%) participants were female. The mean duration of illness in patients accounted for 8.45±6.04 years. There was not any significant difference between the two groups in terms of gender and age (P value of 0.370 and 0.447, respectively).

Among 43 patients with MS, 21 cases (nearly 50%) had previous history of ON. Regarding EDSS, disease severity

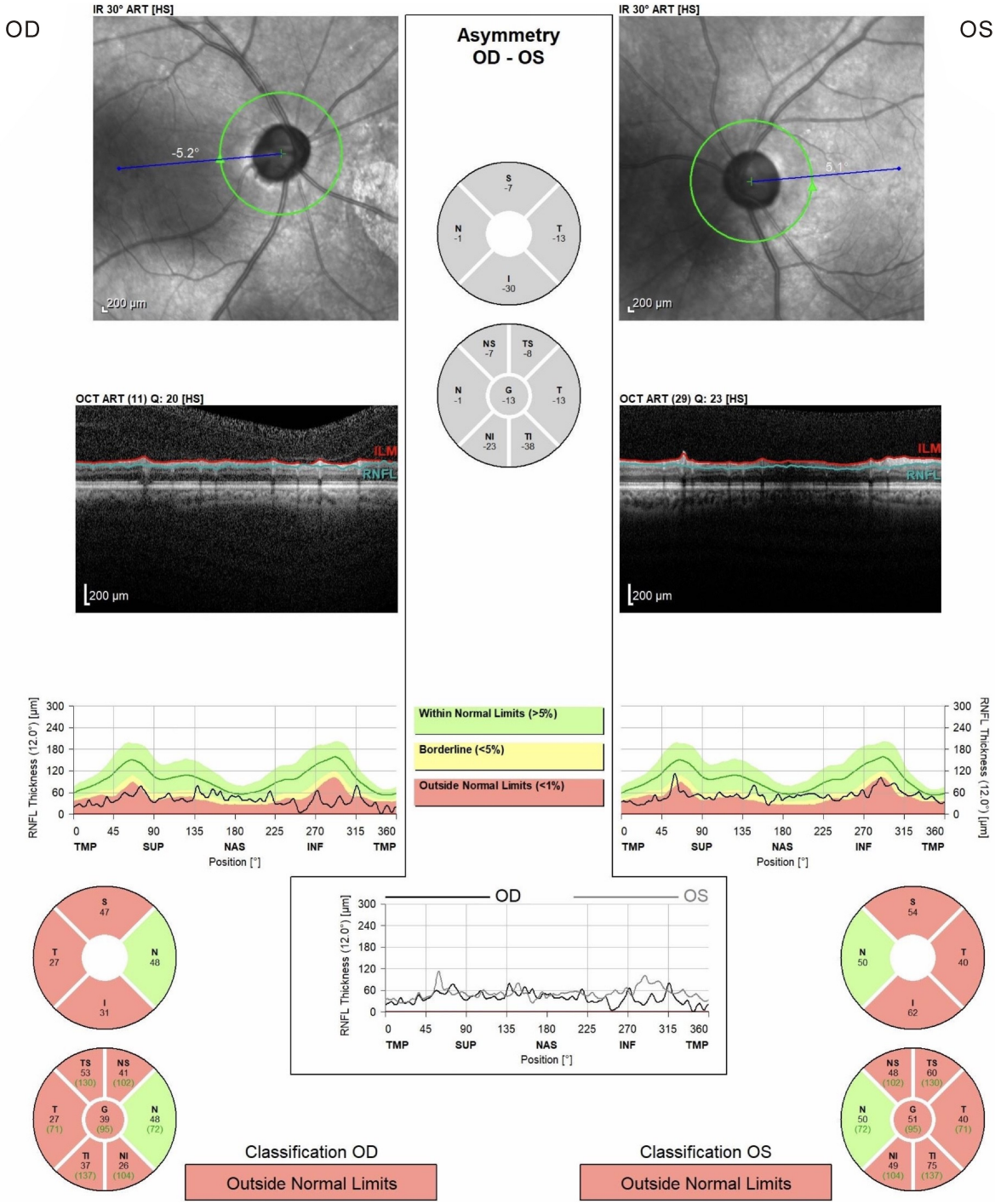

Figure 2 Peripapillary optical coherence tomography of patient with severe multiple sclerosis. OCT: Optical coherence tomography; ILM: Internal limiting membrane; RNFL: Retinal nerve fiber layer.

conferred the hazard interval of 1.0 to 4.5 (2.26±1.03). Dinozol, Rituximab and Fingolimod were the most frequently used drugs by MS patients.

Peripapillary retinal nerve fiber layer thicknesses The comparison of peripapillary RNFL thicknesses of healthy and MS eyes in both right and left eyes were measured (Table 1). Compared with healthy people, MS patients had significantly lower peripapillary RNFL thicknesses in all sections except for nasal part peripapillary region in left eye (72.93±14.74 in healthy eyes *vs.* 67.02±18.22 in MS eyes, $P=0.106$).

Peripapillary retinal thickness Table 2 reveals the comparison of peripapillary retinal thickness of different sections between healthy and MS eyes. In compare to healthy individuals, foveal thickness of left eye of MS group was lower; but not in a significant manner ($P=0.846$). However, compared to healthy eyes, lower foveal thickness in right MS eyes reached the statistically significant level (251.47±17.11 in healthy eyes *vs.* 242.90±20.42 in MS eyes, $P=0.039$). Additionally, retinal thickness in parafoveal, nasal, temporal, superior and inferior regions of both eyes were lower in MS group (all $P<0.05$).

Vessels density of superficial and deep capillary plexuses Table 3 shows the OCTA measurements in two groups, which displays the comparison of vessels density of SCP and DCP in

Table 1 Comparison of peripapillary retinal nerve fiber layer thickness of different sections between healthy and multiple sclerosis eyes

($\bar{x}\pm s$, μm)

Sections	Right eye			Left eye		
	Healthy group	MS group	*P*	Healthy group	MS group	*P*
Supratemporal	139.81±17.24	125.02±27.00	0.004	135.40±18.62	120.69±23.71	0.002
Supranasal	113.07±17.99	93.50±22.73	<0.001	119.70±23.84	103.07±23.70	0.002
Nasal	80.00±13.10	70.81±17.24	0.007	72.93±14.74	67.02±18.22	0.106
Temporal	70.53±11.58	60.57±14.18	0.001	70.49±10.42	58.24±12.59	<0.001
Infronasal	124.42±22.23	107.33±33.54	0.007	118.70±22.68	105.74±30.80	0.030
Infrotemporal	143.33±22.21	126.86±28.12	0.004	148.02±20.61	124.95±33.87	<0.001

MS: Multiple sclerosis.

Table 2 Comparison of peripapillary retinal thickness of different sections between healthy and multiple sclerosis eyes

($\bar{x}\pm s$, μm)

Sections	Right eye			Left eye		
	Healthy group	MS group	*P*	Healthy group	MS group	*P*
Total	319.95±15.83	300.48±19.08	<0.001	315.72±28.50	302.21±17.80	0.011
Foveal	251.47±17.11	242.90±20.42	0.039	246.88±40.55	245.40±27.93	0.846
Parafoveal	330.12±16.10	309.15±20.19	<0.001	326.53±29.85	310.90±18.36	0.005
Temporal	319.93±16.74	301.63±19.47	<0.001	319.43±13.87	303.43±17.78	<0.001
Superior	355.51±15.53	312.98±20.11	<0.001	331.35±28.88	315.74±18.84	0.004
Nasal	333.70±15.34	311.88±21.29	0.001	329.30±36.67	312.81±20.78	0.017
Inferior	331.51±18.31	310.98±20.98	<0.001	332.74±16.05	311.98±18.55	<0.001

MS: Multiple sclerosis.

Table 3 Comparison of vessels density of superficial and deep capillary plexuses in different sections between healthy and multiple sclerosis eyes

($\bar{x}\pm s$, %)

Plexus (sections)	Right eye			Left eye		
	Healthy group	MS group	*P*	Healthy group	MS group	*P*
Superficial capillary plexus						
Total	47.44±2.03	43.66±5.26	<0.001	47.34±3.16	44.94±5.09	0.011
Parafoveal	50.50±2.17	46.53±5.63	<0.001	50.13±3.67	47.90±5.47	0.030
Temporal	48.44±2.27	45.01±5.42	<0.001	48.56±3.55	46.37±4.98	0.023
Superior	52.11±2.45	48.01±6.54	<0.001	51.36±4.19	48.89±6.01	0.030
Nasal	49.21±2.78	45.50±6.49	0.001	48.98±4.64	47.15±5.44	0.100
Inferior	52.14±2.51	47.71±5.90	<0.001	51.84±3.37	49.19±6.11	0.016
Deep capillary plexus						
Total	52.03±4.87	51.21±3.95	0.396	53.41±4.87	52.98±3.31	0.507
Parafoveal	54.39±4.64	53.09±3.96	0.170	55.46±2.73	54.66±3.68	0.265
Temporal	54.28±4.95	53.39±3.72	0.356	55.46±3.14	55.39±2.52	0.909
Superior	54.73±3.66	52.84±4.19	0.030	55.85±3.18	42.54±4.25	0.084
Nasal	54.51±5.19	53.49±3.97	0.309	55.74±2.40	54.82±4.81	0.214
Inferior	53.74±6.37	52.55±4.49	0.322	54.86±3.84	54.43±3.61	0.598

MS: Multiple sclerosis.

different sections between healthy and MS eyes. Regarding SCP, in all sections, VD in healthy group was significantly higher than MS group, except for nasal part of left eye. Considering DCP, although the mean of VD in all sections were higher in healthy eyes, no significant difference was detected; except for superior part of right eye (54.73±3.66 in healthy eyes *vs.* 52.84±4.19 in MS eyes, $P=0.030$).

DISCUSSION

To the best of our knowledge, our study is the first one, which evaluates OCT and OCTA indices differences among MS and healthy individuals of Iranian populations, in a region with a high burden of MS. In compared to healthy individuals, we found that MS patients had significantly decreased peripapillary RNFL and retinal layers' thickness; even who had not experienced ON. Furthermore, considering SCP, OCTA results revealed that MS patients had significantly lower VD in most sections; which this significance was not observed in DCP.

MS is a CNS disease that irreversibly degenerates the neural axons and myelin. Currently, it affects 2.8 million people worldwide and is considered to be as the main cause of disability in young people[12]. MS has emerged as one of the most burdensome illnesses with a mean prevalence of 51.52 cases per 100 000 Iranian population[13]. The incidence of MS in Iranian men and women accounted for 1.2/100 000 (1.0-1.4) and 48.2/100 000 (39.3-59.1), respectively[14]. Evidence reveals that autoimmune, inflammatory, neurodegenerative and vascular pathologies are declared in developing MS. Considering the change of inner retinal layers' thickness and retinal blood flow, OCT and OCTA; as noninvasive precise imaging modalities, enable capturing of high-resolution retinal images and measure these parameters in MS patients[15].

Correlation between vascular network pathology and neural degeneration was basically suggested by Rindfleisch[16] and Charcot[17]. Recent studies have demonstrated that vascular dysfunction plays a vital role in the development of demyelinating lesions of MS. Additionally, in comprehensive review study which was conducted by Caprio and Russo[18] declared that vascular components may be initial simulators for neuronal pathology and subsequent neurological manifestations of MS. It might be attributable to endothelial abnormalities and consequent vascular dysfunction in the brain and retina[19]. The other possible mechanism is that damage to the neural fiber and retinal layers lead to lower metabolism and subsequently reduced blood flow[20].

Reduction in blood flow ofthe optic nerve head and various retinal regions in MS patients is not correlated to previous attacks of ON. In contrast to DCP, we found that reduction of VD in MS patients was significant in SCP. In consensus with our results, Farci *et al*[21] found that in compared to healthy individuals, reduced blood flow was significant in the correlation of the SCP in all retinal subregions which was not related to previous history of ON. This can be interpreted in a way that MS affects the innermost retinal layers, which leads to inner retinal layer thinning. Physiological resistance of more outer retinal layer to retrograde trans-synaptic axonal degeneration preserves the deep retinal layers thickness and blood flow of the DCP[22].

Retinal layers, particularly the RNFL and ganglion layer, have emerged as biomarkers of neuroaxonal damage in MS and their thicknesses can be used as a tool to predict visual function and clinical disability among MS patients[23]. Our present data showed that, compared to HC, retinal layer thicknesses in the foveal, parafoveal and all other regions of retina were reduced in MS patients. In line with our result, previous studies also showed the decreased thickness of retinal layers in MS patients[24-25]. Petzold *et al*[23] demonstrated that peripapillary RNFL and macular ganglion-cell-and-inner-plexiform-layer (GCIPL) thinning could reflect the global CNS deterioration in MS, even in the absence of acute ON. Henderson *et al*[26] found that there is retinal axonal loss in the eyes of progressive MS patients with no history of a previous episode of ON. Additionally, an inverse correlation is observed between RNFL and GCIPL thickness and an increased risk of disability worsening[27-29].

The strengths of our study could be the reasonable size of MS and healthy individuals. Furthermore, we used non-invasive, reliable, and precise imaging modalities including OCTA and OCT to evaluate different parameters. The present results should be interpreted in light of some limitations. First, our study is single-centered and maybe multi-centered studies with more participants would reach different results. Second, we did not evaluate the parameters in various types of MS disease severity. Last but not the least, it is important to address the observed discrepancies in statistical significance between the right and left eyes of the participants. While the results for most items of right eyes yielded a P-value of <0.001, indicating a strong level of statistical significance, the left eyes presented a P-value of <0.05. This difference, while statistically relevant, may not have practical significance in the context of our findings. Such variations can arise from random sampling errors or inherent variability in the data. Given that both results are statistically significant, we assert that the small difference in P-values does not undermine the overall conclusions of our study. Therefore, these results should be interpreted with care, as the primary focus remains on the overarching trends rather than isolated statistical values.

In conclusion, in compared to healthy individuals, we found that MS patients had significantly decreased peripapillary RNFL and retinal layers' thickness; even who had not experienced ON. Furthermore, considering SCP, OCTA results revealed that MS patients had significantly lower VD in most sections; which this significance was not observed in DCP. Future studies with larger sample sizes are recommended to further evaluate these structural and microvascular changes.

Conflicts of Interest: Moghaddasi M, None; Sardarinia M, None; Soltansanjari M, None; Vafajoo A, None; Mohebi N, None; Zare S, None.

Authors' contributions: Moghaddasi M contributes in study design, neurological evaluation of patients, supervision of the study, and critical revision of the manuscript; Sardarinia M contributes in conceptualization and design of the study, leading role in data acquisition, OCT and OCTA imaging, data analysis and interpretation, drafting the manuscript and revising it critically for important intellectual content; Soltansanjari M contributes in ophthalmic examinations, data collection, and preliminary data analysis; Vafajoo A contributes in assistance in data collection, statistical analysis, and interpretation of results; Mohebi N contributes in patient recruitment, data management, and administrative support; Zare S contributes in overall supervision of the project, contribution to study design, and final critical revision of the manuscript.

REFERENCES

[1] Gerardo F, Bárbara E, Cecilia G, et al. Abnormal eye movements

increase as motor disabilities and cognitive impairments become more evident in Multiple Sclerosis: a novel eye-tracking study. Mult Scler J Exp Transl Clin, 2024,10(2):20552173241255008.
[2] Farabi Maleki S, Yousefi M, Afshar S, et al. Artificial intelligence for multiple sclerosis management using retinal images: pearl, peaks, and pitfalls. Semin Ophthalmol, 2024,39(4):271-288.
[3] Abbass NJ, Shaia JK, Shukla P, et al. Prevalence of pediatric and adult optic neuritis in the United States from 2016 to 2023. Eye, 2025, 39(8):1608-1614.
[4] Chisari CG, Toro MD, Cimino V, et al. Retinal nerve fiber layer thickness and higher relapse frequency may predict poor recovery after optic neuritis in MS patients. J Clin Med, 2019,8(11):2022.
[5] Moghaddasi M, Nabovvati M, Koushki A, et al. Randomized control trial of evaluation of Clemastine effects on visual evoked potential, nerve fiber layer and ganglion cell layer complex in patients with optic neuritis. Clin Neurol Neurosurg, 2020,193:105741.
[6] Ulusoy MO, Horasanlı B, Işık-Ulusoy S. Optical coherence tomography angiography findings of multiple sclerosis with or without optic neuritis. Neurol Res, 2020,42(4):319-326.
[7] Mehmood A, Ali W, Song S, et al. Optical coherence tomography monitoring and diagnosing retinal changes in multiple sclerosis. Brain Behav, 2021,11(10):e2302.
[8] Bostan M, Chua J, Sim YC, et al. Microvascular changes in the macular and parafoveal areas of multiple sclerosis patients without optic neuritis. Sci Rep, 2022,12:13366.
[9] Shenoy N, Liu F, Narayanan SP. Loss of cells in the retinal ganglion cell layer as an early indication of neurodegeneration in multiple sclerosis. J Integr Neurosci, 2024,23(7):129.
[10] Schwenkenbecher P, Wurster U, Konen FF, et al. Impact of the McDonald criteria 2017 on early diagnosis of relapsing-remitting multiple sclerosis. Front Neurol, 2019,10:188.
[11] Zurawski J, Glanz BI, Chua A, et al. Time between expanded disability status scale (EDSS) scores. Mult Scler Relat Disord, 2019, 30:98-103.
[12] Dahham J, Rizk R, Kremer I, et al. Economic burden of multiple sclerosis in low-and middle-income countries: a systematic review. PharmacoEconomics, 2021,39(7):789-807.
[13] Fattahi N, Saeedi Moghaddam S, Mohebi F, et al. Burden of multiple sclerosis in Iran from 1990 to 2017. BMC Neurol, 2021,21 (1):400.
[14] Azami M, YektaKooshali MH, Shohani M, et al. Correction: Epidemiology of multiple sclerosis in Iran: a systematic review and meta-analysis. PLoS One, 2019,14(7):e0219466.
[15] Lanzillo R, Cennamo G, Criscuolo C, et al. Optical coherence tomography angiography retinal vascular network assessment in multiple sclerosis. Mult Scler, 2018,24(13):1706-1714.
[16] Rindfleisch E. Histologisches Detail zu der grauen Degeneration von Gehirn und Rückenmark. (Zugleich ein Beitrag zu der Lehre von der Entstehung und Verwandlung der Zelle.). Virchows Arch, 1863,26: 474-483.
[17] Charcot M. Histologie de la sclerose en plaque. Gaz Hosp, 1868, 41:554-556.
[18] Caprio MG, Russo C. Vascular disease in patients with multiple sclerosis: a review. J Vasc Med Surg, 2016,4(2):746-753.
[19] Allen NB, Lichtman JH, Cohen HW, et al. Vascular disease among hospitalized multiple sclerosis patients. Neuroepidemiology, 2008, 30(4):234-238.
[20] Wang XG, Jia YL, Spain R, et al. Optical coherence tomography angiography of optic nerve head and parafovea in multiple sclerosis. Br J Ophthalmol, 2014,98(10):1368-1373.
[21] Farci R, Carta A, Cocco E, et al. Optical coherence tomography angiography in multiple sclerosis: a cross-sectional study. PLoS One, 2020,15(7):e0236090.
[22] Albrecht P, Ringelstein M, Müller AK, et al. Degeneration of retinal layers in multiple sclerosis subtypes quantified by optical coherence tomography. Mult Scler, 2012,18(10):1422-1429.
[23] Petzold A, Balcer LJ, Calabresi PA, et al. Retinal layer segmentation in multiple sclerosis: a systematic review and meta-analysis. Lancet Neurol, 2017,16(10):797-812.
[24] Watson GM, Keltner JL, Chin EK, et al. Comparison of retinal nerve fiber layer and central macular thickness measurements among five different optical coherence tomography instruments in patients with multiple sclerosis and optic neuritis. J Neuro Ophthalmol, 2011,31(2): 110-116.
[25] Saidha S, Syc SB, Ibrahim MA, et al. Primary retinal pathology in multiple sclerosis as detected by optical coherence tomography. Brain, 2011,134(2):518-533.
[26] Henderson APD, Trip SA, Schlottmann PG, et al. An investigation of the retinal nerve fibre layer in progressive multiple sclerosis using optical coherence tomography. Brain, 2008:277-287.
[27] Bsteh G, Berek K, Hegen H, et al. Macular ganglion cell-inner plexiform layer thinning as a biomarker of disability progression in relapsing multiple sclerosis. Mult Scler, 2021,27(5):684-694.
[28] Zimmermann HG, Knier B, Oberwahrenbrock T, et al. Association of retinal ganglion cell layer thickness with future disease activity in patients with clinically isolated syndrome. JAMA Neurol, 2018,75(9): 1071.
[29] Knier B, Leppenetier G, Wetzlmair C, et al. Association of retinal architecture, intrathecal immunity, and clinical course in multiple sclerosis. JAMA Neurol, 2017,74(7):847.