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Combined evaluation of visual field and optical coherence tomography angiography data in multiple sclerosis patients

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ABSTRACT

Aims: To evaluate Humphrey visual field analyzer (HVFA) data and optical coherence tomography angiography (OCT-A) parameters in multiple sclerosis (MS) patients with optic neuritis (ON) attacks.

Methods: 34 eyes of 34 patients with MS diagnosis who had ON attacks were included in the study. After detailed ophthalmoscopic examination, OCT-A and HVFA images were taken. Spearman correlation analysis was used in statistical analysis.

Results: The mean age of the participants was 31.52±10.09 years. In the correlation analysis, a moderate correlation was found between mean deviation (MD) and foveal deep blood flow (DF) (rho=0.52), and a weak correlation was found between MD and foveal superficial blood flow (SF) (rho=0.40) and optic disc head blood flow (ODF) (rho=0.38). A weak negative correlation was found between pattern standard deviation (PSD) and DF (rho=-0.37) and ODF (rho=-0.40).

Conclusion: This study showed that OCTA data were affected in a manner consistent with HVFA data. More practical and quickly applicable OCTA scans may facilitate the estimation of visual field findings in MS patients.

Keywords: Multiple sclerosis, visual field, optic neuritis, optical coherence tomography angiography

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease characterized by axonal loss in the central nervous system.[1] MS occurs mostly in young adults between the ages of 20 and 40, and women are affected more frequently than men. In the clinical course of MS, the most common ocular manifestation is optic neuritis (ON). ON occurs as the first symptom in approximately 20% of these patients.[2]

Recently, retinal imaging has been used to help understand the pathogenesis and follow the disease in central nervous system degeneration. Optical coherence tomography angiography (OCT-A) is a high-resolution, noninvasive method that visualizes blood flow in the retinal vascular structures. In addition to neurodegeneration, cerebral endothelial dysfunction has been detected in MS patients. Decreases in retinal vascular density and optic disc head blood flow indices detected by OCT-A were observed in MS patients.[3]

Visual field (VF) scans provide important information in the evaluation and follow-up of diseases affecting the visual pathways. Naumovska et al.[4] performed VF scans to evaluate the effectiveness of corticosteroid treatment in MS patients with ON attacks. At the end of the study, they revealed that there was no difference in the results of corticosteroid treatment administered orally or systemically. The VF test, which should be applied at certain intervals in MS disease, may be suboptimal depending on the performance of the participants and may need to be repeated.

This study aimed to investigate whether there is a correlation between Humphrey visual field analyzer (HVFA) data and OCT-A parameters in MS patients diagnosed with optic neuritis attacks.

METHODS

This study was conducted at Kahramanmaraş Sütçü İmam University Faculty of Medicine campus between June 2024 and September 2024. It was conducted following the principles of the Declaration of Helsinki with the approval of the Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee (Date: 27.08.2024, Decision No: 210).

In this study, medical records of patients followed up with MS diagnosis were reviewed. Clinical features of ON include

painful or painless subacute monocular or binocular vision loss worsening with eye movements, decreased color vision, and relative afferent pupillary defect (RAPD). Symptoms supporting the diagnosis of ON include acute swelling of the optic disc, increased contrast in the optic nerve and its sheath on magnetic resonance imaging (MRI) of symptomatic patients, delayed P100 wave latency on visual evoked potential (VEP) testing, and deterioration on visual field testing. The presence of these pathologies was considered as having had an ON attack.[5]

Inclusion criteria were having MS between the ages of 18 and 80 years, having had an ON attack, complying with the study procedure (visual field and OCT-A scan), having a visual acuity of at least 20/200, not having had any ON or MS attack for at least three months, and not having used systemic or topical corticosteroid therapy for at least three months. Exclusion criteria were having a refractive status greater than -6.00 and +6.00 diopters in spherical equivalent in both eyes, having a history of intraocular surgery or orbital trauma, and having any additional ophthalmologic pathology (e.g. glaucoma, diabetic retinopathy, hypertensive retinopathy, or age-related macular degeneration). Patients with poorly documented, low-resolution OCT-A images were excluded from the study. Patients who could not adapt to visual field scans had fixation loss of more than 20%, and false positive (FP) and/or false negative (FN) rates of more than 33% were not included in the study. The eye of each participant who met the inclusion criteria for both eyes and had the first attack was included in the study.

A total of 34 eyes of 34 MS patients met the inclusion criteria. All patients underwent a complete ophthalmic examination, including best-corrected visual acuity (BCVA) testing using the Snellen chart (converted to logMAR), color vision examination (Ishihara test), RAPD examination, intraocular pressure measurement using Goldmann applanation tonometry, biomicroscopic anterior segment and dilated fundus examination. After the examination, images were obtained with spectral-domain OCT-A RTVue XR AngioVue (version 2015.1.0.90; Optovue, Inc., Fremont, CA, USA). Visual field acquisitions were performed with the HVFA (Carl Zeiss Meditec, Dublin, CA) at least 2 days later to allow dilation to resolve.

Optical Coherence Tomography Angiography Imaging

Before the OCT-A scan, all patients' pupils were dilated using a combination of 0.5% tropicamide and 2.5% phenylephrine HCL. OCT-A scans were performed by two experienced ophthalmologists (A.M. and S.M.). The OCT-A RTVue XR AngioVue, a spectral domain device based on the erythrocyte motion-dependent split-spectrum amplitude-correlated angiography (SSADA) algorithm, was used for imaging. This device provides volumetric exposure of 304×304 A at 70,000 a-scans per second with an 840 nm light source with a 5 mm axial resolution. The device performs quantitative analysis of the measured data and calculates vascular density and flow area.

Visual Field Imaging

All subjects underwent visual field testing with Humphrey's Field Analyzer 750 I (Carl Zeiss-Humphrey Systems, Dublin, California, USA) using the 30-2 SITA-Fast strategy. Visual fields were considered satisfactory when FP and FN errors did not exceed 33% and fixation errors did not exceed 20%.

The results obtained with HVFA were expressed in three ways: mean deviation (MD), pattern standard deviation (PSD), and the number of significantly depressed test points (DP) at <1% level on the pattern deviation probability map. MD is the mean of the difference between the patient's threshold value and the age-matched control group. PSD indicates the standard deviation of the difference between the threshold values and the expected threshold values in the visual field. It is an indicator of localized defects in the age-corrected area. The indicators of DP on the pattern deviation map are the probability that the obtained values would be found in the current population in this age group. A DP indicates that 99% of normal subjects of the same age would be expected to have a higher sensitivity than the recorded value. This is considered to provide a more sensitive measure of visual field defects than MD. To obtain the DP value, HVFA 30-2 was analyzed by counting and summing the number of significantly DP.

Statistical Analysis

The SPSS (Statistical Package for the Social Sciences; version 23) software program was used for the statistical analysis of the data obtained in this study. Descriptive statistics for the continuous variables were expressed as means ± standard deviations and medians (min-max), while categorical variables were expressed as numbers and percentages. Whether the data conformed to a normal distribution was determined using Kolmogorov-Smirnov and Shapiro-Wilk tests. Spearman correlation coefficients were calculated, and a statistical significance level of $p<0.05$ was accepted.

RESULTS

Demographic and Clinical Features

Of the 34 participants, 6 (17.6%) were male and 28 (82.3%) were female. The mean age was 31.52±10.09 years. The mean BCVA values were 0.10±0.04 (logMAR). Color vision test revealed defects in 11 (32.3%) patients. Additionally, 11 (31.4%) patients had RAPD. Detailed fundus examination revealed optic disc pallor in 15 (44.1%) patients (Table 1).

Table 1. Demographic characteristics of the patients

	MSON+ (n=34)
Age (mean±SD)	31.52±10.09
Gender n (%)	
Male	6 (17.6%)
Female	28 (82.3%)
BCVA (logMAR)	0.10±0.04
Color vision test n (%)	
Affected	11 (32.3%)
Normal	23 (67.6%)
RAPD n (%)	
Positive	11 (32.3%)
Negative	23 (67.6%)
Fundus examination n (%)	
Optic disc pathology	15 (44.1%)
Normal	19 (55.8%)

MSON: Multiple sclerosis optic neuritis attack, SD: Standard deviation, BCVA: Best corrected visual acuity, RAPD: relative afferent pupillary defect

OCT-A and HVFA Measurement Values

The means of OCT-A and HVFA data are given in Table 2. In the correlation analysis, a moderate correlation was found between MD and foveal deep blood flow (DF) (rho=0.525) ($p<0.05$), a weak correlation was found between MD and foveal superficial blood flow (SF) (rho=0.405) (p=0.03), and optic disc head blood flow (ODF) (rho=0.382) (p=0.04). A weak negative correlation was found between PSD and foveal DF (rho=-0.375) (p=0.04) and ODF (rho=-0.400) (p=0.03). There was also a moderate correlation between DP and ODF (rho=-0.528) ($p<0.05$) and a weak negative correlation between DP and DF (rho=-0.407) (p=0.03) was detected. (Table 3).

Table 2. Mean values of OCT-A and HVFA data of MS patients

	MSON+ (mean±SD) (n=34)
SF (μm²)	1.306±0.132
DF (μm²)	1.277±0.232
CCF (μm²)	1.893±0.052
sFAZ (μm²)	0.325±0.096
dFAZ (μm²)	0.414±0.163
Fovea sVD (%)	29.639±5.803
Parafovea sVD (%)	46.188±5.937
Fovea dVD (%)	32.848±8.049
Parafovea dVD (%)	56.648±7.663
ODF (μm²)	1.449±0.211
ONHD (%)	53.170±5.309
MD (dB)	-6.870±5.327
PSD (dB)	3.133±2.045

OCT-A: Optical coherence tomography angiography, HVFA: Humphrey visual field analyzer, MS: Multiple sclerosis, MSON: Multiple sclerosis optic neuritis attack, SD: Standard deviation, SF: Superficial flow, DF: Deep flow, CCF: Choriocapillaris flow, sFAZ: Superficial foveal avascular zone, dFAZ: Deep foveal avascular zone, sVD: Superficial vascular density, dVD: Deep vascular density, ODF: Optic disk flow, ONHD: Optik nerve head dansite, MD: Mean deviation, PSD: Pattern standard deviation, dB: Decibel

Table 3. Correlation coefficients of OCT-A and HVFA data

		SF (μm²)	DF (μm²)	ODF (μm²)
MD (dB)	Correlation coefficient	0.405	0.525	0.382
	p value	0.03	0.00	0.04
PSD (dB)	Correlation coefficient	-0.233	-0.375	-0.400
	p value	0.23	0.04	0.03
DP (<1%)	Correlation coefficient	-0.187	-0.407	-0.528
	p value	0.34	0.03	0.00

OCT-A: Optical coherence tomography angiography, HVFA: Humphrey visual field analyzer, SF: Superficial flow, DF: Deep flow, ODF: Optic disk flow, MD: Mean deviation, PSD: Pattern standard deviation, DP: Depressed test points, dB: Decibel

DISCUSSION

In this study, it was determined that MD, PSD, and DP data obtained from visual field output in MS patients with ON attacks were correlated with foveal SF, DF, and ODF data in OCT-A.

Visual dysfunction is common in MS. This is due to retrobulbar optic neuritis, papillitis, or rarely, demyelinating lesions affecting the retrochiasmal pathways. MS patients with ON attacks develop retinal ganglion cell axon loss.[6] Cheng et al.[7] studied the relationship between VF parameters and retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography (OCT) in MS patients. Pearson correlation coefficients between MD and RNFL thicknesses were found between 0.65 and 0.69 in eyes with ON attacks. However, no agreement was found between the two parameters in eyes without ON attacks. Khalil et al.[8] compared the mean RNFL thickness and MD parameters in VF in 68 MS patients but did not find a significant correlation. They attributed this result to the fact that OCT parameters may indicate subclinical permanent damage despite the VF parameters returning to near-normal levels after the ON attack. In another study comparing anatomical and functional parameters in MS cases, a correlation was found between macular sensitivity determined by microperimetry and macular volume from OCT parameters.[9]

Vascular abnormalities occur in MS patients due to cerebral endothelial cell dysfunction.[10] Based on these findings, retinal microvascular blood flow parameters of MS patients were examined. Wang et al.[11] revealed that there was a decrease in optic disc head flow indices in MS patients who had ON attacks compared to healthy controls. Similarly, decreased vascular density in the perifoveal area was reported in these patients.[3,12] A decrease in superficial and deep capillary vascular density was observed in the optic disc head and macula region in MS patients with or without ON attacks. This result was associated with MS disease activity independently of ON attacks. The authors suggested that the decrease in ganglion cell layer and nerve fiber layer in MS causes retinal hypoxia.[13] The decrease in vascular density in MS patients may be the result of inflammation-related endothelial dysfunction. Another hypothesis is that it may be related to decreased oxygen and metabolite demand due to neuroaxonal degeneration and nerve fiber layer atrophy.[14]

The ganglion cell complex, the nerve fiber layer, the ganglion cell layer, and the inner plexiform layer, are associated with the central nervous system. They are used to determine retinal effects associated with neurological diseases.[8] From OCT-A data, SF represents the blood flow between the internal limiting membrane and the inner plexiform layer. DF is the blood flow between the inner and outer plexiform layers. In the present study, a correlation was found between SF and MD. This result suggested that the decrease in vascular flow in the superficial layers may contribute to the damage in the ganglion cell complex. However, DF was found to be more correlated with VF parameters (MD, PSD, and DP). This finding supports the hypothesis that systemic vascular pathologies may develop in MS and that vascular pathologies may be associated with neuronal dysfunction and degeneration.[15] ODF was correlated with MD, PSD, and DP. In MS patients who have had an ON attack, hemodynamic disorders may develop in the central retinal artery, and optic disc blood flow may decrease.[16] In addition, since axonal loss will develop in the optic nerve after the attack, both OCT-A and VF values will be affected in these cases.

Limitations

The current study includes the limited number of patients and the cross-sectional nature of the study. Future study designs on this topic may benefit from repeated VF and OCT-A measurements. In addition, this study was applied only to MS patients who had ON attacks. Evaluation of cases who did not have ON attacks may provide more detailed information on the subject and help us understand whether the findings are related to MS disease or ON attacks.

CONCLUSION

This study showed that the decrease in retinal vascular parameters in MS patients with ON attacks may be correlated with the deterioration in MD and PSD values in the visual field output. Combining structural and functional tests may be useful in clinical studies of MS patients. Vascular parameters can be used as a fast and simple method to estimate visual functions in MS patients who have difficulty in performing VA and who cannot cooperate.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kahramanmaraş Sütçü İmam University Faculty of Medicine Ethics Committee (Date: 27.08.2024, Decision No: 210).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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