DOI:10.4274/tnd.2023.77906
Turk J Neurol 2023;29:282-286

Original Article / Özgün Araştırma

Sectoral and Quadrant Evaluation of the Peripapillary Retinal Nerve Fiber Layer and Ganglion Cell–inner Plexiform Layer Thickness in Patients with Multiple Sclerosis

Multipl Sklerozlu Hastalarda Peripapiller Retina Sinir Tabakası ve Ganglion Hücre–iç Pleksiform Tabaka Kalınlığının Sektörel ve Kadransal Değerlendirilmesi

Emine Rabia Koç[1], Esin Söğütlü Sarı[2], Alper Yazıcı[3], Furkan Sarıdaş[1], Ömer Faruk Turan[1]

[1]Bursa Uludag University Faculty of Medicine, Department of Neurology, Bursa, Türkiye
[2]Bursa Uludag University Faculty of Medicine, Department of Ophthalmology, Bursa, Türkiye
[3]Private Batigöz Hospital, Clinic of Ophthalmology, Izmir, Türkiye

Abstract

Objective: To evaluate the peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell–inner plexiform layer thickness (GC–IPL) in patients with multiple sclerosis (MS) by sector and quadrant.

Materials and Methods: Seventy-eight eyes of 39 patients with MS and 82 eyes of 41 healthy participants were analyzed using spectral domain optical coherence tomography. Our study defined MS eyes with optic neuritis (ON) as MS ON eyes and those without ON as MS non-ON eyes. Comparisons of the GC–IPL and pRNFL thicknesses were assessed and the measurements compared with healthy controls (HCs).

Results: The comparison of the average and three quadrants (superior, inferior, and temporal) measurements of the pRNFL thickness and the average and six quadrant measurements of the GC–IPL thickness between the MS ON eyes and the MS non-ON eyes revealed statistically significant differences ($P < 0.05$). The average and four quadrants thickness of pRNFL and the average and six quadrants thickness of GC–IPL were significantly reduced in a comparison of MS ON vs. HC with MS non-ON vs. HC eyes ($P < 0.05$).

Conclusion: The evaluation of pRNFL and GC–IPL thicknesses in MS ON and MS non-ON eyes may be beneficial in determining the central nervous system axonal integrity.

Keywords: Multiple sclerosis, optical coherence tomography, ganglion cell layer, retinal fiber layer

Öz

Amaç: Multipl skleroz (MS) hastalarında peripapiller retina sinir lifi tabakası (pRNFL) ve ganglion hücre iç–pleksiform tabaka kalınlığını (GC–IPL) sektörel ve kadransal olarak değerlendirmektir.

Gereç ve Yöntem: Otuz dokuz MS hastasının 78 gözü ile 41 sağlıklı kişinin 82 gözü spektral alan optik koherens tomografi kullanılarak analiz edildi. Çalışmamızda, optik nöritli (ON) olan MS gözlerini MS–ON olan gözler ve ON olmayanları da MS–ON olmayan gözler olarak tanımladık. Her iki grubun aGC-IPL ve aRNFL kalınlıkları ve sektörel kalınlıkları ölçüldü ve değerler, kendi aralarında ve sağlıklı kontrollerle karşılaştırıldı.

Bulgular: MS ON olan gözler ile MS ON olmayan gözler ortalama ve üç kadran (superior, inferior ve temporal) pRNFL kalınlığı ile ortalama ve altı kadran GC–IPL kalınlığı açısından karşılaştırıldığında; gruplar arasında istatistiksel olarak anlamlı fark elde edildi ($P < 0,05$). Ortalama ve dört çeyrek pRNFL kalınlığı ve 6 kadrandaki ortalama ve GC–IPL kalınlığı, MS ON olan grup ile kontrol ve MS ON olmayan grup ile kontrol grubunun gözleri ile karşılaştırıldığında kontrol grubuna göre her 2 grupta da önemli ölçüde azalma saptandı ($P < 0,05$).

Sonuç: MS ON olan ON olmayan gözlerde pRNFL ve GC–IPL kalınlıklarının değerlendirilmesi, santral sinir sistemi akson bütünlüğünün belirlenmesinde ve nörodejenerasyonun izlenmesinde faydalı olabilir.

Anahtar Kelimeler: Multipl skleroz, optik koherens tomografi, ganglion hücre iç pleksiform tabakası, retina sinir lifi tabakası

Address for Correspondence/Yazışma Adresi: Assoc. Prof. Emine Rabia Koç, Bursa Uludag University Faculty of Medicine, Department of Neurology, Bursa, Türkiye
Phone: +90 486 617 04 10 E-mail: erabiakoc@yahoo.com ORCID: orcid.org/0000-0002-0264-7284
Received/Geliş Tarihi: 20.06.2023 **Accepted/Kabul Tarihi:** 13.12.2023

This study was presented in Uludag Neurology Congress in March 2022.

Introduction

Multiple sclerosis (MS) is an immune-mediated, chronic, demyelinating, and neurodegenerative disease of the central nervous system (CNS) and manifests with different clinical entities. Optic neuritis (ON) is one of the most common presentations of MS. The visual pathway is frequently involved, and visual acuity loss occurs due to ON (1,2,3). Although patients do not complain of subjective visual failure, objective assessment of abnormal optic nerve function [i.e., visual evoked potentials (VEPs)] can be detected in ON. Optical coherence tomography (OCT) is a non-invasive examination that provides quantitative measurements and demonstrates peripapillary retinal nerve fiber layer (pRNFL) thinning in MS eyes with and without a history of ON (4). The RNFL is the innermost layer of the retina and comprises unmyelinated axons originating from the retinal ganglion cells (GC) (4,5,6,7). The retina GC bodies and the CNS gray matter are analogous (3). Therefore, retinal changes in MS project the visual system pathology in addition to the overall disease pathology in the CNS (8). OCT is a reliable method for imaging neuroaxonal damage in MS, and the retina is the only area where axons can be directly visualized (9). Previous studies have primarily compared RNFL and GC–inner plexiform layer (PL) thinning between MS ON eyes and healthy controls (HCs) (5,10). This study aimed to compare the average and sectoral measurement of the RNFL and GC–IPL thickness in MS ON, MS non-ON, and HC eyes.

Materials and Methods

Participants

The study was approved by the Balikesir University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2013-026, date: 19.06.2013), and informed consent was obtained from all participants. Seventy-eight eyes in 39 patients diagnosed with MS according to the 2017 McDonald criteria and 82 eyes in 41 HCs were included (11). None of the included patients were diagnosed with progressive MS or a clinically isolated syndrome. In the MS eyes, 35 had ON (clinically, and as assessed by a VEP latency) before enrollment. The eyes of patients with MS who had ON were named MS ON eyes (n = 35) and those without ON were termed MS non-ON eyes (n = 43). All participants were examined to exclude pathological conditions other than MS that affect the eyes, such as neurodegenerative or systemic diseases, diabetes mellitus, hypertension, and glaucoma. The second exclusion criterion was MS patients who had an episode of ON in the previous 6 months before inclusion in the study (12). The medical records of the patients were analyzed for the disease duration, the Expanded Disability Status Scale (EDSS) scores, and any history of ON episodes or VEP analysis (prolonged P100 latency of >120 ms). HCs were collected from medical and non-medical hospital staff. Participants with pathologic hyperopia or myopia or any systemic or ocular disease were excluded.

Optical Coherence Tomography Measurements

OCT was performed on both eyes of each participant using the Cirrus HD-OCT Model 4,000 system (Carl Zeiss Meditec Inc, Dublin, CA, USA). The pupil was dilated with tropicamide 1% (Tropamid, Bilim, Istanbul, Türkiye) before the scanning. The GC–IPL thickness was calculated using the macular cube 200 x 200 analysis protocols. The thickness of the macular GC–IPL was measured within a 14.13 mm^2 elliptical annulus area centered on the fovea, which had the following dimensions: vertical inner and outer radius of 0.5 mm and 2.0 mm, respectively, and horizontal inner and outer radius of 0.6 mm and 2.4 mm, respectively. The average and six sectoral (superotemporal, superior, superonasal, inferonasal, inferior, inferotemporal) GC–IPL thickness values were measured. The average pRNFL and four sectoral (superior, inferior, nasal, and temporal) RNFL thicknesses were also evaluated using a standard protocol that was previously described (13). For the GC–IPL and pRNFL measurements, only spectral domain OCT scans with a signal strength ≥6 were analyzed.

Statistical Analysis

The data were analyzed using SPSS version 15.0 software for Windows (SPSS Inc., Chicago, IL, USA). The mean values were expressed as arithmetic means ± standard error. The χ^2 test, One-Way ANOVA, and Kruskal–Wallis's test were used for comparisons of the groups. A P value of <0.05 was considered statistically significant. Pearson's correlation analysis was used to evaluate correlations between the variables.

Results

OCT scanning was performed for all participants (MS patients: n = 39, 78 eyes; HCs: n = 41, 82 eyes). Table 1 shows the group characteristics. There was no significant difference in age (t-test) or gender (χ^2 test) between the two groups (P = 0.804, P = 0.869, respectively). Among patients' eyes, 35 had a history and finding of ON, whereas 43 patients' eyes were without a history or finding of ON. The average pRNFL and GC–IPL thickness were reduced in the MS ON eyes (74 ± 15 µm, 64 ± 13 µm, respectively) compared with MS non-ON eyes (85 ± 14 µm, 76 ± 10 µm; P < 0.001 for both measures). The comparison of the pRNFL thickness with four quadrants between the MS ON eyes and MS non-ON eyes revealed statistically significant differences in the superior, inferior, and

Table 1. Epidemiology and disease characteristics of participants

	Multiple sclerosis eyes (n = 78)	Healthy eyes (n = 82)
Age, mean (SD) (years)	38 (8)	37.4 (9)
Women: men (% women)	50:28 (65.8)	55:27 (67)
Disease duration, mean (SD) (years)	8.05 (0.5–20)	NA
EDSS score, mean (range)	2.89 (2.23)	NA
Eyes with optic neuritis history, n (%)	35 (42.6)	NA

SD: Standard deviation, NA: Not applicable, EDSS: Expanded Disability Status Scale

temporal quadrants ($P < 0.001$ for each measure) except the nasal quadrant ($P = 0.5$). The average pRNFL and four quadrants of RNFL thickness values were significantly reduced in MS non-ON patients compared with the HCs ($P < 0.05$ per measure) and MS ON vs. HCs ($P < 0.05$ per measure). In addition, a significant decrease was detected in the GC–IPL thickness with six quadrants in MS ON eyes compared with MS non-ON eyes ($P < 0.05$ for each value). The average and six quadrants of GC–IPL thickness were significantly reduced in a comparison of MS ON vs. HCs and MS non-ON vs. HCs ($P < 0.001$ for each measure) (Table 2).

The EDSS scores and the disease duration were not correlated to any studied parameters in the MS subgroups ($P < 0.05$).

Discussion

We demonstrated that the average pRNFL and GC–IPL thicknesses were lower in the MS group with ON or without ON than those in the HCs. The reductions in both average and sectorial measurements of RNFL were higher in MS ON eyes than in MS non-ON eyes, except in the nasal quadrant. Previous studies have also demonstrated a decrease in the RNFL thickness in both MS with ON and non-ON eyes. This pathophysiology in the optic nerve is thought to be due to axonal degeneration. Furthermore, the decrease in the RNFL thickness in unaffected eyes may be related to the reflection of the neurodegeneration process on the clinically unaffected optic nerve (14,15,16,17).

Tatrai et al. (18) evaluated the retinal morphology in patients with MS with or without ON by Stratus OCT. They found a decreased circumpapillary RNFL (cpRNFL) thickness in the MS non-ON eyes compared with the control group only in the temporal quadrant, and the cpRNFL decreased in patients with MS ON eyes in all quadrants compared with the patients with MS non-ON eyes. Furthermore, they found significant differences in all quadrants except the nasal quadrant. In patients with MS ON eyes compared with the controls (18).

Research on retinal pathological changes in MS is not limited to the relaxing–remitting MS form and cross-sectional studies but also includes other forms of MS and prospective cohort studies. Henderson et al. (19) evaluated RNFL thickness longitudinally over 18 months by time-domain OCT in primary and secondary progressive MS patients. They assessed the average and four quadrants of RNFL at the beginning of the study and demonstrated a decrease in the RNFL thickness in the unaffected eyes of patients with MS. In addition, they found that the mean RNFL thickness was significantly decreased in the unaffected eyes of patients with secondary progressive MS compared with controls but not in those with primary progressive MS. However, they measured RNFL values in four quadrants and found the highest thinning in the temporal quadrant in the unaffected eyes of all MS subgroups compared with the controls. They obtained the annualized change in patient groups vs. controls in the same period, and none of the participant groups had a significantly decreased mean RNFL thickness. They only obtained a substantial thinning in the inferior RNFL quadrant in the unaffected eyes of patients with primary progressive MS (19). Sepulcre et al. (20) assessed the RNFL thickness by Stratus OCT in all subtypes of MS with a prospective cohort study, and they found that the RNFL thickness in patients with MS was thinner at study entry vs. the controls. When they analyzed the RNFL quadrants, they found that patients with MS had a reduction in the RFNL thickness in all quadrants except the nasal quadrant. Furthermore, they demonstrated the effect of previous ON, and they found that on average and for each quadrant (except for the nasal quadrant), the RNFL was thinner in ON eyes than in controls. In addition, they found a thinner RNFL in patients with MS without ON compared with controls. However, they found no differences in the RNFL thickness between eyes with and without ON (20). Our study found a reduced pRNFL in MS ON eyes compared with MS non-ON eyes. The comparison of the pRNFL thickness with four quadrants between the MS ON eyes and MS non-ON eyes revealed statistically significant differences in the superior, inferior, and temporal quadrants. The average and four quadrants of the pRNFL thickness were significantly reduced in a comparison of MS ON vs. control and MS non-ON vs. control eyes. According

Table 2. Mean ± SD retinal layer thickness results and comparison of groups

Variable (µm)	Control groups (n = 82 eyes) Mean ± SD	MS non-ON (n = 43 eyes) Mean ± SD	MS ON (n = 35 eyes) Mean ± SD	MS non-ON vs. control *P* values	MS ON vs. control *P* values	MS non-ON vs. MS ON *P* values
Average RNFL	95 ± 10	85 ± 14	74 ± 15	<0.001	<0.001	<0.001
Superior	119 ± 17	109 ± 20	93 ± 20	0.002	<0.001	0.001
Nasal	69 ± 13	64 ± 13	62 ± 14	0.044	0.014	0.500
Inferior	121 ± 23	113 ± 23	94 ± 25	0.037	<0.001	0.001
Temporal	67 ± 10	54 ± 13	44 ± 11	<0.001	<0.001	<0.001
Average GC–IPL	82 ± 7	76 ± 10	64 ± 13	<0.001	<0.001	<0.001
Superonasal	85 ± 8	77 ± 11	64 ± 13	<0.001	<0.001	0.001
Nasal	83 ± 7	75 ± 12	64 ± 16	<0.001	<0.001	0.001
Inferonasal	83 ± 7	76 ± 11	64 ± 15	<0.001	<0.001	<0.001
Inferotemporal	81 ± 8	76 ± 10	64 ± 12	<0.001	<0.001	<0.001
Temporal	82 ± 8	76 ± 11	62 ± 14	<0.001	<0.001	<0.001
Superotemporal	83 ± 8	75 ± 11	64 ± 12	<0.001	<0.001	<0.001

RNFL: Retinal nerve fiber layer, GC–IPL: Ganglion cell–inner plexiform layer, MS: Multiple sclerosis, ON: Optic neuritis, SD: standard deviation

to these findings, some study results indicated that the temporal quadrant had an important role as a more greatly affected part to evaluate RNFL thickness, whereas the other study results emphasized that, except for the nasal quadrant, all quadrants were affected.

In our study, when compared with the patients with MS with and without ON, only the nasal quadrant was spared, and all three quadrants were affected. Differences among the above-mentioned study results are likely related to the patients, including studies with different severities of MS, MS subtypes, and the resolution of OCT devices. Some studies have determined a strong inverse correlation between disease duration and decreased RNFL thickness; however, others have not (20,21,22). Henderson et al. (19) found no significant association between disease duration and the RNFL thickness. In addition, Klistorner et al.(23) did not determine any correlation between the two factors. In contrast to these studies, Talman et al. (17) investigated longitudinal data of 593 eyes that were followed up for more than 3 years, and they indicated that each year of follow-up, there was a significant increase in RNFL thinning both for ON and non-ON eyes. In our study, there was no correlation between the average RNFL thickness and the disease duration in any of the MS subgroups. These opposing findings may be associated with the technique used or population differences in the studies.

The EDSS score is a scale used in clinics to determine the severity of the disease. Previous studies determined an inverse relation between RFNL thickness and EDSS scores, whereas a few studies did not, and some researchers had not looked at correlation analysis (24,25,26,27). There was no correlation between EDSS scores and RNFL thickness.

The retina has several layers known as the GC complex, which contains three innermost layers: the RNFL, the ganglion cell layer (GCL), and the IPL. The RNFL is formed of axons of the GCL, the GCL is formed of the cell bodies, and IPL is formed of retinal GC dendrites. The GC–IPL is located more internally than the RNFL. Most studies in MS have investigated RNFL measures. Since retinal GC loss is thought to play a primary role in the pathogenesis of visual pathologies in MS, GC–IPL measurements have also been obtained in OCT studies. Previous studies indicated that GC–IPL measures had better correlations with visual function than RNFL measures (28,29).

There are several studies regarding GC–IPL thickness and MS subtypes in the literature (10,28,30,31,32). In their study, Ratchford et al. (5) investigated RNFL and GC–IPL thickness in all MS subtypes for baseline and longitudinal measures, including magnetic resonance imaging findings and disease progression clinical evaluation. Patients with more severe disease progression were found to have higher thinning rates for GC–IPL measures than RNFL (5). In another study, Britze et al. (28) found that the GC–IPL thickness significantly decreased and was well correlated with visual dysfunction in MS patients. Similar to this study, Walter et al. (3) demonstrated that the GC–IPL thickness reduced and was related to visual function in ON and non-ON MS eyes. Garcia-Martin et al. (30) also determined that both RNFL and GC–IPL measures decreased in MS eyes with ON and were inversely correlated with EDSS scores. In our study, when MS patients with ON and without ON were compared with the HCs, the GC–IPL thickness was found to significantly decrease in all quadrants. These findings demonstrate that retinal neuronal damage still prevails in MS patients independently of a history of ON.

GC bodies located in the retina are accepted as the analog of the gray matter in the CNS (3). For this reason, a decrease in the GC–IPL thickness can be used as the indicator of cortical atrophy seen in MS patients. In addition, previous studies have shown that gray matter atrophy in MS is a better predictor than white matter disease in terms of foreseeing neurological disability (33). From this perspective, conducting cortical volume measurement and GC–IPL thickness measurement together can yield more helpful information in the examination of cortical atrophy in MS patients.

Conclusion

In conclusion, both RNFL and GC–IPL measurements are non-invasive, easy, and well-predictive techniques for identifying axonal degeneration and neuronal loss of optic nerve in MS patients with or without ON. Since segmental examination of the retina in MS patients without a history of ON will lead us to a detailed evaluation of retinal lower layers, this can shed light on the development of new treatments related to neuroprotection, particularly in patients with early-stage MS. This study provides supporting evidence to previous studies that demonstrate how to evaluate optic nerve damage by measuring the RFNL and GC–IPL thickness in patients with MS. These examinations are easy to administer, non-invasive methods for measuring axonal degeneration and neuronal loss in the optic nerve; therefore, their use as routine laboratory examinations should be considered.

Ethics

Ethics Committee Approval: Balikesir University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2013-026, date: 19.06.2013).

Informed Consent: Obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: F.S., Design: E.R.K., F.S., Data Collection or Processing: E.S.S., F.S., Analysis or Interpretation: Ö.F.T., E.R.K., A.Y., Literature Search: E.R.K., A.Y., Writing: E.R.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Marmoy OR, Viswanathan S. Clinical electrophysiology of the optic nerve and retinal ganglion cells. Eye (Lond) 2021;35:2386-2405.
2. Rodriguez-Mena D, Almarcegui C, Dolz I, et al. Electropysiologic evaluation of the visual pathway in patients with multiple sclerosis. J Clin Neurophysiol 2013;30:376-381.
3. Walter SD, Ishikawa H, Galetta KM, et al. Ganglion cell loss in relation to visual disability in multiple sclerosis. Ophthalmology 2012;119:1250-1257.
4. Minakaran N, de Carvalho ER, Petzold A, Wong SH. Optical coherence tomography (OCT) in neuro-ophthalmology. Eye (Lond) 2021;35:17-32.
5. Ratchford JN, Saidha S, Sotirchos ES, et al. Active MS is associated with accelerated retinal ganglion cell/inner plexiform layer thinning. Neurology 2013;80:47-54.
6. Datta S, Baidya K, Banerjee M, Mahapatra S, Mukherjee S. Retinal nerve fibre layer thinning in patients with thalassaemia, iron deficiency anaemia, and anaemia of chronic diseases. J Ophthalmol 2020;2020:9268364.

7. Tazarjani HD, Amini Z, Kafieh R, Ashtari F, Sadeghi E. Retinal OCT texture analysis for differentiating healthy controls from multiple sclerosis (MS) with/without optic neuritis. Biomed Res Int 2021;2021:5579018.
8. Cettomai D, Pulicken M, Gordon-Lipkin E, et al. Reproducibility of optical coherence tomography in multiple sclerosis. Arch Neurol 2008;65:1218-1222.
9. Mehmood A, Ali W, Song S, et al. Optical coherence tomography monitoring and diagnosing retinal changes in multiple sclerosis. Brain Behav 2021;11:e2302.
10. Oberwahrenbrock T, Ringelstein M, Jentschke S, et al. Retinal ganglion cell and inner plexiform layer thinning in clinically isolated syndrome. Mult Scler 2013;19:1887-1895.
11. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2018;17:162-173.
12. Costello F, Coupland S, Hodge W, et al. Quantifying axonal loss after optic neuritis with optical coherence tomography. Ann Neurol 2006;59:963-969.
13. Leung CK, Cheung CY, Weinreb RN, et al. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography: a variability and diagnostic performance study. Ophthalmology 2009;116:1257-1263.
14. Chan JW. Recent advances in optic neuritis related to multiple sclerosis. Acta Ophthalmol 2012;90:203-209.
15. Cettomai D, Hiremath G, Ratchford J, et al. Associations between retinal nerve fiber layer abnormalities and optic nerve examination. Neurology 2010;75:1318-1325.
16. Khanifar AA, Parlitsis GJ, Ehrlich JR, et al. Retinal nerve fiber layer evaluation in multiple sclerosis with spectral domain optical coherence tomography. Clin Ophthalmol 2010;4:1007-1013.
17. Talman LS, Bisker ER, Sackel DJ, et al. Longitudinal study of vision and retinal nerve fiber layer thickness in multiple sclerosis. Ann Neurol 2010;67:749-760.
18. Tatrai E, Simo M, Iljicsov A, et al. In vivo evaluation of retinal neurodegeneration in patients with multiple sclerosis. PloS One 2012;7:e30922.
19. Henderson AP, Trip SA, Schlottmann PG, et al. A preliminary longitudinal study of the retinal nerve fiber layer in progressive multiple sclerosis. J Neurol 2010;257:1083-1091.
20. Sepulcre J, Murie-Fernandez M, Salinas-Alaman A, et al. Diagnostic accuracy of retinal abnormalities in predicting disease activity in MS. Neurology 2007;68:1488-1494.
21. Al-Mujaini AS, Al-Mujaini MS, Sabt BI. Retinal nerve fiber layer thickness in multiple sclerosis with and without optic neuritis: a four-year follow-up study from Oman. BMC Ophthalmol. 2021;21:391.
22. Feng L, Shen J, Jin X, Li J, Li Y. The evaluation of the retinal nerve fiber layer in multiple sclerosis with special-domain optical coherence tomography. Ophthalmologica 2013;230:116-120.
23. Klistorner A, Arvind H, Garrick R, et al. Interrelationship of optical coherence tomography and multifocal visual-evoked potentials after optic neuritis. Invest Ophthalmol Vis Sci 2010;51:2770-2777.
24. Garcia-Martin E, Ara JR, Martin J, et al. Retinal and optic nerve degeneration in patients with multiple sclerosis followed up for 5 years. Ophthalmology 2017;124:688-696.
25. Grazioli E, Zivadinov R, Weinstock-Guttman B, et al. Retinal nerve fiber layer thickness is associated with brain MRI outcomes in multiple sclerosis. J Neurol Sci 2008;268:12-17.
26. Merle H, Olindo S, Donnio A, et al. Retinal nerve fiber layer thickness and spatial and temporal contrast sensitivity in multiple sclerosis. Eur J Ophthalmol 2010;20:158-166.
27. Torbus M, Niewiadomska E, Dobrakowski P, et al. The usefulness of optical coherence tomography in disease progression monitoring in younger patients with relapsing-remitting multiple sclerosis: a single-centre study. J Clin Med. 2022;12:93.
28. Britze J, Pihl-Jensen G, Frederiksen JL. Retinal ganglion cell analysis in multiple sclerosis and optic neuritis: a systematic review and meta-analysis. J Neurol 2017;264:1837-1853.
29. Seigo MA, Sotirchos ES, Newsome S, et al. In vivo assessment of retinal neuronal layers in multiple sclerosis with manual and automated optical coherence tomography segmentation techniques. J Neurol 2012;259:2119-2130.
30. Garcia-Martin E, Polo V, Larrosa JM, et al. Retinal layer segmentation in patients with multiple sclerosis using spectral domain optical coherence tomography. Ophthalmology 2014;121:573-579.
31. Lambe J, Fitzgerald KC, Murphy OC, et al. Association of spectral-domain OCT with long-term disability worsening in multiple sclerosis. Neurology 2021;96:2058-2069.
32. Park KA, Kim J, Oh SY. Analysis of spectral domain optical coherence tomography measurements in optic neuritis: differences in neuromyelitis optica, multiple sclerosis, isolated optic neuritis and normal healthy controls. Acta Ophthalmol 2014;92:57-65.
33. Fisher E, Lee JC, Nakamura K, Rudick RA. Gray matter atrophy in multiple sclerosis: a longitudinal study. Ann Neurol 2008;64:255-265.