Neurología. 2016;31(6):379—388

NEUROLOGÍA

www.elsevier.es/neurologia

ORIGINAL ARTICLE

Analysis of macular and nerve fibre layer thickness in multiple sclerosis patients according to severity level and optic neuritis episodes☆

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Received 24 February 2014; accepted 6 September 2014
Available online 8 June 2016

KEYWORDS
Macular thickness;
Nerve fibre layer;
Multiple sclerosis;
Expanded disability status scale;
Optic neuritis

Abstract
Introduction: Quantitative assessment of macular and nerve fibre layer thickness in multiple sclerosis patients with regard to expanded disability status scale (EDSS) and presence or absence of previous optic neuritis episodes.
Methods: We recruited 62 patients with multiple sclerosis (53 relapsing-remitting and 9 secondary-progressive) and 12 disease-free controls. All patients underwent an ophthalmological examination, including quantitative analysis of the nerve fibre layer and macular thickness using optical coherence tomography. Patients were classified according to EDSS as A (lower than 1.5), B (between 1.5 and 3.5), and C (above 3.5).
Results: Mean nerve fibre layer thickness in control, A, B, and C groups was 103.35 ± 12.62, 99.04 ± 14.35, 93.59 ± 15.41, and 87.36 ± 18.75 μm respectively, with statistically significant differences ($P < .05$). In patients with no history of optic neuritis, history of episodes in the last 3 to 6 months, or history longer than 6 months, mean nerve fibre layer thickness was 99.25 ± 13.71, 93.92 ± 13.30 and 80.07 ± 15.91 μm respectively; differences were significant ($P < .05$). Mean macular thickness in control, A, B, and C groups was 220.01 ± 12.07, 217.78 ± 20.02, 217.68 ± 20.77, and 219.04 ± 24.26 μm respectively. Differences were not statistically significant.

☆ Please cite this article as: Soler García A, Padilla Parrado F, Figueroa-Ortiz LC, González Gómez A, García-Ben A, García-Ben E, et al. Análisis del grosor macular y de capa de fibras nerviosas en pacientes con escle rosis múltiple en relación con su nivel de gravedad y antecedentes previos de neuritis óptica. Neurología. 2016;31:379—388.

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Conclusions: The mean retinal nerve fibre layer thickness in multiple sclerosis patients is related to the EDSS level. Patients with previous optic neuritis episodes have a thinner retinal nerve fibre layer than patients with no history of these episodes. Mean macular thickness is not correlated to EDSS level.

PALABRAS CLAVE
Grosor macular;
Capa de fibras nerviosas;
Esclerosis múltiple;
Escala expandida del estado de discapacidad;
Neuritis óptica

Análisis del grosor macular y de capa de fibras nerviosas en pacientes con esclerosis múltiple en relación con su nivel de gravedad y antecedentes previos de neuritis óptica

Resumen
Introducción: Evaluar cuantitativamente el grosor macular y de la capa de fibras nerviosas en pacientes con esclerosis múltiple en relación con la escala expandida del estado de discapacidad (EDSS) con o sin antecedentes previos de neuritis óptica.
Métodos: Sesenta y dos pacientes diagnosticados de esclerosis múltiple (53 remitente recidivante y 9 secundariamente progresiva) y 12 libres de enfermedad fueron reclutados para el estudio. Se les realizó una exploración oftalmológica, incluyendo el análisis cuantitativo de la capa de fibras nerviosas retinianas y el grosor macular mediante tomografía óptica de coherencia. Los pacientes fueron clasificados según la escala EDSS en: A: inferior a 1,5; B: entre 1,5 y 3,5, y C: superior a 3,5.
Resultados: El grosor medio ± desviación estándar de la capa de fibras nerviosas en los grupos control, A, B y C fue de 103,35 ± 12,62, 99,04 ± 14,35, 93,59 ± 15,41 y 87,36 ± 18,75 μm, respectivamente, con diferencias estadísticamente significativas ($p < 0,05$). En pacientes sin una historia previa de neuritis, o con un episodio de esta patología entre 3 y 6 meses de evolución o anterior a 6 meses, el grosor medio fue de 99,25 ± 13,71, 93,92 ± 13,30, 80,07 ± 15,91 μm, respectivamente, con diferencias significativas ($p < 0,05$). El grosor macular medio en el grupo control, A, B y C se situó en 220,01 ± 12,07, 217,78 ± 20,02, 217,68 ± 20,77 y 219,04 ± 24,26 μm, respectivamente. Las diferencias observadas entre grupos no fueron estadísticamente significativas.
Conclusiones: El grosor medio de la capa de fibras nerviosas en pacientes con esclerosis múltiple se relaciona con el nivel en la escala EDSS. Los pacientes con historia previa de neuritis óptica cursan con una disminución del grosor de esta capa respecto a aquellos sin antecedentes de neuritis. El grosor macular no se relaciona con el grado de afectación en la EDSS.

Introduction

Optical coherence tomography is an easy-to-perform, non-invasive technique that quantitatively analyses the thickness of the retinal nerve fibre layer (RNFL). It uses low-coherence light, which is produced by a superluminescent diode coupled with an optical fibre interferometer, at a wavelength of 843 nm.[1] Studies using optical coherence tomography in patients with multiple sclerosis (MS) have shown that the RNFL is thinner in these patients than in healthy individuals.[2,3]

In a sample of 14 patients with MS and a history of optic neuritis with complete recovery of visual acuity, Parisi et al.[4] reported a 48% decrease in RNFL thickness. In the contralateral eye, which had not been affected by optic neuritis, RNFL thickness decreased a mean of 28% compared to the control group.

Most published studies have analysed the connection between RNFL thickness and grey matter fraction, brain volume, degree of brain atrophy, optic neuritis, some clinical forms of MS, visual field sensitivity, and the contrast sensitivity test.[2,5–11] However, few studies have addressed the relationship between RNFL thickness and the expanded disability status scale (EDSS) and these include patients with no history of optic neuritis.[12–14]

The purpose of our study was to quantitatively analyse macular and RNFL thickness in patients with MS both with and without a history of optic neuritis, and to assess their association with certain clinical forms of MS and EDSS scores.

Material and methods

We conducted a retrospective study including 62 patients diagnosed with MS (53 with relapsing-remitting MS and 9 with secondary-progressive MS) and a control group of 12 patients without the disease. In compliance with the Declaration of Helsinki, confidentiality of the results was guaranteed and

all patients were apprised of the characteristics of the study before signing informed consent forms.

The patients were recruited from the neurology department at Hospital Universitario Virgen de la Victoria in Málaga, Spain, between February 2012 and January 2013. Controls were randomly selected from the patients with no eye disorders or systemic diseases who visited the ophthalmology polyclinic and who met the following criteria: visual acuity 10/10 on a Snellen chart, intraocular pressure <21 mmHg, and absence of anterior or posterior segment abnormalities. The MS diagnosis was confirmed by the neurology department based on clinical examinations and neuroimaging studies.

The ophthalmological examination of all participants included: a visual acuity test using a Snellen chart (values expressed in decimals), intraocular pressure determination with a Perkins applanation tonometer, and an eye fundus examination with a non-contact biomicroscopy with a Volk 84D lens.

Clinical diagnosis of a previous episode of optic neuritis involved the following clinical findings: visual acuity loss associated with painful eye movements, visual field defects, colour vision defects, afferent pupillary defect, and poor performance on the contrast sensitivity test, with either apparently normal or oedematous papilla. We excluded the patients who less than 3 months prior to the study experienced an episode of optic neuritis.

We used the EDSS[15] to assess neurological impairment. This quantitative scale ranges from 0 (normal) to 10 (death due to MS) in 0.5 unit increments. Scoring is based on a functional scale that assesses pyramidal, cerebellar, brainstem, sensitivity, bowel and bladder, visual, and mental functions, as well as difficulties in walking, communicating, and swallowing. Visual function included 7 grades: 0: normal; 1: scotoma with visual acuity better than 20/30 (corrected); 2: worse eye with scotoma with maximal visual acuity (corrected) between 20/30 and 20/59; 3: worse eye with large scotoma, or moderate decrease in fields, but with maximal visual acuity (corrected) between 20/60 and 20/99; 4: worse eye with marked decrease of fields and maximal visual acuity (corrected) between 20/100 and 20/200; 5: worse eye with maximal visual acuity (corrected) less than 20/200; and 6: grade 5 plus maximal visual acuity of better eye of 20/60 or less.

To study macular and RNFL thickness, we used the Stratus OCT 3000 optical coherence tomography system (Zeiss Humphrey Systems, Dublin, CA, USA) and 2 scan acquisition protocols: Macular Thickness Map, which performs 6 6-mm radial scans in 9 seconds, and the Fast RNFL Thickness, which performs 3 3.4-mm diameter circular scans in a single 1.92-second scan (Figs. 1 and 2).

The Retinal Thickness/Volume Tabular protocol was used to quantitatively analyse macular thickness. This protocol yielded 2 circular maps for measuring macular thickness in the 1000-, 3000-, and 6000-μm-diameter areas centred on the fovea, although we analysed thickness only in the 1000- and 3000-μm-diameter areas.

RNFL thickness was determined with the RNFL Thickness Average protocol, which quantitatively analysed thickness in 4 sectors or quadrants. In our study, we included mean RNFL thickness in the 4 sectors as well as RNFL thickness in each sector (superior, inferior, temporal, and nasal).

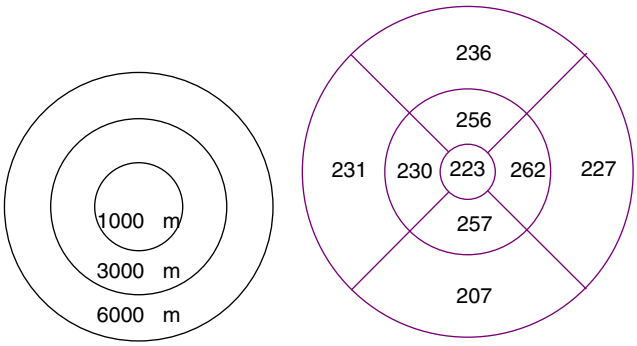

Figure 1 Macular thickness in a patient who experienced an episode of optic neuritis in the right eye more than 6 months previously. Measurements within the central 1000-, 3000-, and 6000-μm-diameter areas.

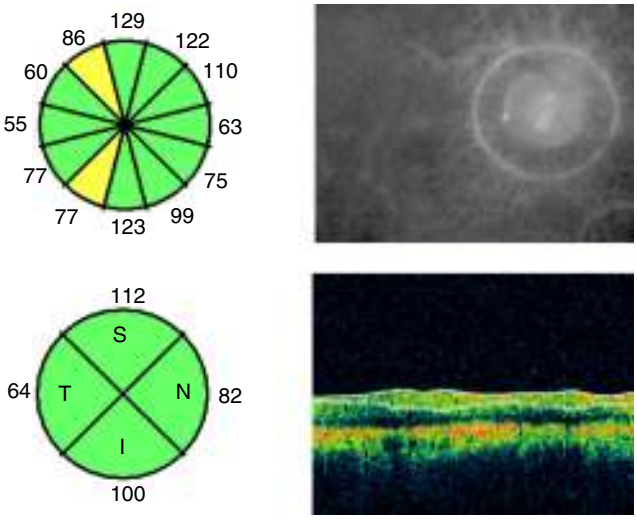

Figure 2 Quantitative analysis of RNFL thickness in a patient who experienced an episode of optic neuritis in the right eye more than 6 months previously. Thickness in all clock-hour sectors and quadrants is expressed in microns.

Data were gathered using FileMaker version 10 for Windows.

Data analysis was performed using SPSS statistical software version 15.0 for Windows. We used the parametric ANOVA test to compare the means between groups. The comparative analysis of quantitative variables was performed with the Pearson bivariate correlation test. Statistical significance was set at $P < .05$.

Results

In our sample, 36.5% of the participants were men, and 63.5% were women. Mean age ± SD was 36.50 ± 8.92 years in the patient group and 32.7 ± 8.33 years in the control group. Disease progression time was 81.54 ± 74.81 months. MS was relapsing-remitting in 85.4% of the patients (53/62) and secondary-progressive in 14.6% (9/62); 70.96% of the patients (44/62) were treated with immunomodulatory drugs (interferon beta).

Table 1 Characteristics of patients with, and controls without, MS.

	Patients	Controls
n	62 Relapsing-remitting: 53 (85.4%) Secondary-progressive: 9 (16.6%)	12
Eyes (*n*)	124	24
Age, years (mean ± SD)	36.50 ± 8.92	32.7 ± 8.33
Disease duration, months (mean ± SD)	81.54 ± 4.81	—
EDSS score (mean ± SD)	2.46 ± 2.04	—
VA (mean ± SD)	0.91 ± 0.21	1.02 ± 0.18
IOP (mean ± SD)	16.3 ± 1.4	16.7 ± 0.9

VA, visual acuity; SD, standard deviation; EDSS, expanded disability status scale; *n*, number; IOP: intraocular pressure.

Table 2 RNFL thickness in patients with MS and controls.

RNFL thickness		Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	Patients	124	94.5418	16.2078	91.6488	97.4348
	Controls	24	103.3590	12.6272	97.4493	109.2687
Superior sector	Patients	124	118.3740	23.1557	114.2408	122.5072
	Controls	24	124.5000	17.6888	116.2214	132.7786
Inferior sector	Patients	124	115.5203	22.1323	111.5698	119.4708
	Controls	24	131.9500	18.4375	123.3209	140.5791
Nasal sector	Patients	124	83.1545	23.4430	78.9700	87.3389
	Controls	24	82.8500	18.1609	74.3504	91.3496
Temporal sector	Patients	124	61.2276	15.6476	58.4346	64.0207
	Controls	24	74.0000	13.1589	67.8414	80.1586

Comparison of mean thickness and thickness in each sector of the RNFL. Values are expressed in microns. 95% confidence intervals for means ± SD.

Eleven patients had a single relapse, 20 had 2, 9 had 3, 10 had 4, and 12 had 5 relapses. Visual acuity was 0.91 ± 0.21 in the patient group and 1.02 ± 0.18 in the control group (Table 1).

We found statistically significant differences in mean RNFL thickness ($P = .02$) and in RNFL thickness in the temporal ($P = .02$) and inferior ($P = .01$) sectors between patients and controls (Table 2). After excluding the patients who had experienced an episode of optic neuritis, differences were significant only for the temporal sector ($P < .05$) (Table 3).

Table 4, which analyses mean RNFL thickness and RNFL thickness in each sector by the clinical form of MS, shows a decrease in thickness in the patients with secondary-progressive MS compared to those with relapsing-remitting MS; however, these differences were not statistically significant. When excluding those patients with a history of optic neuritis, the differences were still not significant (Table 5).

Degree of disability was established based on EDSS scores. The mean EDSS score was 2.46 ± 2.04. We established the following ordinal scale for EDSS scores: A: <1.5; B: 1.5 to 3.5; and C: >3.5. Twenty-five patients were classified into level A, 24 into level B, and 13 into level C. In our sample, none of the patients scored above 6.5.

Table 6 shows RNFL thickness by EDSS level. The statistical analysis revealed significant differences between EDSS levels in terms of mean thickness ($P = .011$), and thickness in the superior ($P = .017$), inferior ($P = .013$), and temporal ($P = .005$) sectors.

After excluding the patients with optic neuritis, the differences between EDSS levels were significant only for mean thickness ($P < .05$) (Table 7).

Table 8 shows mean thickness and thickness of each sector in the eyes both with and without a history of optic neuritis (eyes with optic neuritis are further classified by time elapsed since the episode of optic neuritis). Mean thickness was greater in the patients with no optic neuritis than in those with a history of the disorder (onset between 3 and 6 months or more than 6 months previously). Differences between these groups were statistically significant ($P < .01$) for mean thickness and thickness in the 4 peripapillary sectors.

We found no significant differences between EDSS levels in terms of mean macular thickness in either the

Table 3 RNFL thickness in controls and MS patients without optic neuritis.

RNFL thickness		Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	Patients	88	99.4891	13.1589	96.5940	102.3842
	Controls	24	103.3590	12.6272	97.4493	109.2687
Superior sector	Patients	88	123.2989	21.3623	118.7459	127.8518
	Controls	24	124.5000	17.6888	116.2214	132.7786
Inferior sector	Patients	88	121.6782	18.7135	117.6898	125.6666
	Controls	24	131.9500	18.4375	123.3209	140.5791
Nasal sector	Patients	88	64.3793	14.7334	61.2392	67.5194
	Controls	24	74.0000	13.1589	67.8414	80.1586
Temporal sector	Patients	88	88.0690	22.3808	83.2990	92.8390
	Controls	24	82.8500	18.1609	74.3504	91.3496

Comparison of mean thickness and thickness in each sector of the RNFL. Values are expressed in microns. 95% confidence intervals for means ± SD.

Table 4 RNFL thickness in the patient group, broken down by clinical form of MS.

RNFL thickness		Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	Relapsing-remitting	106	94.6412	16.7450	91.4620	97.8204
	Secondary-progressive	18	93.7679	11.6233	87.0567	100.4790
Superior sector	Relapsing-remitting	106	118.7982	23.9732	114.2467	123.3497
	Secondary-progressive	18	115.0714	15.6227	106.0511	124.0918
Inferior sector	Relapsing-remitting	106	115.5780	22.7340	111.2617	119.8942
	Secondary-progressive	18	115.0714	17.4067	105.0211	125.1218
Nasal sector	Relapsing-remitting	106	83.3486	24.2496	78.7446	87.9526
	Secondary-progressive	18	81.6429	16.4157	72.1647	91.1210
Temporal sector	Relapsing-remitting	106	61.4404	15.7041	58.4588	64.4219
	Secondary-progressive	18	59.5714	15.6731	50.5220	68.6208

Comparison of mean thickness and thickness in each sector of the RNFL. Values are expressed in microns. 95% confidence intervals for means ± SD.

Table 5 RNFL thickness in MS patients without optic neuritis, broken down by clinical form of MS.

RNFL thickness		Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	Relapsing-remitting	76	100.1324	13.8377	96.9486	103.3162
	Secondary-progressive	12	95.4683	11.5748	88.1140	102.8226
Superior sector	Relapsing-remitting	76	124.4933	21.8813	119.4589	129.5278
	Secondary-progressive	12	115.8333	16.6232	105.2714	126.3953
Inferior sector	Relapsing-remitting	76	122.2800	19.0671	117.8931	126.6669
	Secondary-progressive	12	117.9167	16.5609	107.3943	128.4390
Nasal sector	Relapsing-remitting	76	89.0667	22.9925	83.7766	94.3568
	Secondary-progressive	12	81.8333	17.6214	70.6372	93.0295
Temporal sector	Relapsing-remitting	76	64.7600	14.6995	61.3779	68.1421
	Secondary-progressive	12	62.0000	15.3741	52.2317	71.7683

Comparison of mean thickness and thickness in each sector of the RNFL. Values are expressed in microns. 95% confidence intervals for means ± SD.

Table 6 RNFL thickness broken down by EDSS level.

RNFL thickness	EDSS score	Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	<1.5	50	99.0412	14.3548	94.9616	103.1208
	1.5-3.5	48	93.5908	15.4139	89.1151	98.0666
	>3.5	26	87.3688	18.7561	79.6266	95.1110
Superior sector	<1.5	50	122.7800	20.3071	117.0088	128.5512
	1.5-3.5	48	119.7083	24.3720	112.6314	126.7852
	>3.5	26	107.0000	23.2737	97.3931	116.6069
Inferior sector	<1.5	50	120.8400	20.0482	115.1423	126.5377
	1.5-3.5	48	115.4375	20.5404	109.4732	121.4018
	>3.5	26	105.0400	25.8803	94.3571	115.7229
Nasal sector	<1.5	50	85.8400	24.3229	78.9275	92.7525
	1.5-3.5	48	81.9167	21.2531	75.7454	88.0879
	>3.5	26	80.1600	25.9577	69.4452	90.8748
Temporal sector	<1.5	50	66.7000	15.5514	62.2803	71.1197
	1.5-3.5	48	58.0000	14.3764	53.8255	62.1745
	>3.5	26	56.4800	15.4734	50.0929	62.8671

Comparison of RNFL mean thickness and thickness in each sector. Values are expressed in microns. 95% confidence intervals for means ± SD.

Table 7 RNFL thickness by EDSS level in the group of MS patients without optic neuritis.

RNFL thickness	EDSS score	Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Mean thickness	<1.5	38	103.6062	11.8219	99.6646	107.5479
	1.5-3.5	34	96.4023	15.5446	91.0625	101.7420
	>3.5	16	96.5360	10.4546	90.7464	102.3256
Superior sector	<1.5	38	127.5405	19.0271	121.1966	133.8845
	1.5-3.5	34	121.2000	25.9261	112.2941	130.1059
	>3.5	16	117.7333	12.1741	110.9915	124.4751
Inferior sector	<1.5	38	126.0000	17.6839	120.1039	131.8961
	1.5-3.5	34	119.4286	20.0107	112.5547	126.3025
	>3.5	16	116.2667	16.7693	106.9801	125.5532
Nasal sector	<1.5	38	92.4324	22.0511	85.0802	99.7846
	1.5-3.5	34	83.4286	23.2749	75.4334	91.4238
	>3.5	16	88.1333	20.1702	76.9634	99.3032
Temporal sector	<1.5	38	68.3784	15.1847	63.3155	73.4412
	1.5-3.5	34	61.5714	14.2298	56.6833	66.4595
	>3.5	16	61.0667	13.2312	53.7394	68.3939

Comparison of RNFL mean thickness and thickness in each sector. Values are expressed in microns. 95% confidence intervals for means ± SD.

Table 8 RNFL thickness in patients with and without optic neuritis.

RNFL thickness	ON	Eyes	Mean	SD
Mean thickness	ON > 6 months	20	80.0711	15.9168
	ON between 3 and 6 months	16	93.9275	13.3021
	No history of ON	88	99.2555	13.7123
Superior sector	ON > 6 months	20	103.1071	24.6160
	ON between 3 and 6 months	16	121.8750	15.5970
	No history of ON	88	122.9655	21.2660
Inferior sector	ON > 6 months	20	96.2857	21.4973
	ON between 3 and 6 months	16	121.6250	16.1239
	No history of ON	88	121.1494	19.3044
Nasal sector	ON > 6 months	20	70.1429	21.1024
	ON between 3 and 6 months	16	82.5000	19.5375
	No history of ON	88	87.4023	23.1373
Temporal sector	ON > 6 months	20	51.5357	14.1198
	ON between 3 and 6 months	16	54.0000	19.4717
	No history of ON	88	65.0115	15.0838

Comparison of mean thickness and thickness in each sector of the RNFL. Values are expressed in microns. Mean ± SD.
ON, optic neuritis.

Table 9 Retinal thickness in the central 1000- and 3000-μm-diameter areas by EDSS level.

Retinal thickness	EDSS score	Eyes	Mean	SD	95% confidence interval for the mean	
					Lower limit	Upper limit
Macular thickness	<1.5	50	217.7800	20.0268	212.0884	223.4716
	1.5-3.5	48	217.6875	20.7704	211.6564	223.7186
	>3.5	26	219.0400	24.2632	209.0246	229.0554
Superior sector	<1.5	50	265.0600	19.7116	259.4580	270.6620
	1.5-3.5	48	259.2500	19.7263	253.5221	264.9779
	>3.5	26	257.9600	25.4009	247.4750	268.4450
Inferior sector	<1.5	50	261.4200	21.2786	255.3727	267.4673
	1.5-3.5	48	257.7083	20.9649	251.6207	263.7959
	>3.5	26	254.9200	29.6759	242.6704	267.1696
Nasal sector	<1.5	50	250.9000	37.4864	240.2465	261.5535
	1.5-3.5	48	248.0208	29.0088	239.5976	256.4441
	>3.5	26	247.4000	32.7363	233.8871	260.9129
Temporal sector	<1.5	50	245.3600	19.6839	239.7659	250.9541
	1.5-3.5	48	238.8125	21.2869	232.6314	244.9936
	>3.5	26	236.3200	28.2956	224.6401	247.9999

Macular thickness: retinal thickness in the central 1000-μm diameter area. Superior, inferior, nasal, and temporal sectors: thickness in the 3000-μm-diameter area. Comparison of RNFL mean thickness and thickness in each sector. Values are expressed in microns. 95% confidence intervals for means ± SD.
EDSS, expanded disability status scale.

Table 10 Retinal thickness in the central 1000- and 3000-μm-diameter areas in patients with and without optic neuritis.

Retinal thickness	History of ON	Eyes	Mean	SD
Macular thickness	ON > 6 months	20	214.5000	20.9982
	ON between 3 and 6 months	16	212.2500	19.2854
	No history of ON	88	219.6552	21.2235
Superior sector	ON > 6 months	20	247.1429	23.2215
	ON between 3 and 6 months	16	250.6250	15.3244
	No history of ON	88	266.9080	18.2161
Inferior sector	ON > 6 months	20	245.2143	26.8415
	ON between 3 and 6 months	16	250.6250	14.2722
	No history of ON	88	263.7126	20.4813
Nasal sector	ON > 6 months	20	239.4286	29.9313
	ON between 3 and 6 months	16	247.5000	22.6967
	No history of ON	88	252.3103	34.6219
Temporal sector	ON > 6 months	20	228.6071	25.4490
	ON between 3 and 6 months	16	230.7500	12.8480
	No history of ON	88	245.8851	20.2791

Macular thickness: thickness in the central 1000-μm-diameter area. Superior, inferior, nasal, and temporal sectors: thickness in the 3000-μm-diameter area. Comparison of RNFL mean thickness and thickness in each sector. Values are expressed in microns. Mean ± SD.
ON, optic neuritis.

1000-μm-diameter area or the sectors of the 3000-μm-diameter area (Table 9).

When comparing quantitative values of macular thickness in the sectors of the 3000-μm-diameter area between patients without optic neuritis and those with a history of optic neuritis (between 3 and 6 months, or more than 6 months) (Table 10), differences were found to be statistically significant in the superior, temporal, and inferior sectors ($P < .01$).

Discussion

Our study analysed RNFL thickness using time-domain optical coherence tomography. RNFL thickness measurements obtained with this tool are strongly correlated with the values obtained with spectral-domain optical coherence tomography; however, the results from these 2 techniques are not interchangeable.[16]

Our results show a statistically significant decrease in mean RNFL thickness in patients with MS compared to controls. These differences were also statistically significant in the temporal and inferior sectors. However, if we exclude the patients with a history of optic neuritis, differences were significant only in the temporal sector. Pueyo et al.[3] and Bock et al.[11] described a decrease in thickness in the temporal sector exclusively.

Gundogan et al.[17] compared a series of patients with MS with no visual symptoms and a control group without MS, and found a statistically significant reduction in thickness in the temporal sector.

According to Costello et al.,[18] the temporal sector is more sensitive to retinal axonal damage in patients with MS. In this study, decreases in mean thickness manifested 2 months after the episode of optic neuritis, whereas decreases in thickness in the superior and inferior sectors manifested after 3 or 4 months. Decreases in RNFL thickness during progression of MS were independent of immunomodulatory therapy.[10]

In our sample, 85.4% of the patients (53/62) had relapsing-remitting MS and 14.6% (9/62) had secondary-progressive MS. These percentages are similar to those reported by Fisher et al.[2] (80% vs 20%) and Iester et al.[19] (78.2% vs 21.8%) in their studies of RNFL thickness in patients with MS.

We found differences in mean thickness and thickness in each sector between the patients with secondary-progressive and relapsing-remitting MS both before and after excluding the patients with a history of optic neuritis. Although these differences were not statistically significant, our findings suggest that RNFL thickness is lower in patients with secondary-progressive MS than in those with relapsing-remitting MS.

Oberwahrenbrock et al.[20] and Albrecht et al.[13] reported differences in RNFL thickness between these 2 clinical forms of MS. Pulicken et al.,[21] however, found no statistically significant differences in thickness between these 2 groups.

Henderson et al.[22] analysed the differences in RNFL thickness in patients with MS. According to this study, the patients with secondary-progressive MS and no history of optic neuritis showed a significant decrease in thickness compared to controls.

The discrepancies between these results and our own may be due to the heterogeneity of the series, the differences in the number of patients included in each subgroup, and the lack of a model for estimating thickness according to age, sex, and disease duration.

Mean RNFL thickness in patients with MS decreases with disease severity. These decreases are statistically significant in the superior, inferior, and temporal sectors.

In the study by Fisher et al.,[2] thickness decreased as EDSS scores increased, which suggests a direct relationship

between the degree of optic nerve axonal loss and the level of neurological impairment.

The comparative analysis of RNFL thickness between the eyes with and without optic neuritis showed significant differences in terms of mean thickness and thickness in all the peripapillary sectors. García-Martín et al.[23] found more pronounced axonal loss in the eyes with a history of optic neuritis. Optic neuritis episodes in patients with MS cause axonal degeneration during the acute phase. After 6 months, however, RNFL atrophy is associated with MS progression regardless of the history of optic neuritis.

Regarding macular thickness in 1000- and 3000-μm-diameter areas, we found no significant differences between EDSS levels. However, we did find significant differences in macular thickness in the temporal, superior, and inferior sectors of the 3000-μm-diameter area between the patients with a history of optic neuritis and those without. The patients with a history of optic neuritis had greater thickness in those sectors than the patients without optic neuritis.

In our study, we measured thickness in the central 1000-μm-diameter area since it has a higher ratio of bipolar cells to ganglion cells, which led us to hypothesise that there may be a connection between RNFL thickness and retinal thickness. However, the differences between groups were not statistically significant.

Burkholder et al.[24] studied RNFL thickness and macular volume in a series of patients with MS and no history of optic neuritis and found statistically significant differences in both parameters between patients with MS and controls.

In summary, mean RNFL thickness decreases as EDSS scores increase. Patients with a history of optic neuritis usually show a more marked axonal loss; this decrease in thickness has been shown to depend on the time elapsed from the last episode of optic neuritis. In contrast, we found no connection between macular thickness within the central 1000- and 3000-μm-diameter areas and EDSS scores.

Conflicts of interest

The authors have no conflicts of interest to declare.

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