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Original article

Changes in eye parameters measured by optical coherence tomography in patients with multiple sclerosis

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Abstract

Multiple sclerosis is an autoimmune disease that affects young adults with age between 20-40 years. Retinal nerve fiber layer (RNFL) thinning in multiple sclerosis patients was demonstrated in many research papers. The aim of this study is to compare RNFL thickness measured by Optical Coherence Tomography in eyes of the patients with relapsing-remitting multiple sclerosis with healthy control eyes.

Method. Optical Coherence Tomography was performed in patients with relapsing-remitting multiple sclerosis and healthy controls.

Results. RNFL was thinner in multiple sclerosis patients compared to healthy controls.

*Conclusions***.** Optical Coherence Tomography is useful in evaluating multiple sclerosis patients.

Keywords: Multiple sclerosis, Optical Coherence Tomography, retinal nerve fiber layer, optic Neuritis.

Introduction

Multiple sclerosis (MS) is an autoimmnune disease affeacting the central nervous system that causes increasing disability and symptom burden over time (Westergaard, Skovgaard, Magyari et al.,2022)

Its onset is tipically in adults with age between 20-40 years. There is a female predominance of up to 3:1. In 85% of cases the course is relapsing-remitting (RRMS) with episodes of neurologic dysfunction followed by complete or incomplete recovery. The rest of 15% of patients, present a gradually progressive course of from onset, defined as primary progressive MS (PPMS) (Ford, 2020).

The exact etiology of the disease is unknown. A patient with MS can present almost any neurological symptom or sign. (Gomaa, Badawy, Elfatatry et al, 2020).

Visual pathway alterations are one of the main features of MS, and for the patients this is perceived as the second condition causing the greatest decreae in their quality of life, the first one is represented by alteration of the musculoskeletal system (Alcubierre, Sánchez -Dalmau, Muὸoz, et al., 2020).

Optic neuritis (ON) is the first clinical finding in about 20% of MS patients. (Aghdam, Aghajani, Kanani et al., 2021)

It can be recognized for the acute or subacute vision loss, associated with painful ocular movements, dyschromatopsia, contrast sensitivity loss and visual field's scotoma. (Costa, Novo, Felgueiras, 2021)

Thinning of the retina and optic nerve are consequences of inflammation, demyelination, axonal degeneration and neural loss in the central nervous systemthat are typical of multiple sclerosis development (Garcia-Martin, ortiz, Bouquete et al., 2021)

Optical Coherence Tomography (OCT) uses lase interferometry to provide crossectional, detailed image of the retina and its component structures. These high- resolution in- vivo images provided by OCT offer spatial iformation from the retina and volumetric and thickness measurements of each component retinal layer. (Mejia- vergara, Karanjia, Sadun, 2021)

OCT gained increaing attention in MS research and has been suggested as a novel tool to track disease progression. Many OCT studies have shown a pronnounced thinning of average retinal nerve fiber layer (RNFL) thickness in ON and different MS subtypes in comparison to healthy controls. (Boka, Brandt, Dörr et al., 2010)

Thinning of the RNFL has been demonstrated in patients even without history of ON. It was also shown that it is correlated with neurological disability assesed by expanded disability status scale (EDSS) and

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brain volume loss in Magnetic Resonance Imaging (MRI). (Behbehabi, Al-Hassan, Al-Khard et al., 2011)

The aim of this study is to emphasize the differences of RNFL thickness measured by OCT between eyes of multiple sclerosis patients and healthy controls eyes

Method

In the study were included 44 patients (88 eyes) diagnosed with relapsing-remitting multiple sclerosis and 28 healthy controls (56 eyes).

The exclusion criteria for the patients were> age under 18 yeras, history of ON in the last 6 months, history of neurologic or ophtalmologic diseases, evidence of macular disease, diabetes, poor OCT image quality.

In both groups (patients and healthy controls), for each eye we performed OCT using TopCon Dri OCT Triton. We measured RNFL thickness in the four quadrants (superior, inferior, temporal and nasal) and total RNFL thickness.

The statistical analysis was performed using IBM SPSS statistics software version 23. Data are presented as mean +/- standard deviation (SD) for continuous variables in case of symmetric distributions, median and IQR (Interquartile range) for continuous variables in case of skewed distributions os as percentages for categorical variables. The normality of the continuous data was estimated with Kolmogorov-Smirnov test of Normality. For hypotheses testing: Leven's test, Independent Samples t-test, One Way ANOVA Test with Post Hoc Multiple Comparisons analysis (Tamhane/ Bonferroni) were used. The probability of a Type I error (the significance level α was) set at 0.05. If the test statistic for every conducted test, was in the critical region, and the p-value was less than or equal to the significance level, we decided to reject the null hypothesis in favor of the alternative hypothesis.

In the patients group we had 33 women and 11 men. In the healthy control group we had 21 women and 7 men. Mean age for the patients group was 38.48 years with a standard deviation (SD) of 9.15 years. For the healthy controls group mean age was 34 years old, with a SD of 7.80 yeard old. There was no statistical significand differences between the two groups regarding mean age values: $t=1.662$, $df=70$, $p-0.101>\alpha=0.05$ (Independent Samples test). The patients group was divided in subgroups as it follows: eyes with histoy of ON (not in the last 6 months0; eyes with out history of ON, and the congener eye (opposite eye of the one with history of ON).

Results

Total RNFL thickness was measured, and, in the group of congener eyes (N=19), the mean value was 95.93µm, with a SD of 16.13µm; in the group with history of ON (N=19), the mean value was 84.35µm with a SD of 16.95 µm, in the group without history of ON (N=50), the mean value was 101.98µm, with a SD of 12.08 µm, and in the healthy controls group (N=56) the mean value of total RNFL was 108.71µm, with a SD of 9.39µm. There are significant differences between mean values of total RNFL in at least 2 groups: $F=19.412$, $p< 0.001$ $\alpha= 0.05$ (OneWay ANOVA Test). The PostHoc Multiple Comparisons-Tamhane Test (Levene Statistic= 3.357, $p= 0.021 <\alpha =0.05$) shows thate there are signficant differences between mean values of RNFL in the following groups: healthy controls/congener eyes ($p= 0.021< \alpha= 0.05$), healthy controls/ eyes with history of ON ($p= 0.001< \alpha= 0.05$), healthy controls/ eyes without history of ON ($p= 0.012< \alpha= 0.05$), but, there are no significant differences beween congener eyes group/eyes with history of ON ($p= 0.207> \alpha=0 .05$) and congener group/eyes without history of ON ($p= 0.624>\alpha= 0.05$).

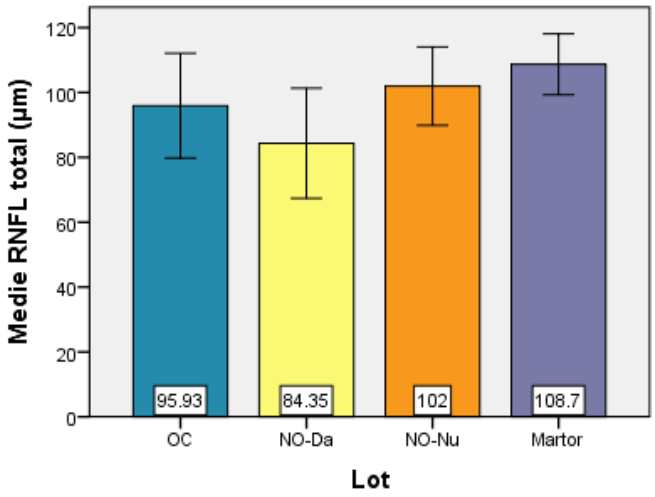

Fig.1. Barr+Error bar chart for mean vales of total RNFL (µm) for the analysed groups

Mean value for **RNFL in the superior quadrant** for congener eyes group was 112.31µm, with a SD of 16.31µm. For the groups eyes with history of ON, mean value for RNFL in the superior quadrant was 101.00µm with a SD of 19.42µm, for the group of eyes without history of ON, mean values for RNFL was 119.26µm, with a SD of 20.96µm, and for healthy cotrols eyes, mean value for RNFL in the superior quadrant was 135.46µm with a SD of 14.21µm. For this situation, there are significant differences between mean vaues for RNFL in the superior quadrant for at least 2 of the analysed groups:).

F=21.818, p< α=0.05 (OneWay ANOVA Test). PostHoc Multiple Comparison- Bonferroni (Levene Statistic= 2.308, p=0.079> α=0.05) indicates that there are significant differences between mean values of RNFL in the superior quadrant in the following groups: eyes with history of ON/healthy control eyes (p= 0.001< α=0.05), eyes with no history of ON/healthy control eyes (p=0.001< α=0.05), congener eyes/healthy control, eyes (p=0.001<α=0.05) and, eyes with history of ON /eyes without history of ON (p=0.001< α= 0.05

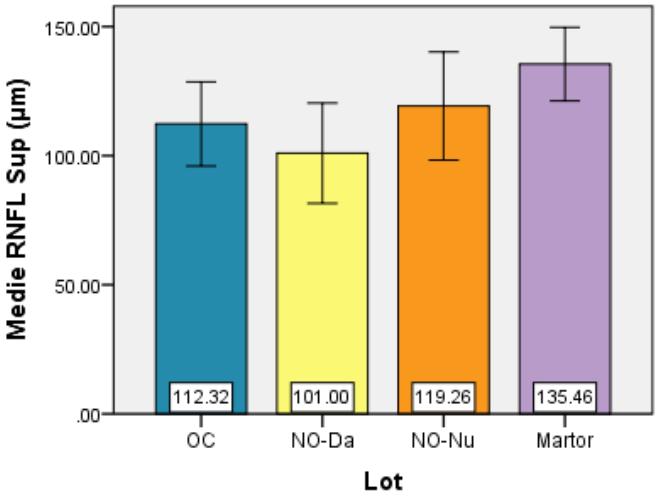

Fig.2 Barr+Error bar chart for mean vales of RNFLin the superior quadrant (µm) for the analysed groups

The mean values for **the RNFL in the inferior quadrant** are the following: for the congener eyes group 124.73µm with a SD of 23.42µm.; for the eyes with history of ON 112.52µm, with a SD of 26.17µm; for the eyes without history of ON 135.72µm with a SD of 18.55µm; for the healthy control eyes 136.32µm with a SD of 17.13µm. There are significantl differences between the mean values for RNFL thickness in the inferior quadrant in at least 2 of the groups: F=8.367, p=0.001<α=0.05 (OneWay ANOVA Test). The PostHoc Multiple Comparisons Bonferoni (Levene Statistic=1.468, p=0.226 >α= 0.05) indicates that there are differences between mean values of the following groups: eyes with history of ON/healthy control eyes (p=0.001<α=0.05) and eyes with history of ON/eyes without history of ON (p<0.001< α=0.05).

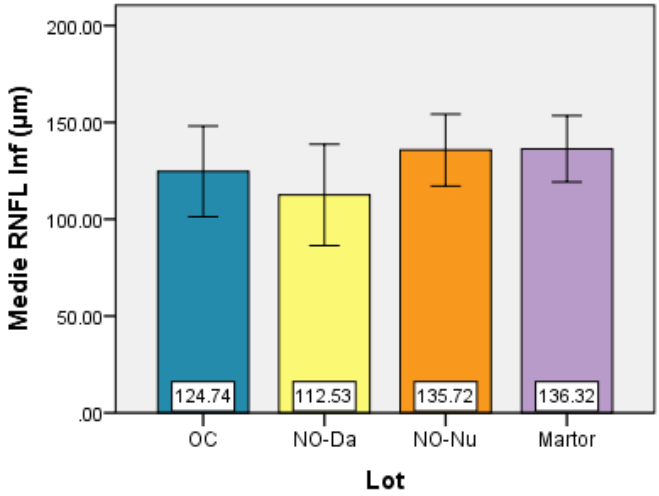

Fig.3 Barr+Error bar chart for mean vales of RNFL in the inferior quadrant (µm) for the analysed groups

For RNFL **measured in the temporal quadrant,** the mean value**s** were: for the congener group eyes the mean value was 62.84µm with a SD of 15.45µm; for the eyes with history of ON the mean value was 49.00µm with a SD of 13.98µm; for the eyes without history of ON the mean value was 64.08µm with a SD of 13.10µm; for the healthy control eyes the mean value was 77.19µm with a SD of 9.91µm. There are significant differences between the mean values for RNFL thickness in the temporal quadrant in at least 2 of the groups: F=27.45, p<0.001α=0.05. (OneWay ANOVA Test). Post Hoc Multiple Comparisons-Tamhane test (Levene Statistic=2.698, p=0.048<α=0.05) indicates thate there are significant differences between mean values of RNFL in the temporal quadrant in the following groups: eyes with history of ON/congener eyes (p= 0.038< α=0.05), eyes with history of optic neuritis/ healthy control eyes (p<0.001<α=0.05).

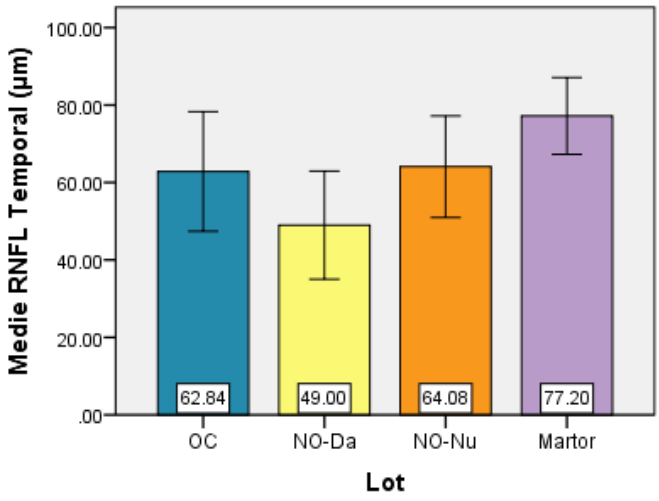

Fig.4 Barr+Error bar chart for mean vales of RNFL in the temporal quadrant (µm) for the evaluated groups

Regarding **RNFL in the nasal quadrant**, the mean values are: for congener eyes group 86.05µm with a SD of 42.67µm; for the eyes with history of ON 74.89µm with a SD of 32.11µm; for the eyes without ON 88.76µm with a SD of 23.30µm; for the healthy control eyes 85.71µm with a SD of 10.01µm. There are no significant differences between mean values of RNFL in the nasal quadrant in the evaluated groups: F=1.495, p=0.218>α=0.05 (OneWay ANOVA Test).

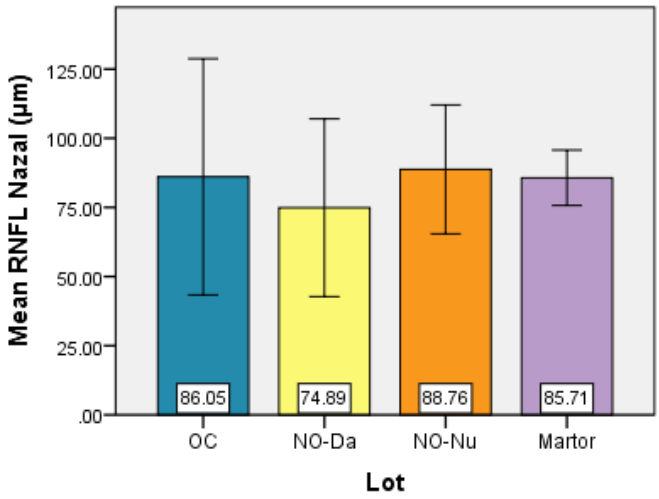

Fig.5 Barr+Error bar chart for mean vales of RNFL in the nasal quadrant (µm) for the evaluated groups

Disscusions

In the study we included 44 patients (88 eyes) diagnosed with relapsing- remittimg MS, and 28 (56 eyes) healthy controls

The highest mean value for **total RNFL thickness** was in the healthy control group eyes, and the lowest in the eyes with history of ON. We found significant differences between mean values of the total RNFL in the following groups: healthy controls/ congener eyes, healthy controls/ eyes with history of ON, healthy controls/ eyes without history of ON. There are no significant differences between congener eyes group/eyes with history of ON, and congener group and eyes without history of ON. It is easy to notice that the mean value of total RNFL in the congener eye group is lower than the one in the group

of patients with no previous history of ON, even if there is no significant difference.

The mean value for RNFL **in the superior quadrant** was also highest in the eyes of the healthy control group, and the lowest was in the eyes with ON history. We found significant differences between the mean values of RNFL in the superior quadrant between the eyes of the patients with history of optic neuritis and healthy controls, the eyes without history of optic neuritis and healthy controls, and congener eyes and healthy controls. We can also notice that the mean value for RNFL in the superior quadrant is lower in the congener eyes group then the mean value in the eyes of the patients without history of optic neuritis.

The assessment of **RNFL in the inferior quadrant** indicates again the highest mean value in the healthy control group and the lowest in the eyes with history of ON. We found significant differences between the mean values of RNFL measurement in the inferior quadrant in the eyes of the patients with history of ON and healthy control eyes, and the eyes of the patients with and without history of ON. In this quadrant also, we notice that the mean value for RNFL is lower in the congener group eye tha in the group of

thinning of the RNFL in clinically unaffected eyes (in which there has not been a previous clinical episode of ON) of patients with MS when compared to healthy controls (Abalo-Lojo, Treus, Arias, et al., 2018).

Conclusions

Our study emphasizes that OCT has an important role in assessing RNFL thinning in multiple sclerosis patients, even in the ones without previous ON attacks. In our study we demonstrate that OCT is very useful in evaluating multiple sclerosis patients, providing information about neurodegeneration and axonal loss**.**

References

Alcubierre R, Sánchez-Dalmau BF, Muñoz S, 2020, La esclerosis múltiple en oftalmología: más allá de la neuritis óptica, Med Clin (Barc). 155 (2):70-76

Alvaro J, Mejia V, Rustum K, Alfredo A, Sadun, OCT parameters of the optic nerve head and the retina as surrogate markers of brain volume in a normal population, a pilot study, Journal of Neurological Sciences 420 (2021) 117213, https://doi.org/10.1016/j.jns.2020.117213

eyes without history of ON even if there is no significant difference.

For the **temporal quadrant**, the highest mean value for RNFL was in the healthy control eyes, and the lowest in the eyes of the patients with ON history. We found significant differences between the groups of eyes with history of ON and congener eyes and between the group with ON and healthy controls. The mean value in the congener group is lower than the mean value of the eyes with no history for ON.

RNFL measurement in the **nasal quadrant** was the highest in the eyes with no history of ON and the lowest in the eyes with history of ON. There were no significant differences in this case.

Indirect measure of axonal and neuronal loss in the anterior visual pathways is provided by quantification of RNFL thickness by OCT. (Lamirel, Newman, Biousse, 2010).

The results we obtained by measuring total RNFL, and in the four quadrants of the eyes of the patients with multiple sclerosis reveal thinning of the RNFL in the eyes without ON history. A number of studies have also reported

Lamirel C, Neuwman NJ, Biousse V, Optical coherence tomography (OCT) in optic neuritis and multiple sclerosis, Revue Neurologique 166 (2010) 978-9986, doi:10. 1016. J. neurol.2010.03.024

Garcia ME, Ortiz M, Bouquete L, Sanchez Morla E M, R. Barea, Cavaliere C, Vilades E, Orduna E, Rodrigo MJ, Early Diagnosis of multiple sclerosis by OCT analysis using Cohen's d method and a neural network as classifier, Computers in Biology and Medicine 129 (2021) 104165, https://doi.org/10.1016/j.compbiomed.2020.104165

Helen F, Clinical Presentation and Diagnosis of Multiple Sclerosis, Clinical Medicine, 2020, Vol 20, No4:380-3

Abalo-Lojo JM, Treus A, Arias M, Gómez-Ulla F, Gonzales F, Longitudinal Study of retinal nerve fiber layer thickness changes in a multiple sclerosis patients cohort: A long term 5 year follow-up, Multiple Sclerosis and Related Disorders, 19 (2018) 124-128

Joana CN, Helena F, Neuro-ophtalmologic manifestations of multiple sclerosis other than acute optic neuritis, Multiple Sclerosis and Related Disorders, 48 (2021) 102730, https://doi.org/10.1016/j.msard.2020.102730

Katrine W, Lasse S, Melinda M, Maria K, Patient perspectives on patient-reported outcomes in multiple sclerosis treatment trajectories: A qualitative study of why, what, and how? Multiple Sclerosis and Related Disorders 58 (2022) 103475, https://doi.org/10.1016/j.msard.2021.103475

Kaveh AA, Ali A, Fatemeh K, Mostafa SS, Samira C, Fatemeh S, Delaram M, Mehdi M, A novel decision tree approach to predict the probability of conversion to multiple sclerosis in Iranian patients with optic neuritis, Multiple Sclerosis and Related Disorders, 47 (2021) 102658, https://doi.org/10.1016/j.msard.2020.102658

Markus B, Alexander UB, Jan D, Helga K, Nicholetta WE, Gunnar G, Caspar FP, Katja He, Helena R, Stephanie O, Judith BSt, Jörn K, Frauke Z, Friedemann P, Patterns of retinal nerve fiber layer loss in multiple sclerosis patients with or without optic neuritis and glaucoma patients, Clinical Neurology and Neurosurgery 112 (2010) 647-652, doi:10.1016/j.clineuro.2010.04.014

Raed B, Abdullah A Al-H, Abdullah Al-K, Devarajan S, Raed A, Retinal nerve fiber layer thickness and neurologic disability in relapsing remitting multiple sclerosis, Journal of Neurological Sclences, 359 (2015) 305-308, https://dx.doi.org/10.1016/j.jns.2015.11.017

Syc SB, Warner CV, Saidha S, Farrel SK, Conger A, Bisker ER, Wilson J, Frohman TC, Frohman E M, Balcer LJ, Calabrese P. A., Cup to disc ratio by optical coherence tomography is abnormal in multiple sclerosis, Hournal of Neurological Sciences, 302 (2011) 19-24, doi:10.1016/ j/jns.2010.12.011

Said GA, Mohamed BB, Elfatatry AM, Elhennawy AA, Visual dysfunction and neurological disability in multiple sclerosis patients in correlation with the retinal nerve fiber layer nd the ganglion cell layer using optical coherence tomography, Egypt J Neurol Psychiatry Neurosurg, 2016, 53:200-205.