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ORIGINAL ARTICLE

Assessment of Retinal Nerve Fiber Layer Thickness in Patients with Multiple Sclerosis using Optical Coherence Tomography

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Abstract

Background: ***Multiple sclerosis (MS) is a chronic autoimmune illness that primarily affects the central nervous system (CNS), damaging the myelin sheath, the cells known as oligodendrocytes, and nerve fibers. It is classified as a central nervous system (CNS) inflammatory and neurodegenerative illness.***

Aim and objectives: ***To evaluate and contrast the thickness of the retinal nerve fiber layer in individuals diagnosed with multiple sclerosis. Compared to individuals without health issues. Evaluating color vision to assess visual impairment in persons with MS.***

Patients and methods: ***This cross-sectional study comprises 80 eyes from 40 individuals. They are divided into groups A (Control) and B (MS sufferers). Every patient underwent a comprehensive ophthalmological examination, including assessing the layer of retinal nerve fibers (RNFL) and color vision using OCT. The collected data were then analyzed for correlations.***

Results: ***Decreased global RNFL thickness (G) in group B (90.1±9.9) when compared with group A (104.4±4.7), with statistically significant (p-value<0.001) also decreased nasal RNFL thickness (N) in group B (66.4±10.3) when compared with group A (81.8±7.9), with statistically significantly (p-value<0.001) also decreased temporal RNFL thickness (T) in group B (59.2±11) when compared with group A (73.1±6.7), with statistically significantly (p-value<0.001).***

Conclusion: ***The primary parameters that can be utilized for early identification and monitoring of MS's impact on the retina and the visual pathway are color vision and OCT parameters for RNFL's various sectors.***

Keywords: Fiber Layer; Color vision; Retinal Nerve; Multiple sclerosis

1. Introduction

An estimated 400,000 Americans and 2.1 million people globally are thought to be afflicted by MS, with a higher geographic distribution of cases in the northern and southern hemispheres. While the average age of diagnosis is thirty years old, the average age of onset varies from fifteen to forty-five years old.

At a ratio of almost 2:1, women are impacted more frequently than men.[1] Approximately 59,671 persons with MS reside in Egypt, which works out to 1 in every 1,500 persons.[2]

The 2010 revised McDonald Criteria is frequently employed to identify multiple sclerosis. The prerequisites include experiencing two or more attacks on two or more clinical lesions or experiencing two or more attacks on a single diagnostic lesion plus evidence of space dissemination from MRI or CSF; having one attack on two or more lesions shown by MRI or followed by another attack; and having one attack on one lesion shown by MRI, CSF, or both. Any subjective or objective 24-hour neurologic disturbance that happens 30 days apart and is not associated with a fever or infection is called an attack. Depending on how the disease progresses clinically, MS can be divided into four subtypes: progressive relapsing, primary progressive, secondary progressive, and relapsing-remitting. [3]

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MS frequently manifests as ocular symptoms. 75% of individuals experience at least one episode of optic neuritis over their lifetime, and up to 20% of patients present with this condition at some point in their lives. MS-related optic neuritis usually manifests as a painful, monocular vision loss that lasts a few weeks and happens over hours to days. Visual acuity changes can be minor or severe; 10% of patients have 20/20 vision, 25% have 20/30-20/40 vision, 29% have 20/50-20/190 vision, and 36% have 20/200 vision or worse. 92% of patients experience orbital pain, which frequently gets worse when they move their eyes. Additionally, patients exhibited decreased contrast sensitivity, visual field loss (most often central scotoma), reduced color vision (dyschromatopsia in 88%; best diagnosed by red desaturation), and a relative afferent pupillary deficit (RAPD). In one-third of patients, an optic disc pallor was detected by slit lamp examination.[4]

The current study aims to determine and contrast the thickness of the retinal nerve fiber layer in patients with MS with that of healthy controls. It also assesses the degree of visual affection in MS patients by examining their color vision.

2. Patients and methods

This cross-sectional study was conducted at the Department of Ophthalmology at Al-Azhar Hospitals, Cairo. Forty eyes of twenty participants, aged between twenty and forty-five, were identified as MS patients with a relapsing-remitting course, and forty eyes of twenty participants, aged between twenty and forty-five, were used as controls in this case-control study.

Ethical approval: The Ethical Committee of the Faculty of Medicine at Al-Azher University approved the operation. Before the operation, each patient provided written consent after receiving a comprehensive explanation of all pertinent data, including the procedure, potential benefits, foreseeable intraoperative and postoperative risks, reasonable expectations, and the potential occurrence of further issues.

Inclusion criteria:

The study cohort comprised individuals of both genders, aged between 20 and 45 years, who had been diagnosed with relapsing-remitting multiple sclerosis diagnosed with MS by standard clinical and neuroimaging criteria (the Revised McDonald's Criteria of 2010) from the Neurology Department at Al-Azhar University Hospitals.

Explicit anterior segment media allowing clear fundus photography and OCT imaging and control subjects were selected from a set of healthy volunteers, who were recruited among the staff, friends, and family members of patients.

Exclusion criteria:

Individuals with any significant systemic disease, such as diabetes mellitus or arterial hypertension, or ocular conditions, such as age-related macular disease or glaucoma. Two more neurodegenerative diseases that affect RNFL thickness are Alzheimer's and Parkinson's

Methodology:

Patients satisfying the inclusion criteria were consented for participation in this study and had the following performed:

History: A systematic history that includes personal history, including the patient's name, age, and sex. History of the present illness, which included the age at the onset of multiple sclerosis. Signs that could indicate optic neuritis include flashes, discomfort, or pain in the area around the eye that gets worse when the eye moves, ophthalmic symptoms other than diminution of visual acuity (e.g., double vision, deviation of eyes), and neurological symptoms (e.g., Motor, sensory, incoordination, and sphincteric abnormalities).

Examination:

Every patient underwent a thorough eye examination, which comprised (an assessment of uncorrected and best-corrected visual acuity, refraction, slit-lamp biomicroscopy, Goldman applanation tonometry, Pupillary reflexes to detect afferent pupillary defect, Ocular Motility and dilated fundus examination) color vision test and Optical Coherence Topography.

Visual acuity testing: VA was measured for each eye of the participants with Landolt's broken rings chart displayed in a consistent indoor environment under diffused artificial light at a distance of 6 meters from the participants. Participants were examined with monocular best-corrected vision letters in each row, and the last row the patient saw was recorded and converted into decimals.

Color vision testing: The Ishihara test assessed Participants' color vision in each eye. A set of sixteen test plates, each including a dot matrix organized to reveal a central shape or numeral that the participant must identify. The plates are intended to be well-appreciated in a space with enough natural light. Seventy-five centimeters separates the plates from the subject. A person who is color blind will only be able to recognize part of the figures.

Figure 1. The Ishihara test plates.

RNFL thickness profile

The RNFL thickness around the disc's center is measured at 3.45 mm in diameter. The thickness measurement is re-sampled concerning the disc center, not the scan beam center, so the measurement will not be impacted by the disc being decentered concerning the scan beam. The measurement is four circular scans, with the optic disc as the center by default for the Temporal, Superior, Nasal, and Inferior TSNI convention.

Method of acquisition of OCT Images:

Relevant personal information about the patient was input into the device's computer program. The patient is situated so that their forehead touches the forehead appliance and their chin rests on the chin rest. The patient was instructed to fix their gaze on the blue dot inside the red background while staring directly through the device aperture. Based on the protocol, the dot would move from the center to the periphery. Photos are selected and stored.

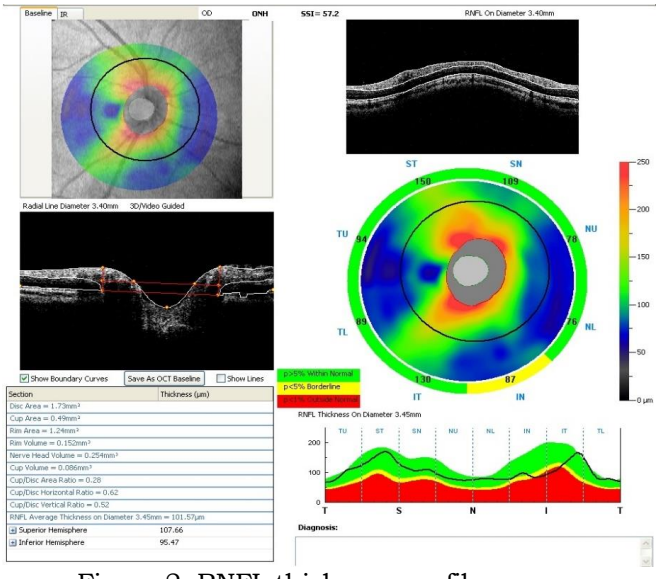

Figure 2. RNFL thickness profile.

Average Egyptian population's thickness of the retinal nerve fiber layer:

The average worldwide RNFL thickness was 101.74±10.05 µm, with a range of 79.0–123.0 µm.[5]

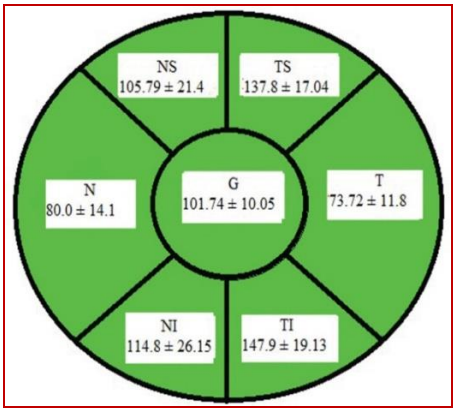

Figure 3. Diagram illustrating the spatial arrangement of the retinal nerve fiber layer. G represents the global sector, N represents the nasal sector, NI represents the nasal inferior sector, NS represents the nasal superior sector, T represents the temporal sector, TI represents the temporal inferior sector, and TS represents the temporal superior sector.

Statistical analysis:

The data was analyzed in version 24 of the Statistical Program for Social Science (SPSS). Frequency and percentage were used to express qualitative data. The statistical information was presented as mean±SD. The mean, or average, is the central value; the arithmetic mean of a discrete set of integers is obtained by taking the total number and dividing its sum of values. The measure of a set of values' dispersion is called the standard deviation (SD). A low (SD) suggests that the values are generally near the set mean, and A high (SD) indicates that the data are spread out over a broader range. The single sample T-test (T) should be used to compare two groups (for normal data distribution). Non-parametric data sets were compared using the chi-square test.

3. Results

As shown in Table 1, A p-value of 0.895 indicates that there was no significant age difference between the two study groups, A and B. The length for group A was 29.7±7.01 years, while the duration for group B was 29.4±7.3 years. Between the two groups under investigation, A and B, there was no statistically significant difference connected to sex (p-value=1.0). Thirteen women (65%) and seven males (35%) made up each study group.

Table 1. Comparison of demographic data between studied groups.

		GROUP A (N=20)		GROUP B (N=20)		STAT. TEST	P-VALUE
AGE (YEARS)	Mean	29.7		29.4		T=0.13	0.895 NS
	±SD	7.01		7.3			
SEX	Male	7	35%	7	35%	X^2=0.0	1.0 NS
	Female	13	65%	13	65%		

T:independent sample T test. X2:Chi-

square test. NS:p-value>0.05 is considered non-significant.

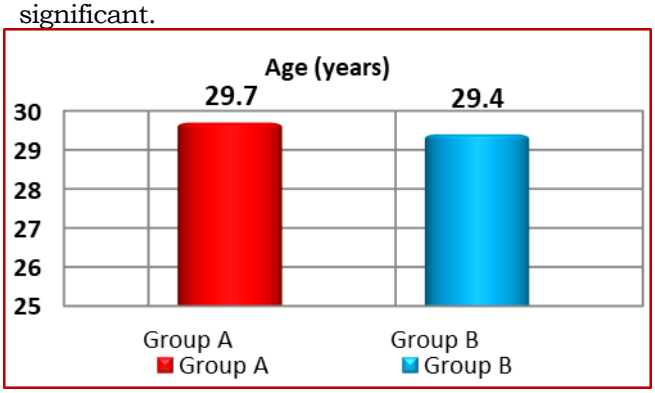

Figure 4. Comparison of age between studied groups.

Regarding the duration of the disease as in Table 2, group B patients had an average disease duration of 5.0±3.1 years, with a maximum of eleven years and a minimum of one year. In terms of the total number of attacks, 7 patients (35%) had 1, 7 patients (35%) had 2, 3 patients (15%) had 3, and the remaining 3 patients (15%) had no attacks at all. Regarding attack side, among group B patients, 3 patients (17.6%) had unilateral attacks, while 14 patients (82.4%) had bilateral attacks. Regarding the most recent attack, group B patients' mean attack duration was 1.4±0.9 years, with a minimum of 0.25 years and a maximum of 4 years.

Table 2. An explanation of the clinical data for participants in group B.

		GROUP B (N=20)	
DISEASE DURATION (YEARS)	Mean±SD	5.0±3.1	
	Min-Max	1-11	
NUMBER OF ATTACKS	No attack	3	15%
	1 attack	7	35%
	2 attacks	7	35%
	3 attacks	3	15%
SIDE OF ATTACK	Unilateral	3	17.6%
	Bilateral	14	82.4%
LAST ATTACK (YEARS)	Mean±SD	1.4±0.9	
	Min-Max	0.25-4	

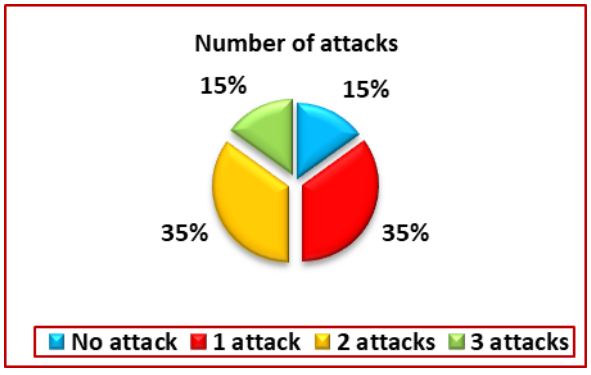

Figure 5. Description of number of attacks in group B patients.

Table 3 showed that, there had been a statistically significant differences (p-value=0.017) between groups A and B in the study. The study found that there were seven individuals (35%) with UA vision (6/6) In group A, two individuals (10%) were present, as opposed to 2 individuals (10%) in group B. In group A, there were nine individuals (45%) with unaided (UA) vision of 6/9, while in group B, there were seventeen individuals (85%) with UA vision. Four individuals (20%) in group A had UA vision of 6/12, whereas no individuals (0%) in group B had this level of vision. Additionally, no individuals (0%) in group A had UA vision of 6/24, while one individual (5%) in group B did.

Table 3. Comparison of UA vision between studied groups.

		GROUP A (N=20)		GROUP B (N=20)		STAT. TEST	P-VALUE
UA VISION	(6/6)	7	35%	2	10%	X^2=10.2	0.017 S
	(6/9)	9	45%	17	85%		
	(6/12)	4	20%	0	0%		
	(6/24)	0	0%	1	5%		

X2:Chi-square test. S:p-value<0.05 is considered significant.

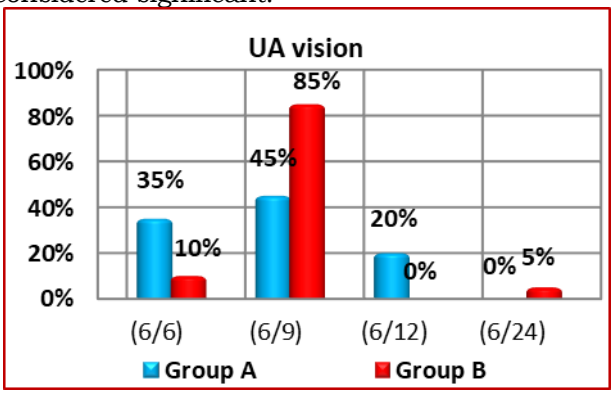

Figure 6. Comparison of UA vision between studied groups.

Between groups A and B in the study, there was definitely a statistically significant distinction in BCV vision (p-value=0.005). Compared to four patients (20%) and six patients (30%) in group A, there were thirteen patients (75%) in group B. With a BCV vision score of 6/9, group B consisted of only one patient (5%) whereas group A included fifteen patients (75%) total. Group A had no patients with a BCV vision score of zero (0%), Table 4.

Table 4. Comparison of the BCV vision of the research groups.

		GROUP A (N=20)		GROUP B (N=20)		STAT. TEST	P-VALUE
BCV VISION	(6/6)	14	70%	4	20%	X^2=10.4	0.005 S
	(6/9)	6	30%	15	75%		
	(6/12)	0	0%	1	5%		

X2:Chi-square test. S:p-value<0.05 is considered significant.

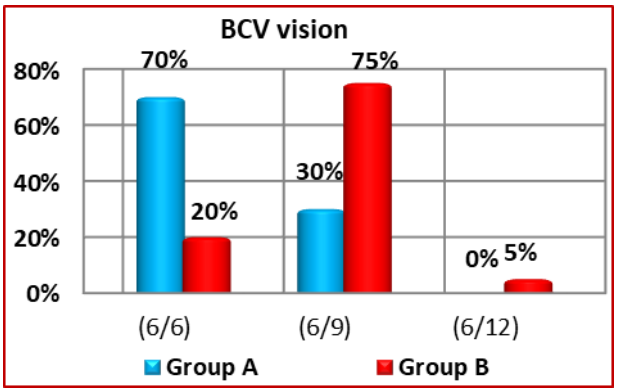

Figure 7. Comparison of BCV vision between studied groups.

Table 5 shows that, there was no statistically significant difference (p-value=0.147) between the two analyzed groups (group A and group B). In group B, 18 patients (90%) and 2 patients (10%) had RRRE and RAPD pupils, respectively, whereas all studied patients in group A (100%) displayed RRRE pupils.

Table 5. Comparison of the student exams between the groups under study.

		GROUP A (N=20)		GROUP B (N=20)		STAT. TEST	P-VALUE
PUPIL	RRRE	20	100%	18	90%	X^2=2.1	0.147
	RAPD	0	0%	2	10%		NS

X2:Chi-square test. NS:p-value>0.05 is considered non-significant.

Between the two examined groups, there was no statistically significant difference in the AC assessment. All patients (100%) in the two study groups underwent a standard AC assessment as in Table 6.

Table 6. Comparison of AC examination between studied groups.

		GROUP A (N=20)		GROUP B (N=20)		STAT. TEST	P-VALUE
AC	Normal	20	100%	20	100%	----	----
	Abnormal	0	0%	0	0%		

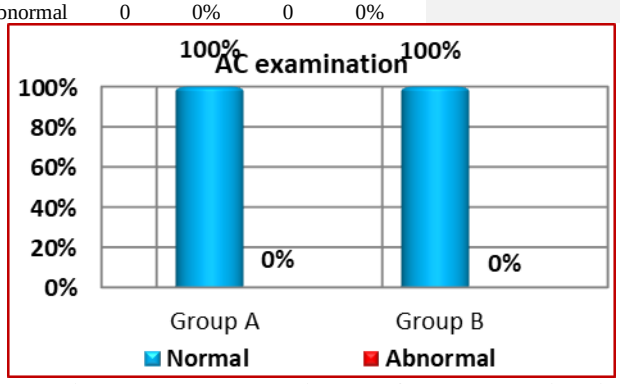

Figure 8. Comparison of AC examination between studied groups.

Table 7 showed that, there was no discernible difference between the two study groups (groups A and B; p-value=0.290). It was 15.8±2.6 mmHg in group A and 15.0±2.4 mmHg in group B.

Table 7. IOP comparison between the groups under study.

		GROUP A (N=20)	GROUP B (N=20)	STAT. TEST	P-VALUE
IOP (MMHG)	Mean ±SD	15.8 2.6	15 2.4	T=1.07	0.290 NS

T:independent sample T test. NS:p-value>0.05 is considered non-significant.

4. Discussion

Our results showed that MS patients' mean RNFL thickness was significantly lower than healthy controls. These findings are consistent with a German study by Bock et al., which showed that the average RNFL loss in MS patients was considerably higher than in healthy controls.[6]

Our study agreed with Haung and Hu et al., who found a statistically significant decrease when comparing the average RNFL thickness of MS patients without ON to the control group.[7]

Saxena et al. found that the RNFL thickness in the nasal (66.23±12.4 µm against 88.93±22.18 µm; P<.001) and superior (106.77±17.92 µm versus 132.33±15.42 µm; P<.001) quadrants differed significantly between the eyes of MS patients and the healthy group. The high axon density of the optic nerve, which predisposes it to atrophy, explains these observations.[8]

According to this study, individuals with MS who had no prior history of ON similarly had a marked decrease in RNFL thickness in their eyes, which indicates the presence of subclinical disease activity. The statistically substantial variation in the average RNFL thickness led to that conclusion. Furthermore, when comparing MS's history of ON to those without, we discovered a noticeably reduced RNFL thickness. Other writers have also reported findings similar to these. When comparing MS patients suffering unilateral optic neuritis to healthy controls, this affection was primarily connected to the duration of the disease, regardless of the prevalence of optic neuritis.[9]

These results agreed with Fisher et al., who discovered a substantial decrease in RNFL in eyes unaffected by ON compared to the eyes of control individuals using the more recent Stratus OCT model. Both neighboring eyes and patients' eyes lack a history of ON in either eye, forming this group of unaffected eyes.[10]

Our findings demonstrated impaired color vision in the study group. Seven individuals (35%) had a red-green deficiency, while 13 patients (65%) had a normal color vision. These findings supported Kollner's rule, which states that optic

nerve disorders impact the red-green channel. One important conclusion of this study is that even in those with MS without ON, color vision loss increases with age and length of disease. The Ishihara test has limited sensitivity for blue-yellow defects because it is primarily intended to detect abnormalities in the red-green color spectrum.

Our study, agreed with Flanagan & Zele, demonstrated decreased sensitivity to color and contrast in people with multiple sclerosis.[11]

In line with our results, Martínez-Lapiscina et al. demonstrated that dyschromatopsia in non-ON eyes is associated with increased clinical disability, aging, a longer duration of the disease, and worse damage to the central nervous system retina. After a year, it was discovered that individuals who experienced color vision impairment without ON had more disability and gray matter atrophy, indicating a connection between dyschromatopsia and diffuse axonal damage that is not related to inflammatory activity.[12]

According to our findings, color vision impairment in multiple sclerosis is linked to diffuse axonal damage, as seen by its correlation with imaging markers of diffuse retinal and brain damage. Using the Ishihara test, color vision changes over three years were found to be relatively minor in a previous study.[13]

Our results showed a pale optic disk in 9 patients (45%) in group B, while 11 patients (55%) showed a normal optic disk. As a result of RNFL damage, this is in line with the reduction of BCV acuity and dyschromatopsia. This means that multiple sclerosis has clear effects on both BCV not related to refractive error and the ability to distinguish different colors. This increases significantly with the disease duration and occurrence of ON.

In line with these results were the results of González de la Rosa M et al. They developed a new method to detect early morphological changes in neurodegenerative diseases such as multiple sclerosis based on measuring the hemoglobin content of different optic disc parts. All Hb percentages were lower in MS patients than in healthy controls, appearing as temporal pallor at the optic disc in the examination.[14]

Regardless of the presence of ON, MS appears to cause gradual alterations in the RNFL thickness over time. As the MS patients' condition worsened over time, a notable decrease in RNFL thickness was observed in the presence of ON. Conversely, MS patients without a history of ON showed less severe RNFL thinning during the same time span. The RNFL thickness of MS patients and healthy controls differed significantly, regardless of ON's presence or absence. Therefore, RNFL thickness measurement could be a valuable biomarker to assess the disease's course and its correlation with ON.

There are notable associations between the EDSS score and the average thickness of the retinal nerve fiber layer (RNFL). Additionally, there is a robust connection between cognitive impairment and the thickness of the inner layer of the retinal nerve. Consistent with previous studies, there is evidence of a correlation between the EDSS scores of patients with multiple sclerosis (MS) and the atrophy of the retinal nerve fiber layer (RNFL).[15]

Overall, our results showed that decreased global RNFL thickness (G) in group B (90.1±9.9) when compared with group A (104.4±4.7), with statistically significant (p-value<0.001) also decreased nasal RNFL thickness (N) in group B (66.4±10.3) when compared with group A (81.8±7.9), with statistically significantly (p-value<0.001) also decreased temporal RNFL thickness (T) in group B (59.2±11) when compared with group A (73.1±6.7), with statistically significantly (p-value<0.001).

4. Conclusion

The measurement of (RNFL) thickness, color vision, and best corrected visual acuity (BCVA) are crucial for closely monitoring the advancement and intensity of the disease.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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