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Assessment of Retinal Nerve Fiber Layer Thickness in Fellow Eye in Patients with Unilateral Optic Neuritis

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Abstract

Background: One of the main progressive consequences of optic neuritis is inflammatory axonal loss manifested by Retinal Nerve Fiber layer (RNFL) thinning on Optical Coherence Tomography. We assessed RNFL thickness in the fellow eye in patients with unilateral optic neuritis.

Methods: Twenty nine patients with unilateral optic neuritis after three months of attack, were enrolled in the study and the RNFL thickness were measured by Optical Coherence Tomography in the quadrants of superior, nasal, inferior, and temporal at both involved and fellow eyes.

Results: The mean RNFL thickness was significantly lower in the involved than in fellow eye in all quadrants except for temporal. Significant differences were only in women. Compared to fellow eyes, lower mean RNFL thickness in superior, inferior, and nasal quadrants in involved eyes was found mostly in the ages below 40. RNFL was less thickened in involved than in fellow eyes only in those patients with final diagnosis of isolated optic neuritis not in those with multiple sclerosis. Mean RNFL thickness was significantly lower in involved eyes in all quadrants (except for temporal) only in those who underwent Optical Coherence Tomography 13 to 24 months after optic neuritis.

Conclusion: RNFL thinning occurs in involved eye compared to fellow eye in patients with unilateral optic neuritis. It is observed in women more than men and in those patients younger than 40. The abnormal change in RNFL thickness was also found in those patients underwent Optical Coherence Tomography 13 to 24 months after optic neuritis. The difference in mean RNFL thickness may be specified to inferior quadrant in MS patients.

Keywords: Optic Neuritis; Retinal nerve fiber thickness; Fellow eye

Introduction

Optic neuritis is an optic nerve inflammatory disorder primarily an isolated phenomenon or secondarily associated with other neurological defects such as neuromyelitis optica or multiple sclerosis or infectious processes such as local or systemic viral infections [1-4]. Some types of optic neuritis may be also resembled by genetic disorders or by neuropathies with unknown origins [4,5]. Inflammatory and immunological nature of optic neuritis has been clearly demonstrated [6]. In pathological investigations, the presence of perivascular lymphocytic infiltration, multifocal demyelination, and reactive astrocytosis in the retrobulbar portion of the optic nerve along with abnormal intrathecal immunoglobulin G (IgG) synthesis has been revealed [7]. Decreased visual acuity is the main manifestation of optic neuritis that is gradually recovered; however, it can remain permanent in a rare of patients. Moreover, defects in color vision and contrast and brightness sensitivity are common permanent symptoms [8]. According to the specific nature of optic neuritis, the definitive diagnosis of disease is based on taking patients' history of inflammatory or infectious disorders along with assessing laboratory inflammatory parameters as well as specific imaging in assessment of inflammatory changes in the optic nerves and peripheral structural lesions [9].

One of the main progressive consequences of optic neuritis is inflammatory axonal loss leading decrease of visual acuity and manifested by Retinal Nerve Fiber layer (RNFL) thinning on Optical Coherence Tomography (OCT). In fact, the visual fields in case of optic neuritis indicate a higher deviation strongly correlated with RNFL loss in optic neuritis patients. In fact, the RNFL thickness measured by OCT showed a significant thinning in the average value and each of the four quadrants in optic neuritis [10,11]. In patients with MS, decrease in RNFL thickness also occurred in an eye affected by ON and some time it can be found even in the fellow eye and without history of ON as well. In patients with NMO, involvement is often bilateral.

It is now hypothesized that the optic nerve atrophy that develops following optic neuritis is due to axonal loss that is

manifested by thinning of the RNFL. The present study aimed to assess RNFL thickness in fellow eye compared to involved eye in patients with unilateral optic neuritis and to determine whether the thickness of fellow eye differs from involved eye affected by different diseases.

Materials and Methods

Twenty-nine patients (23 female, 6 male) with unilateral optic neuritis 3 months after the incidence of ON were enrolled in the study. Six patients were under twenty, 14 were 20-30, nine 30-40 and two were above 40.

A cross-sectional study was conducted at neurology and ophthalmology setup in Rasoul-e-Akram Hospital in Iran in 2015 after prior approval from the research and ethics review boards at Iran University of Medical Sciences. The patients were considered eligible for the study if affected by unilateral optic neuritis. However, based on the study of Costello et al. in 2008 and You et al. in 2013 that specified a significant change in RNFL thickness two months after the incidence of ON, OCT was performed after 3 months of the ON. Thus, the patients with bilateral involvement or with disease duration less than 3 months of ON were excluded. Initially, all patients underwent a detailed history, ocular and neurological examination and investigations to gauge visual functions. The RNFL thickness was measured using the optic nerve cube program on the TOPCON 3D OCT-1000 MK2 (version.3.5.1) and by a trained expert person in the four quadrants i.e. superior, nasal, inferior, and temporal at both involved and fellow eyes. OCT scans with signal strength above 7 were acceptable for analysis else they were repeated. Decreased by more than 5% in the RNFL thickness was considered as abnormal. The study endpoint was to compare the mean RNFL thickness between attack and fellow eyes in terms of demographic characteristics and underlying disorders. Analysis was done using SPSS version 16 (SPSS Inc., Chicago, IL, USA) and Stata 8.0 (Stata Corp LP, College Station, TX, USA) using appropriate tests. Parametric and Non-Parametric tests (T-test and Mann Whitney U) were used for intergroup comparison while the Pearson's correlation coefficient was derived for examining intergroup associations.

Results

Twenty nine patients with unilateral optic neuritis 3 months after the incidence of ON were enrolled in the study. In total, while there was a significant decrease in the mean RNFL thickness of the attack eye, the thickness was normal in the fellow eye, in all quadrants except for temporal quadrant **(Table 1)**. Significant differences were only specified in women not in men. Regarding RNFL thickness in different age subgroups **(Table 2)**, compared to fellow eyes, lower mean RNFL thickness in superior, inferior, and nasal quadrants in attack eyes was revealed mostly in the ages below the 40 years, but not in older adults. RNFL was less thickened in attack than in fellow eyes only in those patients with final diagnosis of isolated optic neuritis not in those with final diagnosis of multiple sclerosis **(Table 3)**. Interestingly, mean thickness was significantly lower in attack eyes than in fellow eyes in all quadrants (except for temporal) only in those who underwent OCT 13 to 24 months after occurring optic neuritis **(Table 4)**.

Table 1 Mean RNFL thickness between affected and unaffected eyes in terms of genders.

Item	Affected eye	Unaffected eye	P-value
Total			
Total	94.03 ± 14.99	104.86 ± 8.21	<0.001
Superior	111.86 ± 20.77	122.83 ± 12.75	0.003
Inferior	114.38 ± 24.47	132.86 ± 16.33	<0.001
Nasal	77.83 ± 14.23	89.24 ± 11.52	<0.001
Temporal	71.93 ± 16.98	74.66 ± 12.20	0.377
Female			
Total	95.70 ± 13.91	104.96 ± 9.02	<0.001
Superior	114.74 ± 18.59	123.52 ± 12.96	0.011
Inferior	116.26 ± 24.63	133.39 ± 17.33	<0.001
Nasal	77.00 ± 14.09	88.83 ± 12.39	<0.001
Temporal	74.70 ± 16.98	74.43 ± 13.23	0.931
Male			
Total	87.67 ± 18.63	104.50 ± 4.37	0.122
Superior	100.83 ± 26.64	120.17± 12.64	0.13

Inferior	107.17 ± 24.57	130.83 ± 12.89	0.135
Nasal	81.00 ± 15.63	90.83 ± 7.99	0.194
Temporal	61.33 ± 13.32	75.50 ± 7.89	0.143

Table 2 Mean RNFL thickness between affected and unaffected eyes in terms of age subgroups.

Item	Affected eye	Unaffected eye	P-value
Total			
Age group 1	99.50 ± 10.47	107.00 ± 13.61	0.027
Age group 2	92.07 ± 18.57	103.29 ± 5.82	0.045
Age group 3	93.00 ± 11.61	105.89 ± 9.80	<0.001
Age group 4	101.50 ± 10.61	107.00 ± 7.07	0.272
Superior			
Age group 1	111.00 ± 9.20	124.50 ± 18.16	0.195
Age group 2	109.21 ± 26.88	120.86 ± 12.17	0.091
Age group 3	115.11 ± 15.60	125.22 ± 13.49	0.011
Age group 4	117.50 ± 14.85	122.50 ± 7.78	0.5
Inferior			
Age group 1	130.25 ± 15.76	142.00 ± 17.05	0.332
Age group 2	110.50 ± 26.63	130.64 ± 16.96	0.016
Age group 3	111.67 ± 22.48	129.89 ± 12.77	0.009
Age group 4	122.00 ± 36.77	143.50 ± 28.99	0.159
Nasal			
Age group 1	84.00 ± 10.89	95.00 ± 15.94	0.031
Age group 2	72.36 ± 14.98	88.64 ± 10.49	<0.001
Age group 3	79.00 ± 8.20	87.22 ± 11.72	0.07
Age group 4	98.50 ± 20.51	91.00 ± 15.56	0.278
Temporal			
Age group 1	72.50 ± 14.08	66.75 ± 15.22	0.324
Age group 2	76.21 ± 21.53	75.14 ± 10.95	0.839
Age group 3	66.00 ± 9.55	78.33 ± 13.61	0.01
Age group 4	67.50± 10.61	70.50 ± 4.95	0.59

Table 3 Mean RNFL thickness between affected and unaffected eyes in terms of final diagnosis.

Item	Affected eye	Unaffected eye	P-value
Total			
ON	94.33 ± 14.78	105.67 ± 8.32	0.001
MS	92.57 ± 17.79	101.14 ± 7.20	0.167
Superior			
ON	113.52 ± 20.18	124.76 ± 12.39	0.004
MS	106.00 ± 24.47	115.14 ± 11.63	0.376
Inferior			
ON	115.57 ± 24.52	133.00 ± 16.29	0.004
MS	109.57 ± 27.30	131.57 ± 18.75	0.004
Nasal			
ON	76.05 ± 12.15	88.86 ± 12.98	<0.001
MS	86.57 ± 17.86	92.86 ± 10.59	0.307
Temporal			
ON	72.00 ± 18.51	75.10 ± 10.66	0.396
MS	67.86 ± 13.04	68.43 ± 7.59	0.904

Table 4 Mean RNFL thickness between affected and unaffected eyes in terms of the time interval between occurring optic neuritis and OCT performance.

Item	Affected eye	Unaffected eye	P-value
Total			
3-6 months	93.50 ± 16.82	104.50 ± 14.71	0.092
7-12 months	103.33 ± 8.74	104.00 ± 4.36	0.053
13-24 months	92.00 ± 13.73	105.59 ± 7.15	0.001
>24 months	95.80 ± 21.98	103.20 ± 9.45	0.372
Superior			
3-6 months	112.50 ± 22.22	114.75 ± 19.81	0.625
7-12 months	129.67 ± 17.95	135.33 ± 3.06	0.589
13-24 months	108.76 ± 19.03	123.06 ± 10.58	0.004
>24 months	111.20 ± 27.56	121.00 ± 14.27	0.467
Inferior			
3-6 months	112.00 ± 29.71	135.50 ± 21.06	0.07
7-12 months	133.67 ± 14.01	126.67 ± 14.15	0.699
13-24 months	110.35 ± 20.45	133.88 ± 15.06	<0.001
>24 months	118.40 ± 37.21	131.00 ± 21.95	0.261
Nasal			
3-6 months	80.00 ± 4.36	89.25 ± 14.98	0.075
7-12 months	73.00 ± 8.00	80.33 ± 3.51	0.221
13-24 months	77.88 ± 15.48	90.71 ± 12.71	0.003
>24 months	83.40 ± 16.07	94.40 ± 11.10	0.173
Temporal			
3-6 months	69.25 ± 11.62	72.50 ± 12.66	0.748

7-12 months	76.33 ± 11.06	72.33 ± 2.31	0.609
13-24 months	71.00 ± 19.96	75.06 ± 11.69	0.324
>24 months	70.00 ± 14.70	71.60 ± 7.70	0.767

Discussion

Because of the revealed association between RNFL thickness and visual parameters including visual acuity, visual field, and color vision and also due to significant visual loss in patients who suffered optic neuritis, we attempted to assess the change in RNFL thickness in patients with unilateral optic neuritis. As the first finding, we showed significantly reducing RNFL thickness in three superior, inferior, and nasal quadrants in attack eyes when compared to fellow eyes, however this difference was not found in temporal quadrant. We also revealed that the mean RNFL thickness in fellow eye was in the normal range of Iranian population [1]. In a similar study by Trip et al. [12], highly significant reductions of RNFL thickness was revealed in affected patient eyes compared with control eyes and clinically unaffected fellow eyes. In another study by Yau et al. [13], although baseline RNFL thickness was similar in both affected and fellow eyes, at three months, the attack eye had a thinner temporal and average RNFL compared to the fellow eye. Also, at three months, the attack eye had significant RNFL thinning in the four quadrants and average thickness compared to baseline. Based on the pathological assessments, inflammatory reactions leading axonal degeneration in parallel with nerve atrophy is described in optic neuritis [14,15]. More interestingly, despite improvement of visual function, the progressive RNFL thinning may be persisted. Contrary to our observation, some studies could show early RNFL thinning in temporal quadrant and thus it has been introduced as the first to be affected by optic neuritis [16-18], but in our study, the temporal quadrant was not ever affected.

As another important finding, reduced RNFL thickness was specified to female patients. Similar finding was revealed in a study by Costello et al. [17] that showed lower mean value of RNFL in men than in women 6 months after disease onset. In their study, men showed more apparent change in RNFL thickness in their optic neuritis eyes from baseline to 6 months of disease than women. According to our research finding, it seems that when affected eyes with optic neuritis were compared to fellow eyes, women had more inter-eye asymmetry in RNFL thickness compared with men. In other word, the results of the present study suggest that women may have worse RNFL thinning than men after optic neuritis, and that the influence of gender may need to be further explored in this phenomenon. As previously shown especially in those patients with multiple sclerosis, although the overall prevalence of disease was notable higher in women as in men, men tend to have worse clinical outcomes, faster disease progression, and higher burden of destructive lesions relative to men [18,19]. Some factors that may be account for gender differences are sex hormones and genetic susceptibility between the genders [20]. As shown in animal studies, estrogen can reduce the severity of neural inflammation [21-24] that was paradoxically shown in present survey. It has been also shown that estrogen can increase retinal blood flow and protect the RNFL in animal and clinical models of optic nerve injury [25,26], but we could not an explainable reason for worsen RNFL thinning in women than in men.

We also showed more reducing RNFL thickness in those who younger than 40 years old, but not in older subjects may be due to small sample size in the latter group. Also, we only observed this abnormal change in those patients underwent OCT 13 to 24 months after occurring optic neuritis. In Costello et al. [17] survey, the difference in the mean RNFL thickness in attack and fellow eyes began 2 months after occurring optic neuritis, progressed within six months and then remained unchanged 7 to 12 months. In their study, the difference in RNFL thickness was not significant between the first and second years after occurring optic neuritis.

In our study, the mean RNFL thickness was found in all quadrants except for temporal quadrant in attack eye compared to fellow eye in patients with isolated optic neuritis, however in MS patients, the between-eye difference was observed only in inferior quadrant. The pointed difference might be due to the simultaneous decrease in RNFL thickness in both eyes in MS condition.

Conclusion

In conclusion, in patients with unilateral optic neuritis, regardless of final diagnosis or time for performing OCT, more thinning of RNFL is detectable in attack eye in comparison with fellow eyes in most quadrants. These pathological changes may be observed more in women than in men, even may be specified to female gender. More reducing RNFL thickness in those patients younger than 40 years was seen. The abnormal change in RNFL thickness was also found in those patients underwent OCT 13 to 24 months after occurring optic neuritis. The difference in mean RNFL thickness may be specified to inferior quadrant in MS patients.

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