Comparison of Retinal Nerve Fiber Layer Profile in Subjects with Myopia and Emmetropia Using Scanning Laser Polarimetry

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Abstract

***Purpose*:** To compare retinal nerve fiber layer (RNFL) profile in subjects with myopia and emmetropia using GDx variable corneal compensator (VCC)

***Methods*:** Besides ophthalmologic standard examination (refraction, visual acuity and slit-lamp examination, applanation tonometry, and funduscopy), perimetry and scanning laser polarimetry (SLP) were performed. 171 healthy age-matched subjects with low to high myopia (90 subjects) and emmetropia (81 subjects) underwent RNFL analysis by means of GDx VCC. The mean value of each parameter was compared in myopic and emmetropic eyes.

***Results*:** Mean myopia was 3.43±1.19 diopter (D) (range, -0.50 to -6.50). Except for ratio parameters, RNFL parameters were significantly lower in myopic patients. TSNIT standard deviation (p=0.026), nerve fiber indicator (NFI) (p=0.027), superior/nasal (p<0.0001), max modulation (p=0.003), ellipse modulation (p=0.0244) and Symmetry (p=0.028) were higher in myopic group. In both groups, all of RNFL measurements were within the normal range. There was a gradual decrease in RNFL thickness associated with aging in myopic patients (simple regression analysis, p<0.05). There was also a gradual decrease in temporal-superior-nasal-inferior thickness (TSNIT) average and superior maximum with increasing degree of myopia (simple regression analysis, p<0.05).

***Conclusion*:** RNFL thicknesses gradually decreased with increasing age in myopic patients. Patients with myopia had significantly lower RNFL thickness than normal subjects and, although weakened by wide age range of myopic group, there was a linear negative correlation between severity of myopia and RNFL thickness in myopic patients.

***Keywords*:** Myopia, Emmetropia, Retinal Nerve Fiber Layer, Scanning Laser Polarimetry, GDx

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Introduction

Myopia is a common ocular disease and is associated with a two to three fold increase in the glaucomatous optic neuropathy, thus early diagnosis of glaucoma in this group is an important clinical issue.[1] The retinal nerve fiber layer (RNFL) in the upper and lower bridges of optic disk is thicker than those of temporal and nasal. Temporal fibers of RNFL do not directly move toward optic disk unlike the other nerve fibers, but after setting a curved direction around papillomacular bundle of macula and leaving a border between upper and lower raphe which is pulled from fovea to retinal temporal area, enter optic disk. In comparison with papillomacular bundle, such curved fibers are more sensitive to glaucomatous changes and their minute defects precede visual field changes as well as optic disk alterations. RNFL changes can be diffused or localized and in advanced glaucoma, such changes lead to complete RNFL atrophy.[1] Myopia may be associated with nerve fiber layer loss, because of elongation of the globe or some degenerative changes associated with myopia.[1] Atrophic area is darker because of greater visibility of pigment epithelium layer. On the other hand, in glaucoma, optic nerve neuropathy causes progressive thinning of RNFL. It has been shown that primary open angle glaucoma causes functional and structural injuries.[2-3] The changes of RNFL become more complex through cross-relation between myopia and glaucoma[4-6] and the optic disc of glaucomatous myopic patients may be more vulnerable than emmetropic and hypermetropic ones even in lower ages.[7]

In addition to the studies which investigate the effects of glaucoma on RNFL and many other studies which evaluate the effects of age and race on the thickness of RNFL,[8-11] there are little reports on the effects of refractive changes on RNFL using scanning laser polarimetry (SLP). Some studies show that compared to emmetropic eyes, RNFL in hyperopic eyes are thinner or thicker[12,13] and in myopic eyes are thinner.[4,12] In one study, it has been shown that RNFL defects in myopic eyes are 8% more common than emmetropic and hyperopic ones.[4]

The conventional visual fields may not sensitive enough in early stages of glaucoma and the structural defects including RNFL can happen sooner than visual field changes.[14-18] SLP is a useful instrument to identify the thickness of RNFL.[15-18] SLP evaluation on patients with open angle glaucoma demonstrates symmetrical reduction of RNFL thickness in upper and lower quadrant of retina.[17]

Due to lack of adequate studies which define the effect of myopic refractive error on RNFL thickness, and also the necessity of diagnosis of retinal nerve defects specially in glaucomatous myopic patients, this study has been conducted to evaluate the effect of myopia on RNFL using SLP with variable corneal compensator (VCC).

Methods

This case-series study was done on 94 patients referring to Farabi Eye Hospital during 2006-2007. The patients did not undertake any charge and all of them signed an inform consent while considering ethical standards based on Helsinki treaty. They were divided into two groups of emmetropia and myopia. Ninty myopic eyes out of 52 volunteers [28 males and 24 females) and 81 emmetropic eyes (range of spherical equivalent (SE) refraction: ±0.50 diopter (D)] out of 42 volunteers (24 males and 18 females) were studied. Myopia was between -0.50 to -6.5 D (mean: -3.4). None of the patients had glaucoma, high intraocular pressure (IOP), cataract, corneal disorders, retinal or optic disk pathologies, strabismus, and a history of eye surgery and best corrected visual acuity (BCVA) less than $^{20}/_{40}$.

Standard ophthalmologic examinations including refractometry, keratometry, visual acuity (VA) measurement, slit-lamp examination, Goldman tonometry, perimetry and fundoscopy along with optic disk examination were done. IOP was less than 21 mmHg. Visual field examination using white on white threshold 24-2 SITA fast strategy (Humphrey Field Analyzer II; Carl Zeiss Meditec, Inc, Dublin, CA, USA) was performed for all of the patients. Patients with unreliable visual fields and visual fields compatible with glaucomatous optic neuropathy were excluded. Patients without any problem in above examinations were included. RNFL parameters were measured by GDx-VCC instrument (Laser Diagnostic Technologies

Inc, San Diego, California; software version 5.5). The parameters included in the analysis were: temporal-superior-nasal-inferior thickness (TSNIT) average, superior average (SA), inferior average (IA), inter-eye symmetry, nerve fiber indicator (NFI) symmetry, superior ratio, inferior ratio, superior/nasal, maximum modulation, superior maximum, inferior maximum, ellipse modulation, normalized superior area, Normalized inferior area, ellipse standard deviation, ellipse average. The mean value of each SLP parameter of myopic eyes was compared with the mean value of the same parameter of emmetropic eyes by the unpaired student test (adjusting the design effect of bilateral cases). Myopic patients were divided into three groups of mild (0 to -2 D), moderate (-2 to -4 D), and severe (>-4 D). These groups were compared to each other as well as to emmetropic group according to RNFL parameters by unpaired student test. Regression analysis was used to evaluate the correlation between RNFL parameters changes with age and myopia in emmetropic and myopic patients respectively. A p-value of less than 0.05 was considered statistically significant.

GDx parameters

Fourteen parameters were automatically calculated using GDx software.

Average-based parameters

Average thickness: The average thickness of all pixels in the image using all 65,536 points

Superior maximum: The average of the 1,500 thickest pixels in the superior quadrant was used to calculate all ratios involving the superior quadrant.

Inferior maximum: The average of the 1,500 thickest pixels in the inferior quadrant was used to calculate all ratios involving the inferior quadrant.

Ellipse average: Average thickness of the nerve fiber layer beneath the ellipse surrounding the optic nerve

Superior average: The average thickness of the nerve fiber layer beneath the superior portion of the ellipse

Inferior average: The average thickness of the nerve fiber layer beneath the inferior portion of the ellipse

Ratio-based parameters

Symmetry: Ratio of the average of the 1,500 thickest pixels in the superior quadrant over the average of the 1,500 thickest pixels in the inferior quadrant

Superior ratio: Ratio of the average of the 1,500 thickest pixels in the superior quadrant over the average of the 1,500 median pixels in the temporal quadrant

Inferior ratio: Ratio of the average of the 1,500 thickest pixels in the inferior quadrant over the average of the 1,500 median pixels in the temporal quadrant

Superior/nasal: Ratio of the average of the 1,500 thickest pixels in the superior quadrant over the average of the 1,500 median pixels in the nasal quadrant

"Other" Parameters

Maximum modulation: First, the average was calculated for the 1,500 thickest points in the superior and inferior quadrants. Next, the 1,500 median points in the nasal and temporal quadrants were calculated. The lowest of these four values was subtracted from the highest, then divided by the lowest value. This gave the difference between the thickest and the thinnest parts of nerve fiber layer.

'Number': A trained neural network assesses all pixels and assigns to an eye a number from 0 to 100 (0 indicates normal and 100 advanced glaucoma). This parameter could be evaluated only for subjects aged 18 years or more because the normative database of GDx software includes only healthy subjects above 18 years of age.

Ellipse modulation: This was calculated by taking the thickest pixel within the elliptical band, subtracting the thinnest pixel within the band and dividing the total by the value of thinnest pixel.

Superior integral: This was calculated as the total area under the curve and within the superior portion of the elliptical band.

Results

The age range was 20-73 years (mean, 38.08±14.24) and 20-76 (mean, 41.58±15.12) in myopic and emmetropic eyes, respectively. There was no significant difference between the average ages of these two groups (p>0.05). The SE range was between -0.5 to -6.5 (mean±SD: -3.4±1.4). Except for IA symmetry, superior ratio, and inferior ratio, other RNFL parameters decreased significantly with the age in the myopic group in regression analysis (p≤0.038).

All values related to myopic patients were lower than emmetropic patients except for mean of TSNIT standard deviation, NFI, symmetry, superior/nasal, maximum modulation, ellipse modulation that were significantly greater than emmetropic patients. All of the GDx parameters in both myopic and emmetropic groups were in the normal range according to the data base of GDx VCC (Table 1).

The mean of TSNIT average in each of mild, moderate, and sever myopia group was significantly less than that in emmetropic group (p<0.0001). The mean of SA in both moderate and sever myopia group was significantly less than that in emmetropia group (p=0.013 and p=0.042 in moderate and sever myopia group, respectively) (Table 2). The mean of IA in moderate myopia group was significantly less than that in emmetropia group (p=0.009). The mean of NFI in sever myopia group was significantly more than that in emmetropia group (p<0.0001). The mean of superior ratio in moderate myopia group was significantly more than that in emmetropia group (p=0.004). The mean of inferior ratio in moderate myopia group was significantly more than that in emmetropia group (p=0.038). The mean of superior/nasal in both moderate and sever myopia groups was significantly more than that in emmetropia group (p=0.009). The mean of ellipse modulation in both moderate and sever myopia groups was significantly more than that in emmetropic group (p=0.026 and p=0.009 in moderate and sever myopia group, respectively).

Based on regression analysis, there was a significant linear correlation between myopia severity and NFI, superior maximum, and TSNIT average parameters (p values of 0.019, 0.004, and 0.009, respectively). (r values of 0.30, 0.27 and 0.25, respectively) (Figures 1 and 2).

Table 1. Comparison of different parameters between myopic and emmetropic subjects

	Myopic eyes	Emmetropic eyes	p
TSNIT average	53.54±4.59	65.19±19.06	<0.0001
Superior average	65.67±6.91	72.95±16.87	<0.0001
Inferior average	63.36±9.64	70.20±17.43	0.002
TSNIT standard deviation	23.55±4.91	21.57±6.40	0.026
NFI	18.81±8.20	15.91±8.65	0.027
Symmetry	0.99±0.11	0.94±0.17	0.028
Superior ratio	2.85±1.50	3.36±1.25	<0.0001
Inferior ratio	3.10±1.64	3.75±1.24	0.004
Superior/nasal	2.80±0.84	2.11±0.74	<0.0001
Maximum modulation	3.30±1.20	2.40±0.52	0.003
Superior maximum	74.78±14.67	92.94±28.14	<0.0001
Inferior maximum	76.16±14.99	99.98±32.39	<0.0001
Ellipse modulation	4.62±1.84	3.47±2.00	0.0244
Normalized superior area	0.14±0.08	0.15±0.05	0.503
Normalized inferior area	0.13±0.02	0.15±0.04	<0.004
Ellipse standard deviation	23.69±5.15	22.32±5.98	0.11
Ellipse average	53.23±5.78	65.08±19.17	<0.0001

TSNIT: Temporal-superior-nasal-inferior thickness
NFI: Nerve fiber indicator

Table 2. Correlation between age and TSNIT average in myopic eyes

	Myopic eyes (90 eyes)	Emmetropic eyes (81 eyes)	p
Sex (Male/Female)	34.4	39.1	0.326
Age	38.08±14.24	41.58±15.12	0.476

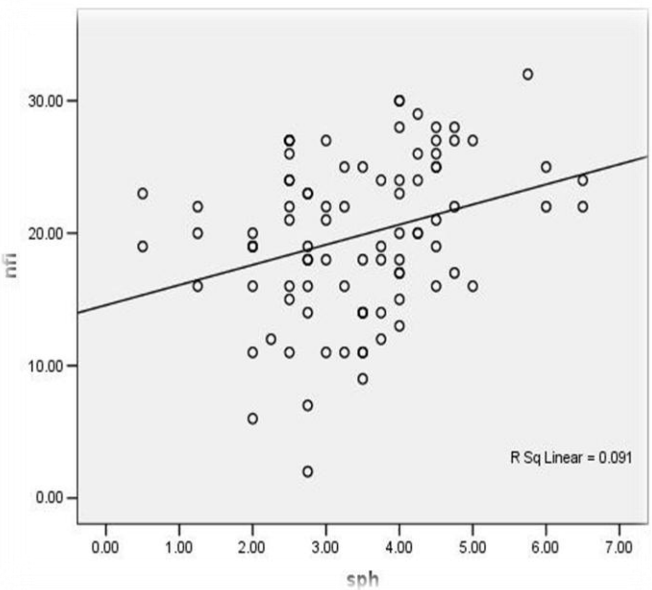

Figure 1. Correlation between myopia severity and nerve fiber indicator

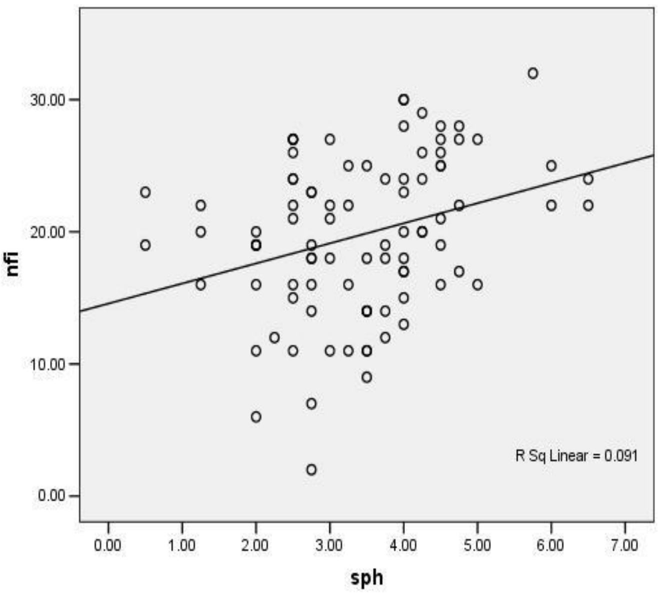

Figure 2. Correlation between myopia severity and Temporal-superior-nasal-inferior thickness average

Discussion

The rationale behind studying NFL thickness in patients with myopia is contributing role of myopia in primary open angle glaucoma.[19] In the present study, RNFL thickness related parameters (prominently SA, IA, TSNIT average and NFI) in myopic eyes showed significantly lower thicknesses of RNFL than emmetropic subjects; although ratio parameters (maximum modulation, ellipse modulation, TSNIT standard deviation, superior ratio, inferior ratio and superior/nasal) did not confirm such difference between myopic group and emmetropic group. Notably, superior and inferior ratios are defined as the ratio of superior and inferior thickness to temporal thickness. For example, in moderate myopic group, superior ratio, inferior ratio and superior/nasal were significantly higher than emmetropic group, it could be related to the thicker temporal and nasal NFL thickness in emmetropic group compared to moderate myopic group. It has been reported that maximum modulation, ellipse modulation and inferior ratio are part of the best GDx parameters to discriminate early glaucoma.[20] In practice, these parameters also may be very helpful in detecting glaucoma in myopic subjects because they should not be affected by lowering effect of myopia on RNFL thickness.

Kremmer et al using a third generation GDx fixed corneal compensation (GDx FCC) (an earlier version of GDx) in patients with myopia ≤-8.50 D stated that GDx values decrease with increasing level of myopia. They also suggested that there is no significant differences between myopic patients and hyperopic patients and thus reported that it is the refractive error not axial length that resulted in such a decrease in NFL parameters.[20] They stated that the average thickness, ellipse average, SA, IA, and superior integral in both myopic and hyperopic eyes had significantly lower values in comparison with the emmetropic control eyes; there was an association between the amount of reduction in GDx parameters and level of myopia.[20]

In an earlier study Ozdek et al performed first-generation polarimetery in 110 eyes with ≤-15.00 D of myopia. They found that superior and inferior NFL retardations, and the S/I ratio in myopic patients were significantly lower compared to those of age-matched normal subjects. There was an association between the level of the myopia and decrease in retinal NFL thickness.[21]

It was in contrary to another study performed by Vetrugno et al. They included one hundred and seventy-four healthy age-matched subjects with low to high myopic (up to -8.50 D) and emmetropic eyes who underwent retinal NFL evaluation by means of GDx VCC. TSNIT average ($p=0.0111$), SA ($p=0.0244$), symmetry ($p<0.0001$) and ellipse average ($p=0.0111$) were higher in myopic group. Superior ratio and inferior ratio were higher in emmetropic eyes ($p=0.0179$ in both cases). In both groups, compatible with our study, all measurements of the RNFL were within the normal range. They concluded that there was no clinically significant variation in myopia NFL parameters as measured by GDx VCC compared to emmetropic eyes.[22] In the present study, there was a significant correlation between NFI and TSNIT and severity of myopia ($p=0.019$ and $p=0.009$, respectively). It has been confirmed by formerly mentioned studies[20,21] using enhanced corneal compensation (GDx ECC) by Wang et al did not support this association.[23] They found that using Cirrus OCT, there was significant correlations between both SE ($r=0.291$, $p<0.001$) and axial length ($r=-0.322$, $p<0.001$) and average RNFL thickness ($p<0.001$). On the other hand, a significant correlation was found in RNFL measurement between GDx ECC and Cirrus OCT ($p<0.001$); however there was not significant correlation between RNFL thickness measured with GDx ECC and axial length/SE. But using GDx ECC could result in fewer ARP in relation to GDx VCC. Thus these associations may be less detectable in GDx VCC.[24,25] Atypical retardation pattern (ARP) is seen as alternating peripapillary circumferential bands of low and high retardation and areas of high retardation arranged in a spoke like arrangement on the nasal and temporal side of the disc. It seems that ARP is more common in eyes with a low signal to noise ratio due to thinning of the retinal pigment epithelium. Such condition may be seen in myopia. SLP with GDx ECC has been developed addressing this problem, however it is still a possible problem in this situation, using this software.[23,24] The rationale behind the difference in our study and aforementioned studies[22,23] may be the lower diopters of myopia included in our study, resulting in lower amounts of ARP. It supports the role of ARP associated with higher degrees of myopia in partially degradation of the image captured by SLP. However the recent studies using OCT supports decrease in RNFL thickness in myopic patients compared to emmetropic subjects.[23-28]

Ageing is associated with a significant retinal NFL thinning. De pozzo et al reported 0.08 µm, 0.16 µm and 0.12 µm decrease per year for TSNIT, SA and IA, respectively; (p<0.001). They showed a 9.5%, 16.2% and 11.7% decrease from baseline values for TSNIT average, SA and IA in a 65-year lifespan, respectively.[29] Consistent with the previous studies,[29,30] there was a gradual decrease in NFL thickness in our study with increasing age.

In our study, GDx parameters in myopic patients were in normal range. However Melo et al reported that GDx was not a suitable device to differentiate between glaucomatous and non-glaucomatous myopic patients.[31] Therefore, we did not perform such a comparison to detect the power of GDx in glaucomatous myopic patients.

Conclusion

In conclusion, NFL thicknesses gradually decreased with increasing age. Patients with myopia had significantly lower NFL thickness than normal subjects and, although weakened by wide age range of myopic group, there was a linear relation between severity of myopia and NFL thickness in myopic patients. In relation to study RNFL thickness in myopic patients using SLP, caution should be applied and in this situation application of OCT could be considered.

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