Retinal Nerve Fiber Layer Thickness and Physiological Central Corneal Thickness in Healthy Myopic Eyes

Amir-Houshang Behesht-Nejad, MD[1] • Reza Ghaffari, MD[2] • Sasan Moghimi, MD[3]
Mahmood Jabbarvand, MD[1] • Abolghasem Hajilaari, MD[3]
Mohammad-Ali Zare, MD[1] • Abasat Bashiri, MD[2]

Abstract

***Purpose*:** To examine the relationship between retinal nerve fiber layer (RNFL) measurements obtained using scanning laser polarimetry with variable corneal compensation (VCC) and central corneal thickness (CCT) measurements using pentacam in myopic patients

***Methods*:** The study included 45 eyes from 45 myopic patients with intraocular pressure (IOP) measurements≤21 mmHg. All participants had normal optic discs and normal standard automated perimetry visual fields. All patients underwent imaging with the GDx VCC and pentacam. We examined the relationship between GDx VCC RNFL measurements and CCT.

***Results*:** Mean spherical equivalent (SE) was -3.65±1.1 D (range: -1.00 to -6.5 D). Mean CCT was 530.9±24.32 µm with a range of 488 to 596 µm. TSNIT (temporal, superior, nasal, inferior, temporal) average, inferior average, superior average, TSNIT standard deviation (SD) and nerve fiber indicator (NFI) were not correlated with CCT. There were no correlations between RNFL thickness and refraction, age, corneal volume and mean keratometry. However, RNFL in patients with CCT≤530 µm was significantly thinner than in those with thick corneas.

***Conclusion*:** RNFL measurements obtained using GDx VCC may not correlate with corneal thickness (CCT) and refraction in myopic patients. Myopic patients with CCT≤530 have thinner RNFL than in those with thick corneas.

***Keywords*:** Retinal Nerve Fiber Layer, GDx VCC, Myopia, Corneal Thickness

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Introduction

Retinal nerve fiber layer (RNFL) is affected in some pathological processes affecting retinal ganglion cells, optic nerve or visual pathways. Thus, RNFL thickness measurement has an important role in evaluation of diseases associated with RNFL loss, most notably glaucoma.[1-3]

GDx VCC (laser diagnostic technologies, San Diego, California) is a scanning laser polarimeter (SLP) capable of objective and quantitative measurement of RNFL thickness, in a noncontact method.

1. Associate Professor of Ophthalmology, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences
2. Resident in Ophthalmology, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences
3. Assistant Professor of Ophthalmology, Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences

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Correspondence to: *Sasan Moghimi, MD*
Eye Research Center, Farabi Eye Hospital, Tehran, Iran, Tel:+98 21 55414941-6, Email: sasanimii@yahoo.com

It measures RNFL thickness based on the amount of retardation of linearly polarized light, as it passes through RNFL, after compensating for birefringent properties of the cornea.[1,4] Several studies have demonstrated GDx as a valuable tool for detection of early glaucomatous damage.[2,3,5]

Ocular hypertension treatment study (OHTS) has demonstrated decreased central corneal thickness (CCT) as a major risk factor for development of glaucoma in ocular hypertension[6] and now there is strong evidence that decreased CCT is a risk factor for development of glaucoma in these patients.[6,7] However it is not completely understood whether this increased susceptibility to glaucoma is due to low tonometric readings and underestimation of actual intraocular pressure (IOP). Some authors proposed that a thinner cornea might be a manifestation of an abnormality in ocular connective tissue or a biomechanical abnormality, which might be associated with increased risk of optic nerve damage and retinal nerve fiber loss.[7] CCT has been associated with structural changes with optic nerve head and optic disc area in healthy eyes which may be responsible for a part of its association with glaucoma.[8]

Myopia may, also have an effect on RNFL thickness. It has been associated with increased risk of glaucoma in some studies; so changes in RNFL thickness should be taken into consideration when measuring it by GDx or OCT in these patients.[9-12] The goal of this study was to determine the relationship between RNFL thickness and CCT in healthy myopic eyes. As peripapillary atrophy in myopic degeneration, commonly observed in high myopic patients, may be associated with increased retardation values by GDx, patients with high myopia.

Methods

Forty five eyes of 45 myopic patients were consecutively recruited for this prospective longitudinal study. Only one eye (right eye) of each patient was included in the study. Inclusion criteria were best corrected visual acuity (BCVA) of $^{20}/_{30}$ or more, IOP of ≤21 mmHg, and normal visual field. Refractive error had to be in the range of mild to moderate myopia (up to -6.00 diopters (D)). Exclusion criteria were keratoconus or other corneal thinning disorders, cylinder more than three D, peripapillary atrophy, tilted disc appearance, congenital optic disc anomalies, generalized or asymmetric cupping, systemic disease including diabetes, and a history of intraocular surgery.

Informed consent was obtained from all patients. All patients underwent complete ophthalmologic examination including cycloplegic refraction, slit lamp examination, Goldman tonometry and funduscopy. CCT was measured by pentacam (Oculus, Inc, Wetzlar, Germany) and RNFL by GDx VCC (laser diagnostic technologies INC, San Diego, California).

Visual field was evaluated with SITA standard C-24-2 program (Humphrey visual field analyzer). Visual field was considered normal when fixation loss<33%, false-positive<4%, false-negative<12%, GHT within normal limit, normal mean deviation and PSD and no more than of one missing point in visual field.

GDx

All patients underwent SLP using GDx VCC. GDx VCC incorporates eye specific anterior segment birefringence properties to improve sensitivity of RNFL measurements. Pupil was not dilated and images were obtained by a single experienced technician. Only sharp and well focused images with a sore of at least of eight were considered acceptable. Patients with atypical birefringence pattern images as defined by peripapillary high retardation arranged circumferentially or in a spokelike pattern or splotchy areas of high retardation nasally and temporally, were excluded from study.

Five main GDx and 12 accessory parameters recorded in our study. Five main GDx parameters were TSNIT (temporal, superior, nasal, inferior, temporal) average, inferior average, superior average and TSNIT standard deviation (SD) and nerve fiber indicator (NFI).

Pentacam

CCT was measured with pentacam. Pentacam utilizes a rotatory scheimpflug camera to image the anterior segment of the eye. All measurements were obtained between 8 to 12 o'clock after at least three hours of waking, by a single experienced

technician. Calibration of the pentacam (software version 1.14) was checked by the manufacturer at the beginning of the study. Pentacam's five CCT measurements from the central four mm of cornea were averaged and recorded.

Statistical analysis

Data were analyzed by SPSS 10.0.1 (SPSS Inc, Chicago, Illinois, USA). Only right eyes of patients were used for analyses. A multivariate analysis was used to assess the association between different RNFL parameters and age, refraction, CCT, and mean keratometry.

Results

There were 13 (28.9%) male and 32 (71.1%) female patients in this study. The age (mean±SD) of participants was 26.5±4.9 years (range: 20-43 years). Mean SE was -3.65±1.1 D (range: -1.00 to -6.5 D). Mean CCT was 530.9±24.32 µm with a range of 488 to 596 µm.

The TSNIT average and superior average were 53.56±4.61, and 65.67±6.91, respectively. TSNIT SD was 23.55±4.91 and NFI was 18.38±8.20. Mean and SD of other parameters are shown in table 1. There was not statistically significant difference between mean of GDx measurements and CCT in males and females.

TSNIT average, inferior average, superior average, TSNIT SD and NFI were not corrected with CCT. Pearson correlations coefficients and P-values are given in table 1. Statistically, there was correction between some of GDx parameters and CCT. Max modulation (r=0.35, P=0.02), ellipse average (r=0.30, P=0.03) were correlated with CCT. There were no correlations between RNFL thickness and SE, age, corneal volume and mean keratometry.

When mean of GDx parameters of subjects with a CCT≥530 µm and less than 530 µm were compared, there was a significant difference between NFI (P=0.008), maximum modulation (P=0.002), ellipse average (P=0.009), Ellipse SD, inferior average (P=0.023) and superior average (P=0.005).

Table 1. Mean±SD of GDx parameters and their correlations with central corneal thickness (CCT)

	Mean±SD	R	P-value*
TSNIT average	53.56±4.61	0.17	0.20
Superior average	65.67±6.91	0.37	0.00
Inferior average	63.42±9.68	0.13	0.34
TSNIT SD	23.55±4.91	0.10	0.94
NFI	18.38±8.20	-0.21	0.98
Superior ratio	3.63±1.25	-0.01	0.93
Inferior ratio	3.75±1.24	0.17	0.88
Superior/nasal	2.80±0.84	0.24	0.02
Maximal modulation	3.03±1.20	0.04	0.72
Superior maximum	74.78±14.67	0.26	0.01
Inferior maximum	76.16±14.99	-0.05	0.62
Ellipse modulation	4.64±1.83	0.01	0.91
Ellipse average	53.27±5.77	0.05	0.61
Normalized superior area	0.14±0.8	0.02	0.79
Normalized inferior area	13±0.024	0.02	0.72
Ellipse SD	23.76±5.14	-0.00	0.95
Symmetry	0.99±0.11	0.05	0.61

NFI: Nerve fiber indicator, SD: Standard deviation, *: Multiple regression

Discussion

CCT measurement, now considered as an important biological entity in ocular biometry, is widely used in ophthalmology. Recent investigations have implicated its role in the pathogenesis of glaucoma; and now CCT measurement is an important consideration in these patients.[7,13-15] OHTS has demonstrated that a thin CCT is a risk factor for the development of glaucoma. In fact, it was the strongest risk factor that was identified in that study.[6] This has been validated in other studies and now, there is strong evidence that decreased CCT is a risk factor for the development of glaucoma in ocular hypertension (OHT).[7]

Despite these findings, it is debated whether this effect is due to the effect of CCT on the accuracy of IOP measurements, or another additional biomechanical effect or ocular connective tissue abnormality, could make the optic nerve vulnerable to damage and cause retinal nerve fiber loss. Goldman applanation tonometry is based on the assumption of the mean CCT of 550 µm and decreased CCT results in underestimation of the true IOP.[13] In OHTS, a thin cornea was still an independent risk factor after compensation of its effect on the IOP. In addition, the CCT has a relationship with the optic nerve head structure and optic disc area in healthy nonglaucomatous eyes,[8] which may account partly, for its effect on development of glaucoma.

In CCT measurement, it is important to note the diurnal variations of human corneal thickness and its changes associated with contact lens wear, ocular disease, medications and ophthalmic surgery and on endothelial cell health status.[13] In addition, mean CCT varies among racial groups[14-16] and also may be influenced slightly by age.[6]

Instruments, used in measurement of CCT are based on either ultrasound or optical methods.[13,17,18] Although ultrasound pachymetry has shown high degree of reproducibility in normal eyes[17,18] and is currently, the clinical method most widely used to measure corneal thickness, some newer optical based anterior segment imaging technologies have evolved to allow corneal thickness measurement in a noncontact method. Several studies have shown pentacam accurancy in measurement of CCT in normal eyes[19-21] and after refractive surgery.[22] In our study, pentacam also had the added benefit of detecting early keratoconus, not evident on clinical examination and form fruste keratoconus which may have an effect on CCT, which were excluded from the study.

Myopia has been associated with changes in RNFL thickness. A point that emphasizes the importance of retinal nerve fiber measurements in myopic population is that myopia may be associated with an increased risk of glaucoma. In some population based studies, myopia has been a risk factor for glaucoma but the data is inconclusive.[9-12] In OHTS myopia was not an independent risk factor for glaucoma.[6] In low to moderate myopia, SLP parameters,[23] has been shown to be within normal range and have not been associated with clinically relevant variations, although there may be differences with the emmetropes. Moreover, GDx and optical coherence tomography (OCT) may not be useful to discriminate nonglaucomatous and glaucomatous subjects with high myopia.[24]

Our study did not find a significant correlation between RNFL thickness and CCT in patients with low to moderate myopia, although there was significant correlation of some parameters with the CCT. To our knowledge, we were unable to find another study addressing this relationship, in this population. There are mixed results about the peripapillary RNFL thickness measurements in myopic patients with regard to the degree of the refractive error or axial length (AL). Ozdek et al found that SLP measurements of RNFL were thinner in the myopic patients than the emmetropic controls and that there was a linear relationship between the severity of myopia and RNFL thickness.[10] There was also a decline in the RNFL thickness with age. Sek-Tien Hoh et al, in a study of 132 young male myopic patients with the SE of -0.50 to -14.25 D, noticed that the RNFL thickness, measured by OCT did not vary with the SE or AL of the eye.[9] But others[11,12] observed that with increasing the level of myopia, the peripapillary RNFL thickness decreased.

Several studies have investigated the relationship among the CCT and the RNFL thickness in normal and OHT patients. Lester et al in a study found no significant correlation between RNFL thickness, measured by GDx,

and CCT. Although, some GDx parameters including symmetry, superior ratio, inferior ratio, the number and maximum modulation had statistically significant correlation with CCT.[25] Henderson et al found that OHT patients with thinner corneas had significantly thinner RNFL and higher NFI scores, by GDx VCC than OHT patients with thicker corneas and healthy subjects.[26] In our study, there were statistically significant differences in some GDx parameters, when patients were stratified into groups with a CCT>530 and CCT<530. Likewise Kaushik et al,[27] found that RNFL thickness, measured by OCT in OHT patients with CCT<555 was significantly thinner than RNFL thickness of normal subjects and OHT patients with CCT>555. In another study[8] CCT had negative correlations with the optic nerve parameters including: disc area, rim area, rim volume, and RNFL area. So, in addition to its effect on the IOP measurements, CCT and its relationship to optic nerve head structure may explain its role in development of glaucoma.

Conclusion

Our findings are consistent with the other studies about correlation of the RNFL thickness and CCT in the healthy eyes or the normal controls in the studies, also including ocular hypertensive patients. As previously discussed, in most of these studies,[9-12,25-27] no significant correlation was detected between the RNFL thickness and CCT. Although this correlation was shown in ocular hypertensive patients which is compatible with observed increased risk of glaucoma in these patients in clinical practice. Also, some hypothesize that ocular hypertensive patients with thin corneas may be a subset of early undetected glaucoma patients or increased structural susceptibility to glaucoma. In our study there was a statistically significant difference in some GDx parameters, when patients were stratified to groups with a CCT>530 and CCT<530. The significance of these finding is not known and should be verified in larger studies.

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