Peripapillary Retinal Nerve Fiber Layer Thickness in Normal Iranian Children Measured with Optical Coherence Tomography

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Abstract

Purpose: This study aimed to measure the peripapillary retinal nerve fiber layer (RNFL) thickness using spectral-domain optical coherence tomography (SD-OCT) in normal Iranian children aged below 18 years.

Methods: Peripapillary RNFL imaging was performed in the right eye of normal Iranian children aged below 18 years using Spectralis SD-OCT (Heidelberg Engineering; Vista, CA). The effects of age, gender, cup-to-disc ratio, and spherical equivalent (SE) on global and sectoral RNFL thicknesses were evaluated.

Results: A total of 115 eyes were imaged. Approximately 51 (44.3%) of the cases were female children. The mean age was 12.44 ± 2.52 years. The SE of refractive error was 0.39 ± 1.38 diopters (range: −3.00 to +4.5 D). The RNFL thickness measurements in the superior, inferior, nasal, and temporal quadrants were 129.25 ± 14.52, 128.16 ± 13.46, 76.76 ± 10.58, and 69.58 ± 9.94 µm, respectively. The global RNFL thickness was 101.01 ± 7.74 µm. In both univariate and multiple regression analyses, SE was the only determinant of RNFL thickness (all P values < 0.05).

Conclusion: OCT analysis can effectively measure RNFL thickness in children, and SE is the only determinant of RNFL thickness in normal Iranian patients aged below 18 years.

Keywords: Children; Iranian; Optical Coherence Tomography; Retinal Nerve Fiber Layer

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INTRODUCTION

Children with suspected disc appearance are frequently referred to glaucoma clinics for optic nerve assessment and ruling out glaucoma. In these cases, functional (by visual field examination) and structural assessment (by optic nerve and peripapillary retinal nerve fiber layer (RNFL) imaging) should be performed.

Structural examinations are very useful especially in uncooperative children who would not perform well in perimetric tests. Spectral domain optical coherence tomography (SD-OCT) is a reproducible and reliable method of measuring RNFL and has been proven to be suitable for following up the patients over time.[1-3] Some studies have shown that OCT is a useful tool for...
differentiating early stages of glaucoma in children as well as adults.\textsuperscript{[4–6]} Having normative reference range for children helps in diagnosing this serious disease and in treating it in earlier stages.

The normal amounts of adult RNFL thickness have been studied by many investigators. In fact, the normative database of Spectralis OCT machine (Heidelberg Engineering; Vista, CA) and Stratus OCT (Carl Zeiss Meditec, Dublin, CA) include participants over 18 years of age. Because the normal amounts of RNFL thickness in Iranian children have not been previously reported, this study was conducted to measure the peripapillary RNFL thickness in normal Iranian children using Spectralis OCT.

\textbf{METHODS}

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee of Teheran University of Medical Sciences. Informed consent was obtained from the parents or legal guardians of the participants.

\textbf{Participants and Clinical Examinations}

A total of 120 healthy Iranian children aged 8–17 years were included in this study. Only the right eye of each participant was studied. Children who were born preterm (<37 weeks), with any kind of systemic or ophthalmic disease such as neurologic or metabolic problems, with best corrected visual acuity (BCVA) less than 8/10, with spherical equivalent (SE) outside the range of −7 to +5 diopters or astigmatism greater than 3 diopters, with strabismus or amblyopia, with intraocular pressure (IOP) higher than 21 mmHg, and with family history of glaucoma or any kind of optic nerve problems such as very small or very large discs were excluded.

All children were examined in our glaucoma clinic. Uncorrected visual acuity and BCVA were measured using E charts. The numbers were converted to logarithm of minimum angle of resolution for statistical purposes. A comprehensive ophthalmic examination including ocular alignment and motility assessment, cycloplegic refraction, slit lamp biomicroscopy of the anterior segment, Goldmann applanation tonometry, and dilated fundus examination were conducted on all participants.

\textbf{Peripapillary Retinal Nerve Fiber Layer Imaging}

Peripapillary RNFL imaging was obtained using Spectralis SD-OCT (Heidelberg Engineering; Vista, CA) after pupillary dilation. Scans were centered on the optic disc, and the 12° scan circle was positioned exactly in the middle of the optic nerve head. Images with a quality score less than 20 or erroneous segmentation, illumination, or centration were not included in the final analysis. The fovea-to-disc alignment line was manually adjusted if it did not point to the center of the fovea. The global, superior, inferior, nasal, temporal, superotemporal, superonasal, inferotemporal, and inferonasal RNFL thickness measurements were recorded in micrometers (\(\mu m\)) and analyzed.

\textbf{Statistical Analyses}

Statistical analysis was performed using SPSS 22.0 software (SPSS Inc., Chicago, Illinois, USA). Global and all sectoral RNFL parameters, SE, age, and other data were tested for normality using Shapiro-Wilk test. Scattered plots were created between each of the sectoral RNFL values and age, SE, cup-to-disc ratio, and gender to visually assess the presence of linear relationship between the parameters and excluding any outliers if present. The relationship between the RNFL thickness and age, SE, cup-to-disc ratio, and gender was analyzed using both univariate and multivariate regression analyses. A \(P\) value of <0.05 was considered significant.

\textbf{RESULTS}

A total of 120 eyes of 120 normal Iranian children aged 8–17 years were studied. Five images were excluded due to poor quality. Approximately 51 (44.3\%) of the participants were female children. The mean age was 12.44 ± 2.52 years (range: 8–17) [Figure 1]. The spherical equivalent of refractive error was 0.39 ± 1.38 diopters (range: −3.00 to +4.5 D), and the spherical refractive error was 0.45 ± 1.25 (range: −3.00 to +6.00 D) [Figure 2]. IOP was 13.67 ± 1.94 mmHg (range: 10–18), with cup-to-disc ratio between 0.0 and 0.6.

The quality value of the images ranged from 20 to 44. The RNFL thickness measurements in the superior, inferior, nasal, and temporal quadrants were 129.25 ± 14.52, 128.16 ± 13.46, 76.76 ± 10.58, and 69.58 ± 9.94 \(\mu m\), respectively. The global RNFL thickness was 101.01 ± 7.74 \(\mu m\) [Table 1]. The RNFL thickness in
Different peripapillary locations is shown in a box plot in Figure 3.

Simple regression analysis showed that neither age nor cup-to-disc ratio had a significant effect on global or individual quadrant RNFL thickness values. Gender was not a determinant of RNFL thickness either. On the contrary, SE was significantly associated with RNFL thickness (both global and sectoral) [Table 2 and Figure 4]. A multiple regression analysis was also conducted to determine the difference between SE, gender, age, and cup-to-disc ratio as predictor variables and RNFL thickness values as dependent variables. SE was the only variable that had a significant association with RNFL thickness (global and quadrant values); a lesser SE indicated a thinner RNFL thickness [Table 3].

DISCUSSION

Since the normative database of OCT machines for RNFL thickness does not include the measurements of children aged below 18 years, we conducted this study to measure the peripapillary RNFL thickness in normal Iranian children using Spectralis spectral domain OCT. The results of this study will serve as a basis for future evaluation of optic nerve diseases and RNFL in this age group. Although some studies have found no difference in RNFL thickness among various ethnic populations, others have suggested that ethnicity was among the determinants of these parameters.

The mean global RNFL thickness was 101.01 ± 7.74 µm. This value was the same with that obtained by Lee and others in children under 18 years using Spectralis OCT. The RNFL thickness in the superior and inferior quadrants was more than that in the nasal and temporal quadrants, which conformed to the “double-hump” pattern of peripapillary RNFL.

While no significant association was found between RNFL thickness and age, a negative correlation was observed between RNFL thickness and SE. In studies...
involving normal adults with wide age range, a negative correlation was found between RNFL thickness and age.\cite{8,16} However, this correlation did not exist among children aged below 18 years, and only the SE or axial length (AL) was reported to be associated with RNFL thickness.\cite{14,15,17,18} Histopathologic studies have found that ganglion cell loss and loss of their axons and thinning of the retinal nerve fiber layer were a prominent feature of aging in people older than 60 years.\cite{19} The lack of significant correlation between RNFL thickness and age in the pediatric population can also be explained from a statistical point of view: the narrow age range in pediatric population studies made it difficult for researchers to find a correlation between RNFL thickness and age, and extremely large sample sizes may be required to reveal such relationships.

Although some studies have not found any association between RNFL thickness and refractive error,\cite{20} many others (like our findings) have reported thinner RNFL in myopic people either children or adults.\cite{8,12,14,15,17,21}

Spectralis has underlying mechanisms that can compensate refractive error. However, extreme forms

Table 2. The \( R^2 \) and regression coefficient in the simple regression analysis between spherical equivalent as independent variable and the global, superior, inferior, nasal, and temporal retinal nerve fiber layer thickness values as dependent variables

|                      | \( R^2 \) | Regression coefficient (P) |
|----------------------|-----------|-----------------------------|
| Global               | 0.314     | 3.14 (<0.001)               |
| Superior             | 0.155     | 4.14 (<0.001)               |
| Inferior             | 0.171     | 4.03 (<0.001)               |
| Nasal                | 0.047     | 1.66 (0.02)                 |
| Temporal             | 0.086     | 2.10 (0.002)                |

Table 3. The regression coefficient and their corresponding P values in the multiple regression analysis between age, cup to disc ratio, spherical equivalent and gender as predictors and global, superior, inferior, nasal and temporal retinal nerve fiber layer thickness as dependent variables

|                      | Regression coefficient for age (P) | Regression coefficient for cup to disc ratio (P) | Regression coefficient for SE (P) | Regression coefficient for gender (P) |
|----------------------|-----------------------------------|-----------------------------------------------|---------------------------------|-------------------------------------|
| Global               | 0.258 (0.290)                     | 0.245 (0.955)                                 | 3.10 (<0.001)                   | 0.893 (0.469)                       |
| Superior             | 0.220 (0.665)                     | −4.19 (0.640)                                 | 4.03 (<0.001)                   | 1.080 (0.675)                       |
| Inferior             | 0.381 (0.413)                     | 8.00 (0.330)                                  | 4.14 (<0.001)                   | −0.529 (0.822)                      |
| Nasal                | 0.398 (0.311)                     | −0.925 (0.893)                                | 1.574 (0.031)                   | 1.625 (0.413)                       |
| Temporal             | 0.254 (0.483)                     | −0.062 (0.992)                                | 2.044 (0.003)                   | 1.950 (0.287)                       |

SE, spherical equivalent

Figure 4. Scatter plot showing the relationship between global (a) and sectoral (b-e) peripapillary retinal nerve fiber layer thickness and spherical equivalent.
of refractive error were not included in our study, but at least part of observed RNFL thinning in myopic can be due to magnification error.

RNFL thickness was similar between boys and girls in the present study, and this result is in agreement with those of other studies conducted among young population.[8,15]

This study is just a start point for further investigations about RNFL and other optic nerve variables in Iranian children and therefore has some limitations that should be kept in mind; small sample size is one of them. In addition, we did not measure the optic nerve head parameters or axial length and did not include those with high degrees of refractive errors.

In conclusion, RNFL thickness in Iranian children aged below 18 years positively correlated with SE, but age, gender, and cup-to-disc ratio had no influence on the measurements.

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Conflicts of Interest
There are no conflicts of interest.

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