The Relationship between Retinal Nerve Fiber Thickness and Retinal Functional Sensitivity during OCT and Static Perimeter Examinations

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SUMMARY

Aims: To demonstrate the relationship of dependency between the thickness of the retinal nerve fiber layer and the functional sensitivity of the retina in healthy young individuals. We also secondarily investigated the relationship between refractive error and mean retinal thickness in the macula.

Material and methods: The basic cohort contained 30 subjects with an average age of 23.4 ±4.2 years. These were young, generally healthy individuals without serious ocular pathologies. The average value of spherical equivalent in both eyes of all individuals was -1.2 ±2.5 D. We measured the thickness of the retinal nerve fiber layer (RNFL) in the papilla area and the average thickness of the retina in the area of the macula using the device OPKO Spectral OCT SLO Combination Imaging System (Opko Health, USA). We performed a functional examination of the retina within an area up to 30° using a perimeter with a stimulus with a Frequency Doubling Technology (FDT) from the company Humphrey (Carl Ziess Meditec, Inc., Dublin, CA). As a significant variable for comparison, we determined the mean value of retinal sensitivity deviation (MD).

Results: In our study, we did not demonstrate a statistically significant relationship between the average thickness of the retinal nerve fiber layer (RNFL) and the average value of retinal functional sensitivity (r = 0.18, p = 0.34) in either right eyes or the left eyes of the examined subjects (r = 0.20, p = 0.29). We also did not find a statistically significant relationship secondarily between the variable called the spherical equivalent of refractive error (SE) and the average retinal thickness in the macula in either the right eyes (r = 0.34, p = 0.06) or the left eyes (r = 0.18, p = 0.32).

Conclusion: When comparing the average thickness of the nerve fibers in the papilla with the help of OCT examination and the functional sensitivity of the retina measured on an FDT perimeter, we did not find a statistically significant dependence in the group of right eyes or in the group of left eyes. We also achieved a similar result when examining the interdependence of the variables of spherical equivalent of refractive error of the eye and the average thickness of the retina in the macula.

Key words: RNFL, OCT, FDT perimeter, SE, macula, papilla

INTRODUCTION

Measurement of the retinal nerve fiber layer (RNFL) with the aid of optical coherence tomography (OCT) is performed especially for the purpose of determining its diminution upon affliction by glaucoma. The cause of the onset of glaucoma is unknown, and as a result it is necessary to determine the stage of the pathology especially by quantifying changes of "clinical neuropathy" [1]. RNFL thickness can be determined very precisely with the aid of the method known as optical coherence tomography (OCT). Measurement with the aid of an OCT instrument is a functional measurement in which the patient's RNFL is compared with data stored in the database of the OCT instrument. In several published studies [2,3] it has been determined that demonstrating structural changes of the RNFL helps us diagnose this pathology and predetermines the size of functional changes [4,5]. Functional examination in glaucoma is usually performed with the aid of a static automatic perimeter (SAP). At present a professional consensus exists regarding the matter of a mutual co-

rrelation of structural examinations, which demonstrate loss of retinal ganglion cells (RGCs) and thinning of the RNFL, for example with the aid of OCT and functional examinations that enable the detection of loss of function and sensitivity of the retina. This for example concerns examination with the aid of a static automatic perimeter (SAP). For example, in one study [6] the authors reached the conclusion that the diminution of fibers of the RNFL measured with the aid of an OCT instrument correlates well with a decrease of retinal sensitivity as determined with the aid of a perimeter. The results in this study also predict that a relationship exists between structural and functional changes on the retina of eyes in advanced glaucomatous optic neuropathies. The authors of the study [7] describe a correlation between thinning of the RNFL and the final value of visual acuity (r = 0.807, p = 0.005) in patients with glaucomatous optic neuropathy. Loss of 1 row upon examination of visual acuity corresponds to a reduction of RNFL thickness by 5.4 μm. A study by the authors [8] points to a significant correlation between the region of the neural rim area (RA) of the optic nerve, RNFL thickness (SD-OCT) and the mean value of retinal sensitivity deviation (MD) obtained with the aid of perimetry with SITA technology. Average RNFL thickness was 85.6 ±5.7 μm, RA 1.0 ±0.3 mm2 and MD -1.3 ±1.9 dB. A stronger correlation was determined between the values of RA and MD (p = 0.005).

In the case of the second hypothesis, we were interested in the relationship between the thickness of the central part of the retina in the macula and the size of the refractive error. It is known from several studies [9] that an increase in short-sightedness can lead to changes on the ocular pole leading for example to chorioretinal atrophy, pigment degeneration, posterior staphyloma, or even as far as retinal detachment. An increase in the size of the sclera is linked with a diminution of retinal thickness. OCT examination is a noninvasive method which enables us to determine central retinal thickness with high precision. This technology enables in vivo comparison of retinal thickness and the size of the refractive error measured by a refractometer. Several studies [11,12] have compared retinal thickness in the macula and size of refractive error or axial length of the eye. Zhao et al. [9] in their study state the mean value of central foveal retinal thickness at 191.1 ±15.3 μm. Retinal thickness in the macula is generally larger in women than in men. Central retinal thickness demonstrates a significant positive correlation with axial length of individuals, and a negative correlation with the spherical equivalent (SE) of their refractive error.

MATERIAL AND METHODS

The basic cohort was composed of 30 subjects with an average age of 23.4 ±4.2 years, of whom one subject was male and 29 subjects were female. These were primarily young, generally healthy individuals in whom no serious ocular pathologies had been diagnosed. The average value of spherical equivalent in both eyes of all individuals was -1.2 ±2.5 D. The cohort was therefore composed predominantly of subjects with myopia, or myopia with astigmatism without presbyopia.

We measured the thickness of the retinal nerve fiber layer (RNFL) in the papilla area and the average thickness of the retina in the area of the macula using the device OPKO Spectral OCT SLO Combination Imaging System (Opko Health, USA). An RNFL analysis was recorded with the aid of an Optic Disc Cube 200*200 for the purposes of verifying the first hypothesis, and mean retinal thickness (ILM–RPE) from the macular region was obtained using a Macular Cube 512-128 scan for the purposes of the second hypothesis. We performed a functional examination of the retina within an area up to 30° using a perimeter with a stimulus with a Frequency Doubling Technology (FDT) from the company Humphrey (Carl Ziess). The examination was conducted monocularly and with correction of refractive error in the given proband. For our study, as a significant variable for comparison, we determined the mean value of retinal sensitivity deviation (MD).

Examination of the refractive state of the eye was conducted on the instrument Topcon TRK-2P without cycloplegia. The average value from three measurements on each eye was used. With regard to the dependency of measurement between the right and left eye, we divided the cohort into two subgroups (OD and OS), and conducted an evaluation of the mutual dependency of the variables separately for the right and left eye.

The results of the examination were recorded in an MS EXCEL table, and were subsequently evaluated with the aid of the statistical program Statistika version 12 from the firm STATSOFT and MedCalc. A Kolmogorov–Smirnov test was used to determine the normality of the data. In order to determine the mutual correlation of the variables we subsequently used a non-parametric Spearman rank-order correlation coefficient. The statistical level of significance was set at p = 0.05.

RESULTS

The average value of RNFL thickness from OCT in the right eyes was 109.1 ±12.0 μm and in the left eyes 107.7 ±16.5 μm. The mean MD (Mean Deviation) value from the perimeter, which shows a medium deviation from the mean value pertaining to the specific age group in the right eyes was -0.6 ±2.5 dB and in the left eyes -0.4 ±2.2 dB.

The mean value of spherical equivalent of refraction from the refractometer of the right eyes in our cohort was -1.2 ±2.3 D, and in the left eyes -1.1 ±2.8 D. A total of 17 individuals out of 30 (i.e. 57%) were myopic according to spherical equivalent. Astigmatism was recorded according to the refractometer in 24 individuals (80%). Mean retinal thickness in the area of the macula according to OCT examination was 264.3

±13.4 in the right eye and 270.6 ±30.6 μm in the left eyes.

The results of our study unfortunately did not demonstrate a statistically significant relationship between the studied variables in either of the hypotheses. In the first case only a weak positive correlation was calculated with the aid of the statistical software between the average thickness of the retinal nerve fiber layer (RNFL) and the average value of retinal functional sensitivity in the right eyes (r = 0.18, p = 0.34, Graph 1), and also in the left eyes of the examined subjects (r = 0.20, p = 0.29, Graph 2). We also did not find a statistically significant relationship secondarily between the variable called the spherical equivalent of refractive error (SE) and the average retinal thickness in the macula in either the right eyes (r = 0.34, p = 0.06, Graph 3) or the left eyes (r = 0.18, p = 0.32, Graph 4).

The study may be limited by the relatively small size of the cohort (n = 30). The results of the study are also influenced by the fact that the research group comprised young probands without significant general or ocular pathologies, whose average spherical equivalent of refractive error manifested only mild short-sightedness (-1.2 ±2.5 D).

DISCUSSION

Several studies appear in the professional literature dealing with the dependency between structural and functional changes of the retina. In the case of patients with glaucoma there is a decrease in the average value of RNFL thickness, as is documented for example by the study conducted by Yasmeen et al. [12]. In this study a statistically significant difference (p = 0.02) was found in the average value of RNFL thickness for the group of patients with pseudoexfoliation glaucoma compared with healthy patients.

Similarly, thanks to clinical trials it has also been possible to demonstrate a decrease in the value of retinal sensitivity in these patients using measurement with the aid of a static/automatic perimeter. We can find evidence for example in the study conducted by Giammaria et al. [13], which determined a more rapid decrease of sensitivity on the perimeter in patients with glaucoma in comparison with healthy individuals by -0.032 dB per year.

Thanks to guided progression analysis (GPA), a sophisticated instrument such as OCT is able to show

Retinal sensitivity in relation to the RNFL

$R^2 = 0{,}0357$
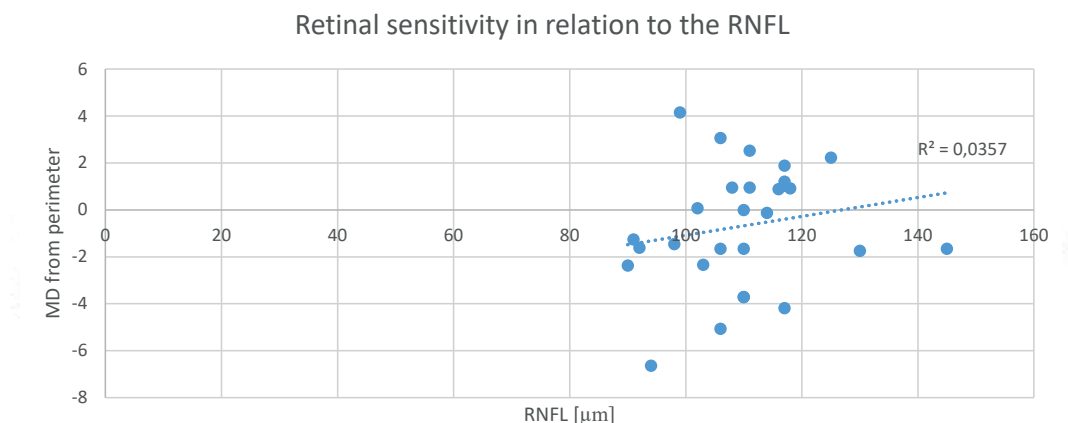
Graph 1. Correlation between mean retinal nerve fiber thickness (RNFL) and mean retinal functional sensitivity (MD) in right eyes

Retinal sensitivity in relation to the RNFL

$R^2 = 0{,}0426$
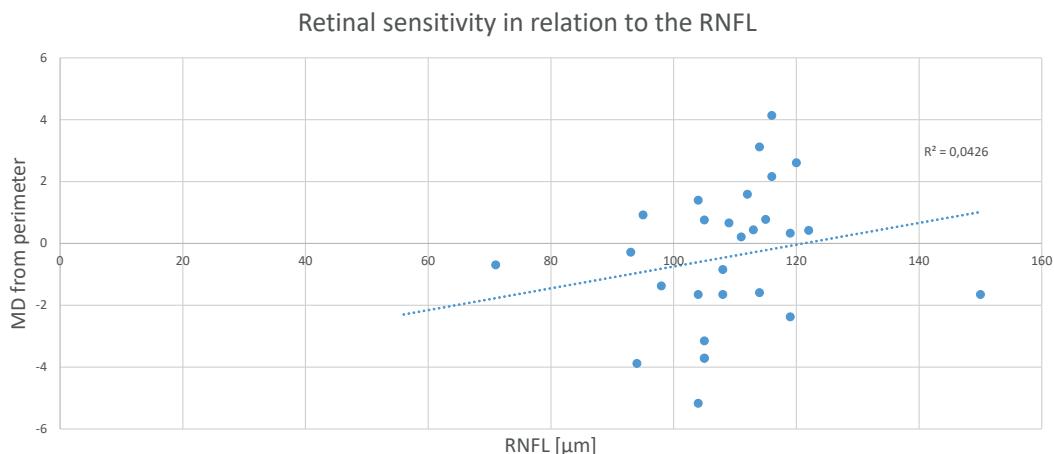
Graph 2. Correlation between mean retinal nerve fiber thickness (RNFL) and mean retinal functional sensitivity (MD) in left eyes

changes in RNFL thickness in patients with glaucoma over time, such as in the study conducted by Leung et al. [14], who thanks to GPA demonstrated an average decrease in RNFL thickness by -1.2 to 15.4 μm per year, as well as a decrease of the visual field index (VFI) from the perimeter by -0.5% to -7.2% per year.

In a study conducted by the author Holló [15], the relationship between peripapillary angioflow vessel density (PAFD) on the instrument Angiovue OCT and the mean defect of retinal sensitivity measured with the aid of an Octopus perimeter was examined. A strong negative correlation was determined between these variables (r = -0.552, p ≤ 0.002). This means that an increase in the density of peripapillary vessels leads to a diminution of retinal sensitivity measured on an automatic perimeter.

A study conducted by Salman et al. [16] also used examination of RNFL from OCT and a perimetric record in order to confirm the difference between a research group of patients with migraine and a control group. The results of the study demonstrated a statistically significant difference between the research group and the control group upon perimetric examination (p < 0.05), while contras-

tingly no difference was demonstrated (p > 0.05) upon examination of RNFL on an OCT instrument.

Sato et al. [17] in a clinical trial compared the relationship between RNFL thickness and retinal sensitivity measured on a microperimeter, which was a component of the instrument OCT Stratus (Carl Zeiss, Meditec). The result demonstrated a relationship between RNFL thickness and retinal sensitivity (r = 0.42, p < 0.0001). A reduction of RNFL thickness is accompanied by a reduction of sensitivity to stimuli.

In our study we did not demonstrate a statistically significant relationship between RNFL thickness and retinal sensitivity measured on an FDT perimeter up to 30 degrees. The reason is probably that this concerned young, healthy individuals whose MD value was -0.6 ±2.5 dB for the right eye and -0.4 ±2.2 dB for the left eye, and according to the size of the standard deviation did not fluctuate significantly. The same applies also to the other studied variable of RNFL thickness from an OCT instrument, where the standard deviation in the right eye comprises 13% of the mean value, and 17% in the left eye.

The resulting values of RNFL thickness from OCT
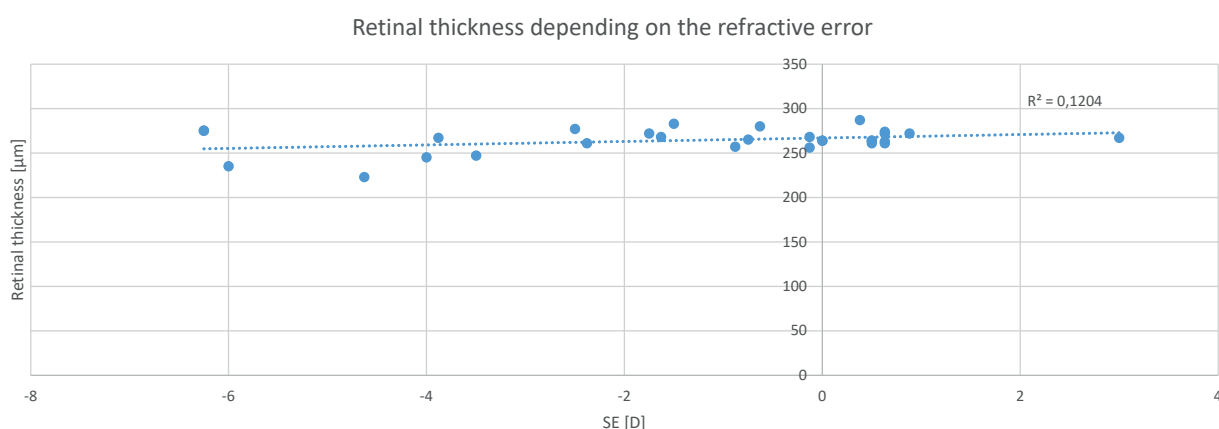
Graph 3. Correlation between refractive error spherical equivalent (SE) and mean macular retinal thickness in right eyes
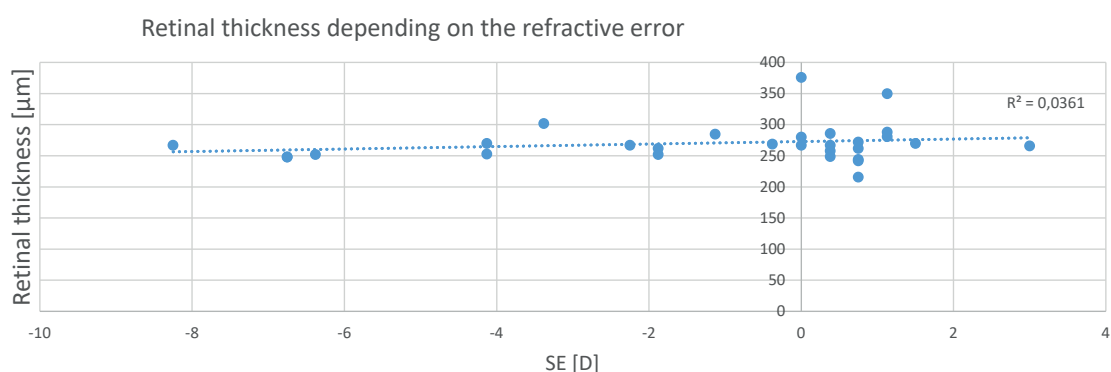
Graph 4. Correlation between refractive error spherical equivalent (SE) and mean macular retinal thickness in left eyes

examination according to our study (average of right eye 109.1 ±12.0 μm, average of left eye 107.7 ±16.5 μm) correspond with the average values of healthy individuals aged from 20 to 78 years from the study conducted by the author Ocansey et al. [18]. In this study the OCT HD Cirrus 500 instrument was used to measure an average RNFL thickness of 102.3 ±7.45 μm in 100 healthy patients, and 90.7 ±14.5 μm in patients with glaucoma.

The mean retinal thickness in the area of the macula (ILM–RPE) measured on our instrument (OPKO Spectral OCT SLO Combination Imaging System, Opko Health, USA) and evaluated with the aid of a Macular Cube 512-128 scan was 264.3 ±13.4 μm in the right eye and 270.6 ±30.6 μm in the left eye. In the study conducted by the authors Viladés et al. [19] the average value was 266.8 ±9.3 μm for the nasal quadrant of the retina in the age group of 20 to 34 years, measured on an instrument with OCT swept source technology. The results of both studies are therefore comparable.

CONCLUSION

When comparing the average thickness of the nerve fibers in the papilla (RNFL) in our study with the aid of OCT examination and the functional sensitivity of the retina measured on an FDT perimeter, we did not find a statistically significant dependence either in the group of right eyes or in the group of left eyes. We also achieved a similar result when examining the interdependence of the variables of spherical equivalent of refractive error of the eye (SE) and the average thickness of the retina in the macula on an OCT instrument. No statistically significant relationship of these variables was determined for the groups of right or left eyes, thus neither of the hypotheses was confirmed on a statistically significant level.

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