

Optic Nerve Head and Retinal Nerve Fiber Layer Thickness Analysis in Healthy and Ocular Hypertensive Eyes Using Optical Coherence Tomography

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Abstract

Purpose: To assess and compare optic nerve head and retinal nerve fiber layer thickness measurements in healthy and ocular hypertension subjects using optical coherence tomography (OCT).

Material and Methods: The study enrolled 63 Caucasian patients (126 eyes) of the same Azeri ethnicity. 25 healthy people (50 eyes) and 38 patients (76 eyes) with ocular hypertension. Peripapillary RNFL assessment was performed using "RNFL Thickness Average Analysis Report" and the head analysis with "Optic Nerve Head Analysis" program, Stratus OCT (Carl Zeiss Meditec, Inc., Dublin, CA). Student and Wilcoxon tests were used to statistically evaluate the results.

Results: The study revealed that considerable thinning of TRNFL (95% confidence interval) when compared to the control group was detected in the inferior quadrant by 8.2% ($p < 0,01$) and nasal one by 9.1% ($p < 0,05$), as well as RNFL aver - 6,4% ($p < 0,01$) and I max - 6,4% ($p < 0,05$). However, hourly in-depth analysis of the study group when compared to the control one showed a significant thinning of TRNFL that was greater at the nasal quadrant clock: 2:00 by 8,0%; 3:00 - 7,8%; 4:00 - 13,2% ($p < 0,01$) and only at 5:00 of the inferior quadrant- 11,7% ($p < 0,01$); the smallest shortening in TRNFL was at 12:00 - 1.6% in the superior quadrant. The study of bioretinometric indicators of ONH in the second group when compared to the control one revealed that there was a 38.6% increase in the cup area ($p < 0,01$), cup/disk area ratio by 25,1% ($p < 0,05$), cup/disk vertical ratio by 11,7% ($p < 0,05$) and optic nerve disc diameter by 8.8% ($p < 0,05$). No gender differences were found.

Keywords: Ocular Hypertension; Optical Coherence Tomography; Retinal Nerve Fiber Layer; Optic Nerve Head

Abbreviations

RNFL: Retinal Nerve Fiber Layer; TRNFL: Thickness Retinal Nerve Fiber Layer; OCT: Optical Coherence Tomography; ONH: Optic Nerve Head; CDR: Cup-Disc Ratio; OH: Ocular Hypertension; IOP: Intraocular Pressure

Introduction

As a rule, ocular hypertension (OH) is regarded as a condition with intraocular pressure (IOP) exceeding 21 mm Hg. It is not limited to the specific time frame when the elevated pressure was measured, and it does not manifest itself in any glaucomatous changes. Increased IOP can be observed in one or both eyes in all (2 and more) subsequent measurements [1-4].

Ocular hypertension occurs 10 - 15 times more frequently than primary open-angle glaucoma, i.e. approximately every tenth out of a hundred patients over 40 has a pressure higher than 21 mm Hg, but glaucoma develops only in 1 patient out of these people [2-4]. Unfortunately, pathomechanism and etiology of OH development still remain unstudied [5].

Long-term studies (since 1994) of American and European scientists within the framework of programs The Ocular Hypertension Treatment Study (OHTS) and European Glaucoma Prevention Study (EGPS) have revealed that in 9.5% cases in patients with untreated ocular hypertension glaucoma developed within 5 years, in 13 years the frequency was 22% or about 2% per year, while with timely treatment the risk of development decreased by about 50%.

It has also been found that the risk of glaucoma development can increase:

- With age (by 26% for every decade)
- With IOP increase (by 9% for each 1 mm Hg)
- With a change in cup-to-disc ratio (Vertical and horizontal cup-to-disc ratio). And the risk increases by 19% with a 0.1 increase in size [1,2,5-8].

Glaucoma is the second leading cause of blindness worldwide. Approximately 2% - 2.5% of the world's population currently suffer from glaucoma [9-11].

Many times glaucomatous progression by field of vision is detected only after significant RNFL loss has already occurred. RNFL measurements using repeated OCT scans at different time points (months or years) are needed to detect glaucoma progression, which can appear earlier than field of vision changes. Measuring RNFL thickness by OCT enables an objective and quantitative assessment of glaucomatous structural loss [12-14].

Optical coherence tomography (OCT) is nowadays an important diagnostic tool for retinal diseases in the clinical practice. It provides cross-sectional or three-dimensional images by measuring the echo time delay and magnitude of backscattered or back-reflected light. OCT gives a kind of optical biopsy with quantitative and reproducible measurements RNFL thickness parameters using near-infrared light [14-17].

Among the latest technologies recently used for structural evaluation of ONH and RNFL, OCT is the most interesting one regarding the possibility of simultaneous study of retinal parameters and ONH. As practice shows, sometimes it is not enough to use routine research methods for early diagnosis, so in 50% cases the disease remains undiagnosed even after a full-scale conventional study (tonometry, perimetry, ophthalmoscopy) [5,12,18-20].

The importance of TRNFL determination in the early diagnosis of glaucoma cannot be overstated, because RNFL thinning may in theory be the earliest structural change clinically detectable and has been shown to precede functional loss by as much as 5 years [14-17,22-24].

OCT has proven itself as one of the most sensitive and specific methods used to diagnose glaucoma [18,26-30]. At the same time, if the method sensitivity at quadrant study is equal to 14.8%, at hourly study it is 85.2-95%, and the specificity of the method ranges from 86.6 to 92.5% [31]. A Kiernan DF, Hariprasad SM. (2010) believe that the sensitivity and specificity of Stratus OCT is equal to 80% and 94% respectively [32].

In view of the said above, the Purpose of this research is to evaluate and compare TRNFL in peripapillary zone and ONH in the patients with ocular hypertension by means of optical coherent tomography - OCT (Stratus OCT 3000).

Materials and Methods

The retrospective study included outpatient records and examination protocols of 63 Caucasian patients (126 eyes) of the same Azeri ethnicity.

Among them there were 19 women and 44 men with the average age of the patients of 50.0 ± 3.2 . The examined were divided into 2 groups. The first - control - group consisted of 25 people (50 eyes). The selection criteria were: IOP not exceeding 21 mm Hg; no marked lens opacity (e.g. back capsular cataract); no ocular pathology, congenital ONH abnormalities or neurological symptoms in the history.

The second group was composed of 38 patients (76 eyes) with ocular hypertension. The selection criteria were: IOP exceeding 21 mmHg, (IOP ≤ 24 mm Hg in 2 cases at least), gonioscopically - open anterior chamber angle, no glaucoma-specific changes in the field of vision and ONH, no signs of hemorrhage, incision, notching or RNFL defect, no history of myopia, congenital ONH abnormalities or neurological symptoms.

All clinical material was collected at the National Centre of Ophthalmology named after acad. Zarifa Aliyeva, the observation period was 2010 - 2013. All the patients underwent a complete ophthalmologic examination that included both standard and additional methods of examination: Visometry, Refractometry, Biomicroscopy, Biomicrophthalmoscopy (Ocular HighMag 78 D), Tonometry (applanation tonometry according to Maklakov). There was also a study of peripapillary TRNFL using OCT (Stratus OCT 3000 software v.4.0.2; Carl Zeiss Meditec, Inc., Dublin, CA) under the program "RNFL Thickness Average Analysis Report, 3.4 mm scan protocol" and assessment and comparison of optic nerve head (ONH) parameters under the program of "Optic Nerve Head Analysis". The following criteria were used to statistically process the observation results: parametric Student's t-test (and estimation of difference between the lobes) was used to preliminary estimate difference between variation rows, and non-parametric Wilcoxon's U-test was used to verify and refine the results obtained.

Results and Discussion

In total, there were 2 groups with almost the same average age of all the examined, but men outnumbered women. In the first group, the average age was 52.2 ± 3 , of them 17 men (68%) and 8 women (32%); in the second group, 51.3 ± 2.8 , of them 27 men (71.1%) and 11 women (28.9%), respectively. The average value of intraocular pressure in the control group was equal to $17,8 \pm 0,3$ (12,2 - 21,4) mm Hg and with ocular hypertension - $19,2 \pm 0,3$ (12 - 25) mm Hg accordingly, statistically significant difference with the first group indices was ($p < 0,01$).

As it can be seen from table 1 visual acuity in both groups with and without correction was relatively equal.

Assessment and comparison of the peripapillary TRNFL was performed in four quadrants and 12 hours according to table 2.

Groups	IOP, mm Hg	Visual acuity without correction	Visual acuity with correction
1 - Control (n = 50)	$17,8 \pm 0,3$ (12,2 - 21,4)	$0,638 \pm 0,052$ (0,1 - 1)	$0,847 \pm 0,039$ (0,4 - 1)
2 - Ocular hypertension (n = 76)	$19,2 \pm 0,3$ (12 - 25)**	$0,510 \pm 0,042$ (0,01 - 1)	$0,758 \pm 0,045$ (0,4 - 1)

Table 1: Distribution of IOP and visual acuity ratio in the study groups.

Note: statistically significant difference with indicators: control group: * - $p < 0,05$; **: $p < 0,01$.

As follows from table 3, a significant thinning of TRNFL (95% confidence interval) when compared to the control group was detected in

Quadrants		Degrees	Hours
T	Temporal	316 - 450	8:00,9:00,10:00
S	Superior	46 - 1350	11:00,12:00,1:00
N	Nasal	136 - 2250	2:00,3:00,4:00
I	Inferior	226 - 3150	5:00,6:00,7:00

Table 2: Diagnostic reference points for the quadrant and hourly distribution of RNFL thickness.

the inferior quadrant by 8.2% ($p < 0,01$) and nasal one by 9.1% ($p < 0,05$) and also RNFL aver - 6.4% ($p < 0,01$) and I max - 6.4% ($p < 0,05$).

Indicators	Groups		Statistically significant difference with control group indicators
	Control group	Ocular hypertension	
I	132,1 ± 2,1 (109 - 164)	121,3 ± 2,5 (44 - 158)	< 0,01
S	123,1 ± 2,3 (86 - 148)	118,7 ± 2,1 (66 - 146)	> 0,05
N	82,4 ± 2,5 (47 - 121)	74,9 ± 2,0 (47 - 117)	< 0,05
T	71,9 ± 2,0 (50 - 110)	67,5 ± 1,6 (32 - 103)	> 0,05
RNFL aver	102,4 ± 1,5 (79,49 - 125)	95,9 ± 1,7 (51,96 - 127)	< 0,01
I max	165,2 ± 2,9 (125 - 206)	154,7 ± 3,0 (63 - 196)	< 0,05
S max	151,5 ± 3,2 (101 - 189)	146,0 ± 2,3 (96 - 181)	> 0,05

Table 3: Distribution of average values of RNFL thickness by quadrants in research groups.

Bowd Ch., *et al.* have published similar results. They have obtained the following results: the average RNFL was significantly thinner (by 15%) in the eyes with ocular hypertension than in the normal eyes (the control group) - 72.8 μm (66.4 - 78.1 μm) and 85.8 μm (80.2 - 91.7 μm), respectively. The lowest RNFL values were found in the inferior quadrant, 84.8 μm (75.6 - 94.0 μm) versus 107.6 μm (99.3 - 115.9 μm); and in the nasal quadrant, 44.1 μm (37.5 - 51.7 μm) versus 61.8 μm (53.0 - 65.6 μm) when compared to the control group. Given the racial differences in measuring the parameters of optic nerve disk and RNFL, the authors indicate that the patients participating in the study were mostly Caucasian (88%) [33].

Myung G Choi., *et al.* mention the thinning only in the inferior quadrant. In addition to ethnic differences another reason for that could be probably the age of the patients which was in the following proportions: 41.7 ± 6.5 in the group of healthy patients and 45.5 ± 8.5 in the patients with OH [34].

Patel D., *et al.* reported that the best parameter to differentiate ocular hypertension at risk from normal eyes was found to be TRNFL in superior quadrant in SD-OCT RNFL thickness parameters [35].

Chen H-Y., *et al.* in course of TRNFL study in patients with ocular hypertension (32 eyes; mean age 32.88 ± 15.55, Chinese) on Stratus 3000 OCT found the following quadrant distribution: mean TRNFL (RNFL aver.) was 108.81 ± 9.08; temporal - 98.06 ± 21.91; superior - 129.75 ± 12.73; nasal - 73.41 ± 13.73 and inferior - 133.91 ± 19.35, that considerably did not differ from the control group and conform to the following data: RNFL aver. 110.48 ± 9.79, T - 97.00 ± 20.75, S - 135.92 ± 15.03, N - 73.90 ± 17.05 and I - 135.24 ± 17.8 [26].

Given the size of the optic nerve disc and corneal thickness Vessani RM., *et al.* showed from an overall optic disc area of 2.13 mm² mean RNFL thickness in ocular hypertensive patients (mean ± standard error of the mean) was 98.27 ± 2.53 μm and 106.50 ± 2.28 μm in normal controls and from an overall optic disc area of 2.08 mm², mean RNFL thickness (mean ± standard error of the mean) in ocular hypertensive patients (CCT < 540 μm) was 92.98 ± 5.55 μm and 101.77 ± 4.08 μm in ocular hypertensive patients (CCT > 540 μm) [36].

Mahadevan A., *et al.* reported that the mean RNFL was 102.12 ± 12.28 μm in the OHT group; RNFL was measured with spectral-domain optical coherence tomography [37].

Brijesh P., *et al.* showed with Optovue spectral Domain OCT, that mean RNFL thickness was 83.83 ± 26.20 μm in ocular hypertension and 103.27 ± 16.23 μm in normal eyes. In the ocular hypertensive group, RNFL was thinner in the superior (107.40 ± 35.39 μm), inferior

(100.80 ± 26.77 μm), nasal (67.10 ± 19.26 μm) and temporal (58.30 ± 24.99 μm) quadrants when compared to normals (P < 0.001, unpaired ‘t’ test) [38].

In-depth hourly analysis of the examined group (Table 4) when compared to the control one showed a significant thinning of TRNFL that was greater in the nasal quadrant: 2:00 by 8.0%; 3:00 - 7,8%; 400 - 13,2% (p < 0,01) and only at 5:00 in the inferior quadrant - 11.7% (p < 0,01); the smallest reduction of TRNFL was detected at 12:00 - 1,6% in the superior quadrant.

Hours	Groups		Statistically significant difference with control group indicators
	Control group	Ocular hypertension	
1:00	118,0 ± 2,9 (71 - 169)	113,8 ± 2,7 (57 - 159)	> 0,05
2:00	96,9 ± 3,5 (47 - 147)	89,1 ± 2,8 (42 - 141)	> 0,05
3:00	66,8 ± 2,4 (37 - 113)	61,6 ± 2,1 (31 - 112)	> 0,05
4:00	83,7 ± 2,7 (54 - 128)	72,7 ± 2,2 (34 - 116)	< 0,01
5:00	117,2 ± 3,2 (75 - 158)	103,4 ± 2,9 (29 - 154)	< 0,01
6:00	139,8 ± 3,1 (100 - 181)	130,8 ± 3,3 (50 - 181)	> 0,05
7:00	139,5 ± 4,0 (85 - 193)	129,4 ± 3,0 (55 - 173)	< 0,05
8:00	75,9 ± 2,8 (51 - 121)	71,1 ± 1,9 (35 - 127)	> 0,05
9:00	56,3 ± 1,5 (40 - 82)	53,7 ± 1,1 (29 - 79)	> 0,05
10:00	83,5 ± 2,6 (50 - 140)	79,2 ± 1,9 (32 - 125)	>0,05
11:00	126,6 ± 3,5 (83 - 172)	119,6 ± 2,8 (52 - 173)	> 0,05
12:00	124,7 ± 3,0 (80 - 164)	122,8 ± 2,7 (73 - 169)	> 0,05

Table 4: Hourly distribution of RNFL thickness in study groups.

Şahli E and Tekeli reported that no difference was found between the OHT group and the control group in any OCT parameter in four quadrants and clock hours with scanned Cirrus HD-OC [14].

The results (Table 5) of bioretinometric indicators of the ONH in the second group when compared to the control one revealed that there was an increase in the cup area by 38.6% (p < 0,01), in the cup/disk area ratio by 25.1% (p < 0,05), in the cup/disk vert. ratio by 11.7% (p < 0,05) and in the optic nerve disc diameter by 8.8% (p < 0,05).

ONH indicators	Groups		Statistically significant difference with control group indicators
	Control	Ocular hypertension	
Vert. inteq. rim area (vol.)	0,365 ± 0,033 (0,065 - 1,026)	0,355 ± 0,035 (0,012 - 1,67)	> 0,05
Horiz. inteq. rim width (area)	1,637 ± 0,035 (1,154 - 2,151)	1,62 ± 0,037 (0,79 - 2,278)	> 0,05
Disk area	2,363 ± 0,054 (1,804 - 3,26)	2,570 ± 0,057 (1,769 - 4,35)	< 0,05
Cup area	0,832 ± 0,059 (0,167 - 1,863)	1,153 ± 0,083 (0,07 - 4,35)	< 0,01
Rim area	1,529 ± 0,063 (0,742 - 2,442)	1,416 ± 0,067 (0 - 3,034)	> 0,05
Cup/disk area ratio	0,350 ± 0,023 (0,07 - 0,715)	0,438 ± 0,025 (0,037 - 1)	< 0,05
Cup/disk horiz. ratio	0,620 ± 0,023 (0,292 - 0,902)	0,674 ± 0,022 (0,19 - 1)	> 0,05
Cup/disk vert. ratio	0,542 ± 0,018 (0,264 - 0,788)	0,605 ± 0,020 (0,146 - 1)	< 0,05

Table 5: Distribution of bioretinometric ONH data by research groups.

It is interesting to note that the Korean authors (Myung G Choi, *et al.*) conducted the study of bioretinometric ONH data in the patients with OH when compared to the control group of healthy people and mention the difference was observed for all parameters except for the diameter of the optic nerve disc and Disk area. These indicators were almost identical in both study groups, which may be explained by ethnic differences [34].

No distinct gender differences have been found in the study. Vessani RM, *et al.* have published the similar results [37].

Conclusion

1. Distinct thinning of TRNFL (95% confidence interval) when compared to the control group was detected in the inferior quadrant by 8.2% ($p < 0,01$) and nasal one - 9.1% ($p < 0,05$), as well as RNFL aver - 6.4% ($p < 0,01$) and I max - 6.4% ($p < 0,05$).
2. However, in-depth hourly analysis of the examined group when compared to the control one showed a significant thinning of TRNFL that was greater at the nasal quadrant clock: 2:00 by 8,0%; 3:00 - 7,8%; 4:00 - 13,2% ($p < 0,01$) and only at 5:00 in the inferior quadrant - 11,7% ($p < 0,01$); the smallest reduction of TRNFL was detected at 12:00 - 1,6% in the superior quadrant.
3. The study of bioretinometric indicators of ONH in the second group when compared to the control one revealed that there was an increase in the cup area by 38.6% ($p < 0,01$), cup/disk area ratio by 25.1% ($p < 0,05$), cup/disk vert. ratio by 11.7% ($p < 0,05$) and diameter of the optic nerve disc by 8.8% ($p < 0,05$).
4. No distinct gender differences have been found.

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Conflict of Interest

None declared.

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