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Measuring optic nerve sheath diameter and lens thickness by b-mode sonographic evaluation in glaucoma

Kenan Dagdelen

Department of Ophthalmology, Beytepe Murat Erdi Eker State Hospital. Ahlatlibel Mh. 1746 Sk. 06800 Beytepe, Cankaya, Ankara, Turkey.

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Abstract

Aim: This study was conducted to measure optic nerve sheath diameter (ONSD) and lens thickness (LT) with B-mode USG in patients with glaucoma and compare them with a healthy control group.
Materials and Methods: Seventy-two individuals were recruited, 35 with glaucoma and 37 age- and gender-matched controls without glaucoma. Patients with systemic hypertension, diabetes mellitus, and cataract, history of ocular trauma, higher refractive error, active ophthalmologic infection and smoking were excluded from the study. The ONSD and LT values of both eyes were measured in the supine position using 10MHz frequency B-scan ultrasound. Data analysis was performed by transferring to the SPSS version 25 program.
Results: The mean ONSD of glaucomatous eyes (3.60 mm and 3.50 mm on the right and left, respectively) was found to be significantly thinner than the controls (4.20 mm and 4.55 mm on the right and left, respectively). The mean LT of eyes with controls (4.25 mm and 4.15 mm on the right and left, respectively) was significantly lower compared to glaucoma (4.40 mm and 4.30 mm on the right and left, respectively).
Conclusion: In glaucoma, sonography is a reliable tool of evaluating the optic nerve sheath diameter and lens thickness.

Introduction

Glaucoma refers to a group of eye disorders that differ in their pathophysiology, risk factors, symptoms, treatments and prognosis (1). Common features are progressive degeneration of the optic nerve, loss of retinal ganglion cells, thinning of the retinal nerve fiber layer and progressive atrophy of the optic disc. Intraocular pressure was found to be normal in 30% of all glaucoma cases in a study evaluating people of European origin (2). To briefly mention the pathophysiology of glaucoma, high intraocular pressure and low perfusion pressure increase the gradient along the lamina cribrosa and cause papillary hypoperfusion. It causes impaired axonal transport in optic nerve fibers with structural changes and remodeling of lamina cribrosa (3). Increased loss of retinal ganglion cells in the field of vision progresses from the periphery until only a central intact visual island remains. Other functional disturbances are impaired contrast or color perception and reading difficulties (4). The different types of glaucoma are classified according to the structural changes in the anterior segment of the eye. Aqueous humor is excreted mainly through the trabecular meshwork and Schlemm's canal and partly through the uveoscleral outlet (root of the iris, ciliary body). The anterior chamber angle lies between the iris and the peripheral posterior surface of the cornea, and is localized under the trabecular meshwork at the end of the Schlemm canal. In open angle glaucoma, the chamber angle is open macroscopically, but it is blocked by the iris in acute angle closure. In secondary open-angle glaucoma, there are different forms of chamber deposits that can be seen under the microscope (gonioscope), including pigment deposition (in pigmentary glaucoma) (5) or protein deposition (in pseudoexfoliation glaucoma) (6).

The mechanisms that cause increased intraocular pressure in primary open-angle glaucoma are not fully understood. Glaucomatous optic neuropathy is the primary functional and structural disorder in glaucoma (7). Even when intraocular pressure is within normal limits (normal pressure glaucoma), glaucomatous changes may occur in the optic nerve. Ocular sonography is a known method to scan the optic nerve sheath. Only a few studies with ocular sonography have shown a reduction in the optic nerve sheath diameter (ONSD) of eyes with glaucoma (8, 9) and ONSD correlates with the level of axonal loss leading to optic atrophy in cases with glaucoma. Since optic nerve damage precedes visual field and pressure changes (9) and early diagnosis is very important to reduce the burden of the disease in glaucoma, it may be possible to utilize ocular sonography to achieve early and rapid evaluation of patients suspected to have glaucoma. The aim of our study was to demonstrate the possible changes in ONSD and lens thickness (LT) in patients with

Email address: ysfknn@hotmail.com (Kenan Dagdelen)

glaucoma via sonography and to compare the results with the eyes of a control group.

Materials and Methods

This study was carried out as a prospective, descriptive, cross-sectional study conducted in a four-month period by the Department of Ophthalmology of our institution. The study protocol was approved by the Clinical Researches Ethics Board of the Republic of Turkey Ministry of Health Ankara City Hospital. Ethics Board registration number is E1/1449/2020. Informed consent was obtained from each participant included in the study. Thirty-five adults ($\geq$ 30 years old) who were previously diagnosed with glaucoma (IOP > 21mmHg- Goldmann applanation tonometry and visual field showing the glaucomatous pattern as determined by an Ophthalmologist at the Ophthalmology clinic of our institution) were included in the glaucoma group. Patients who were diagnosed with glaucoma at least 3 months ago and did not receive any invasive treatment (laser or surgery) other than topical drop therapy were included in the study. Intraocular pressure was measured ten minutes before the sonographic examination in all patients. Thirty-seven volunteers who were age- and gender-matched and had normal IOP (< 21 mmHg- goldmann applanation tonometry), normal visual field and no other ocular disease were included in the control group. Exclusion criteria were: Systemic hypertension (Systolic blood pressure > 140mmHg and / or diastolic blood pressure > 90mmHg), diabetes mellitus (Hemoglobin A1c > 5.7%), cataract, history of ocular trauma, higher refractive errors, active ophthalmologic infection, patients with a history of eye-orbital-cranial surgery, previously treated with cranial and orbital radiotherapy, with congenital optic disc pathology, any neurophthalmologic disease and smoking.

After a detailed description of the procedure, each patient was examined in the supine position. Trans-orbital scan of both eyes was performed using a Sonomed® real-time ultrasound device (ultrasound scanner model E-Z Scan 5500+ by Sonomed Inc. NY) with a linear transducer (Frequency = 10MHz). All sonographic examinations were performed by the author who already had 10 years of experience with ocular sonography. After the subjects were instructed to close their eyes, a large amount of acoustic gel was applied on the upper eyelid. The transducer was then placed on the coupling gel on the temporal region of the eye lid. Throughout the procedure, minimal pressure was applied to the probe to prevent discomfort to the patient. The probe was moved from the superotemporal region to the optic nerve entrance area and was appropriately angled to view the optic nerve in its axial plane. To achieve this, the patient was asked to direct his/her gaze to the primary position with respect to the probe marker that had been centered on the cornea. Transverse (cross-section) and longitudinal scans of both optic nerves were obtained to evaluate ONSD. Transverse scanning was performed by bi-directional visualization after placing the probe marker in the nasal or superior region. Longitudinal scanning was performed from the periphery of the limbus, with the probe marker perpendicular to the limbus. ONSD was measured by placing cursors on the outer contours of the dural sheath –in the retrobulbar position with placement performed 3 mm behind the optic disc (optic nerve head). ONSD was measured as the horizontal distance between cursors and each eye measurement was bilaterally repeated three times in a row; the mean value was calculated and recorded as ONSD value (Figure 1).

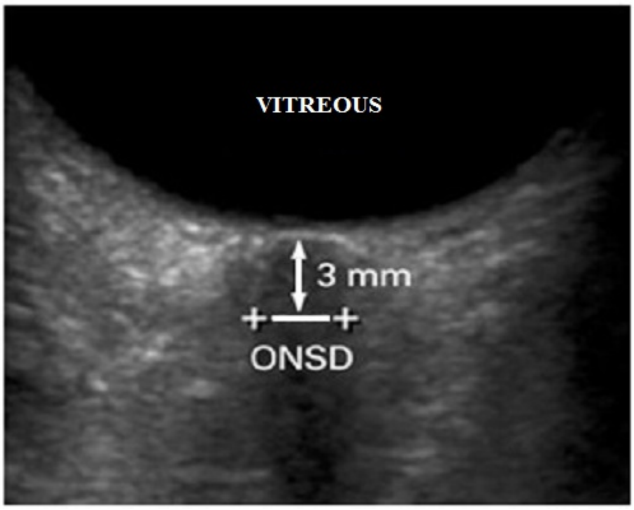

Figure 1

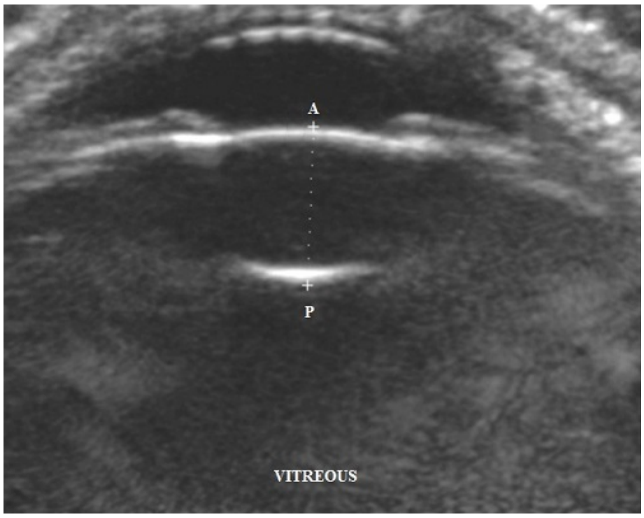

Figure 2

The cursors were placed on the outside of the anterior and posterior lens capsules and axial LT was measured. LT was also measured three times in a row and the mean value was recorded for each eye B-mode sonographic image of the eye (axial plane) showing measurement of the lens thickness (A-P, white arrow) as the anechoic space between the echogenic anterior (A) and posterior (P) lens capsules (delimited by cursors) (Figure 2).

Statistical Analyses

The data were recorded on a spreadsheet and analyses were performed after transfer to the SPSS version 25 software. Frequency and percentage values were used to describe categorical data, and chi-square tests were used for comparison. The compatibility of continuous data to normal distribution was tested using the Shapiro-Wilk test. Since the continuous data did not conform to normal distribution and parametric assumptions were not met, these variables were described with median and 25%–75% interquartile range (IQR) values. The Mann–Whitney U test was used to compare quantitative variables. Any p-value of < 0.05 was accepted to demonstrate significance.

Results

The demographic characteristics and examination findings of the study groups are presented in Table 1.

Of the 35 patients included in the glaucoma group, 18 (51.4%) were female and 17 (48.6%) were male and median age was determined as 64 (52–75) years. Of the 37 volunteers included in the control group, 19 (51.4%) were female and 18 (48.6%) were male, with median age of 60 (49–70) years.

There were no statistically significant differences between the demographic characteristics of the study groups. The Cup / Disc (C/D) ratio of patients with glaucoma was significantly higher than that of the control group ($p < 0.05$). Average spherical values of glaucoma group +1.00 and control group +0.50 were measured. The ONSD values of glaucomatous eyes (3.60 mm and 3.50 mm on the right and left, respectively) were significantly lower than controls (4.20 mm and 4.55 mm on the right and left, respectively) ($p < 0.001$). The LT values of eyes with controls (4.25 mm and 4.15 mm on the right and left, respectively) were significantly lower compared to glaucoma (4.40 mm and 4.30 mm on the right and left, respectively) ($p < 0.001$). Comparison of demographic characteristics and examination findings of glaucoma and control group (Table 1).

There were no statistically significant differences between the right and left eyes of glaucoma patients and the right and left eyes of the control group in terms of C/D Ratio, ONSD and LT ($p > 0.05$) (Table 2).

Regarding to the correlation analysis of cup/disc ratio, optic nerve sheath diameter and lens thickness for the glaucoma, control and overall group. No statistically significant correlation was found (Table 3).

Discussion

Glaucoma is the second most common cause of irreversible blindness after age-related macular degeneration (10). Between 1990 and 2010, 2.1 million people worldwide experienced vision loss due to glaucoma (11). Traditionally, glaucoma is evaluated by a trio of tonometry, visual field testing, and optic nerve evaluation (12). However, due to ocular and non-ocular factors, this trio requires an alternative examination method (8, 13, 14). Despite the fact that magnetic resonance imaging (MRI) and computed tomography (CT) have relatively higher spatial resolution and are non-invasive, their use is associated with high costs and may delay diagnosis in resource-limited settings. Optical coherence tomography has a very important place in the diagnosis and follow-up of patients with glaucoma. With this imaging technique, the optic nerve head and retinal nerve fiber layer can be evaluated very well. However, non-globe optic nerve evaluation cannot be evaluated with this imaging method (15-19). Ultrasound evaluation of ONSD is an easily applicable method which is cost effective and may consume less time. The advantages of this method include the fact that results are reproducible and that it is a noninvasive modality that may cause only slight discomfort (20). In prior research, ONSD measurement by ultrasound has been accepted as a reliable method to estimate intracranial pressure (21, 22). This is due to the fact that the pressure exerted by cerebrospinal fluid can cause expansion of the optical nerve sheath, and studies have demonstrated that this expansion can be quantified via USG examination (23). Therefore, the measurement of ONSD (and LT) via ultrasound may carry the potential to be a reliable method to detect underlying changes in glaucoma.

The aim of this study was to evaluate ONSD and LT with B-mode USG in glaucoma patients and to compare results with the control group. In our study, 35 patients were included in the glaucoma group, while there were 37 healthy controls in the control group. There was no statistically significant difference in the demographic characteristics of the two groups. The average ONSD of the glaucoma group was 3.6 mm, and the LT was 4.2 mm. These results showed that glaucoma patients had significantly lower values relative to the control group. In addition, when the right and left eyes were compared separately between the two groups, we found that the ONSD and LT values were significantly lower in both the right and left eyes of patients with glaucoma. The bilateral mean C/D ratio of glaucoma patients was significantly higher, as expected. This reduction in ONSD is similar to the findings of previous studies using USG and MRI (8, 9, 14, 20). It has been widely reported that glaucomatous optic neuropathy is due to optic nerve atrophy secondary to the loss of the retinal nerve fiber layer. Therefore, it is not surprising to observe a reduction in ONSD in glaucoma patients compared to healthy eyes. However, there are other studies of ONSD using CT scanning (24) and USG (25) reporting different results. While Jaggi et al. (24) found that patients with normal tension glaucoma had higher ONSD than control subjects, Pinto et al. (25) suggested that ONSD did not differ between these groups. These inconsistencies in ONSD results may reflect differences in patient selection. Differences such as age, head position, sample size and imaging method can alter the final outcome of such comparisons. While we utilized USG in our study, Jaggi et al. (24) used CT in a sample size of only 18 subjects. It is also important to consider the position of the head during image capture. In our study, images were taken with USG in the supine position, while Jaggi et al. (24) obtained images in the prone position. The prone position has been shown to affect cerebrospinal fluid distribution in the central nervous system due to the effect of gravity. In addition, while measurements were taken at a distance of 3 mm behind the globe in our study, Jaggi et al. (24) measured ONSD value from a point in the orbit that provided the highest ONSD value for each patient. Regarding the study of Pinto and colleagues, it can be considered that the fracture state of patients can cause bias, since sclera properties differ from hyperopia to myopic patients. The mean spherical values of the glaucoma group in our study were found to be +1.00 and the control group as +0.50. In the study of Pinto et al. (25),due to the use of 7.5 MHz B-scan ultrasound probe (Antares echograph device, Siemens, Munich, Germany), it is evident that the resolution of sonographic images is considerably lower than those obtained by the 10 MHz probe used in our study. Thus, the emergence of artefacts would have been more likely in the study by Pinto et al., and may have affected the accuracy of measurements, especially with respect to ONSD.

The LT values measured in our study also demonstrated that patients with glaucoma had higher values bilaterally when compared to the control group. In our study, a strong positive correlation was found between LT and C/D ratio. Omatiga et al. found that only left-sided LT was significantly different between the glaucoma and control groups. They stated that they could not determine the reason for this unilateral difference (8). In the literature review, lens thickening was reported in closed-angle glaucomatous eyes compared to controls (26, 27); however, this is not an expected result in other forms of glaucoma.

Table 1. Comparison of demographic characteristics and examination findings of glaucoma and control group

Variables		GLAUCOMA (n =35)	CONTROL (n = 37)	P value
Gender	Male	17 (48.6%)	18 (48.6%)	0.995
	Female	18 (51.4%)	19 (51.4%)	
Eye	Right	18 (51.4%)	19 (51.4%)	0.995
	Left	17 (48.6%)	18 (48.6%)	
Age		64 (52-75)	60 (49-70)	0.743
Spherical Equivalent (Diopter)		1.00 (-4.25- 2.25)	0.50 (-3.50-2.75)	0.320
Intraocular Pressure (mmHg)		17.2 (10-25)	15.5(11-19)	0.045
Height (cm)		166 (151-185)	169 (154-190)	0.977
Weight (kg)		69 (56-97)	67.5 (49-94)	0.572
HbA1c (%)		5.3 (4.8-5.7)	5.1 (4.7-5.6)	0.562
Cup/Disc (C/D) Ratio		0.40 (0.2-0.7)	0.25 (0.1-0.4)	0.001
Optic Nerve Sheath Diameter (ONSD) (mm)		3.6 (3.4-4)	4.45 (4.00-4.90)	0.001
Lens Thickness (LT) (mm)		4.35 (3.80-4.70)	4.2 (3.7-4.5)	0.041
Duration of glaucoma(months)		13.2 (3-35)	NA	

Table 2. Differences in ONSD and LT between eyes in the study groups

Variables		Right	Left	P value
Optic Nerve Sheath Diameter (ONSD) (mm)	Glaucoma	3.60 (3.50-4.00)	3.50 (3.40-3.90)	0.782
	Control	4.20 (4.00-4.60)	4.55 (4.00-4.90)	0.355
Lens Thickness (LT) (mm)	Glaucoma	4.40 (3.90-4.70)	4.30 (3.80-4.60)	1.000
	Control	4.25 (3.70-4.50)	4.15 (3.80-4.50)	0.757

Table 3. Correlation analysis between Cup / Disc Ratio, ONSD and LT

Variables		ONSD	Lens Thickness
Cup/Disc Ratio	Glaucoma (r;p)	-0.068; 0.697	0.215; 0.216
	Control (r;p)	-0.192; 0.263	0.201;0.240

The C/D ratio of glaucoma patients was found to be significantly higher in comparisons for both the left and right side, as expected. In a study in which cup / retrobulbar optical nerve diameter (C/OND) measurements were made with a 20 MHz high-resolution ultrasound probe, it was reported that the results showed a strong correlation with C/D ratio (28). Based on this finding, it can be assumed that this method of measurement may be useful for patients with glaucoma in whom fundus examination cannot be performed.

Conclusion

It is important to have demonstrated that ONSD measurement via B-scan sonography can an alternative for examination in cases where tonometry, visual field test and optic nerve evaluation are not possible in patients with eyes suspected to have glaucoma. Future sonographic studies of LT and C/OND values in glaucoma patients are required. The limitations of our study include the lack of simultaneous intraocular pressure measurement and the fact that the study was not conducted in patients with a specific type of glaucoma.

Ethics approval and consent to participate:
All procedures performed in studies involving human participants (including the use of human cell and/or tissue samples) were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The informed consent was obtained from all subjects or, if subjects are under 18, from a parent and/or legal guardian. The study was approved by the Clinical Researches Ethics Board (registration number: E1/1449/2020).

Availability of data and materials:

The data sets during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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