·Investigation·

Optic nerve sheath diameters in healthy adults measured by computer tomography

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Abstract

• AIM: To measure optic nerve sheath diameters (ONSD) in different locations by computer tomography (CT) and to recommend the best location for cases when ONSD is used for intracranial pressure monitoring.

• METHODS: In a prospective cohort study, CT data of 300 healthy adults were analyzed (600 eyes). In all cases, the CT investigation was performed at the Emergency Department because of the various conditions that proved not to be connected with ophthalmological or neurological pathology. The ONSD were measured at 3 mm and 8 mm distance from the globe, and 3 mm from the anterior opening of the optic canal. The correlation analysis was performed with gender, age, and ethnic background.

• RESULTS: The right/left ONSD are 4.94±1.51/5.17±1.34 mm at 3 mm, 4.35 ±0.76/4.45 ±0.62 mm at 8 mm from the globe, and 3.55±0.82/3.65±0.7 mm at 3 mm from the optic canal. No significant differences correlated with gender of the patients, their age, and ethnic background were found.

• CONCLUSION: In healthy persons, the ONSD varies from 5.17±1.34 mm to 3.55±0.82 mm in different locations within the intraorbital space. The most stable results with lesser standard deviation can be obtained if it is measured 8–10 mm from the globe.

• **KEYWORDS:** optic nerve sheath; computer tomography; intracranial pressure
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INTRODUCTION

At least since 1780, when Zinn and Wrisberg [1] republished his classical "Descriptio anatomica oculi humani", it was well known that the optic nerve "arrives at the back of the eye, enclosed in a strong sheath, continued from the dura mater", but optic nerve sheath diameter (ONSD) did not attract immediate attention and no normative measurements were published during the next 200y. ONSD is however important because the optic nerve is surrounded by subarachnoidal cerebrospinal fluid and all three meningeal layers, and changing of the ONSD can indicate some changes of the intracranial pressure. In the 1990s, it was postulated that the presence of enlarged optic nerve sheaths suggests that raised intracranial pressure is transmitted to the perineural subarachnoid space[2,3].

The term "enlarged" is not clear. Improper assessment of normal anatomical data led the authors of various publications on the subject to invent their own indicators. Different authors indicated a normal/abnormal threshold (a cutoff value) of the diameter from 4.8 mm to 5.9 mm with numerous variations between these numbers [4,5]. The second problem is that different authors estimated the ONSD at different distances from the globe measuring it 3 mm[6,7], 4 mm[8], 2 to 5 mm behind the globe or even not mentioning this distance at all[9,10]. In 1996, Helmke and Hansen[11] presented their explanation of how to choose the specific distance for the measurement. These authors found that at 3 mm distance from the globe the ONSD experienced wider changes than in other intraorbital sections of the optic nerve. The intraorbital part of the optic nerve is about 15-24 mm long; its sheath however is not a single-diameter tube and each mm counts. In normal subjects, the subarachnoid space is widest behind the globe, then narrowed toward the orbital apex [12]. The study of ONSD application to the intracranial pressure is not perfected yet, and the recent review on methods of intracranial pressure monitoring estimated the accuracy of the ONSD method as low[13].

The purpose of the current research was to establish normative data of the ONSD in various locations within its intraorbital path with the help of data obtained by computer tomography (CT) technique. We planned to measure the ONSD in several distances from the globe, analyze these data, and recommend the most convenient normative distance to be used in practice especially in cases when ONSD is

measured for the purpose of detection of elevated intracranial pressure.

SUBJECTS AND METHODS

In a prospective cohort study, the CT data of 300 consecutive adult patients (>18) who were admitted to the Department of Radiology at our Medical Center from January 2011 to June 2013 were collected and analyzed. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki (amended 2008) as reflected a priori after approval by the institution's Helsinki committee. We examined CT data from the patients who were scheduled for routine CT investigation that included the head and neck region. In all cases, the CT investigation was performed by the Emergency Department request because of the various medical conditions that proved not to be connected with ophthalmological or neurological pathology.

Exclusion procedure was organized in three steps. First, the patients with documented ophthalmological, cerebral, or neuro-ophthalmological disorders were excluded as well as patients with injuries around the eyeballs and the orbits. Second, the selected patients were examined by an ophthalmologist and by a neurologist in order to exclude overlooked eye disorders or cerebral pathology. Special attention was paid in order to exclude cases with ischemic, toxic, hereditary, nutritional, or compressive neuropathies, glaucoma, cataract, *etc*. Third, in order to exclude further any possibility of the optic nerve (normative area 4-6.25 mm^2) compression. We also excluded from the study all cases with narrow optic foramen (the diameter of the foramen <4.5 mm, the area <6.6 mm^2). The patient flow was as follows: from the 460 consecutive patients, 89 were excluded at the first step, 41 were excluded at the second step, and 30 were excluded at the third step. The data collection was stopped when we obtained 300 ophthalmologically and neurologically healthy cases.

ONSD were measured at 3, 8 mm distance from the globe, and 3 mm from the anterior opening of the optic canal. Superior ophthalmic vein was used as the landmark for the middle third for the orbital path of the optic nerve. All the CT scans were obtained by the 256-slice CT scanner (Brilliance iCT, Philips Healthcare) (Figure 1) with NanoPanel 3D spherical detectors in axial (transverse) plane that were used further for reconstruction of coronal (frontal) and sagittal planes. The standard Philips protocols [14,15] for head and neck imaging were implemented in all cases with slices performed at 25 degrees to the skull base. The pixel size of the used scans was 1.6 mm, with an average slice distance of 3 mm. When the CT scans were obtained, the left and right ONSD were measured by the computer program (spine window, middle third; window parameters: WW 60, WL 360, accuracy 1 pixel). All measurements were made using the same window, contrast and brightness. The error margin was expressed by means of the technical error of measurement (TEM) to calculate the intra-evaluator variability and inter-evaluator variability between two evaluators. The same equipment and methodological procedures for measurements were adopted by both evaluators.

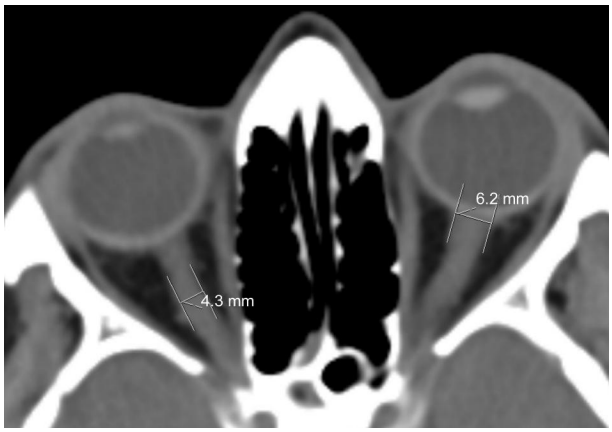

Figure 1 Optic nerve sheath diameters as measured by CT in transverse projection ONSD in various locations is indicated in mm (4.3 mm: ONSD at the middle third of the orbital path of the optic nerve; 6.2 mm: ONSD 3 mm behind the globe). At this picture, the left ONSD was measured precisely (6.2 mm), and the 4.3 mm represents preliminary detection of the right optic nerve sheath that was measured precisely at the following CT scan slices.

Statistical Analysis A within-group repeated measures experimental statistical analysis was used to test the variables. To verify the normality of the data, normal probability plots and basic descriptive statistics [mean, standard deviation (SD), min, max] were calculated for every variable (three diameters). The data obtained from the left optic nerve and from the right nerve were compared. The correlation analysis was performed with the following variables: gender, age group (group I: 18-30y, n=67; group II: 30-65y, n =134; group III: >65y, n =99), and ethnic background. The data were statistically evaluated by three-dimensional analysis of variance, SPSS, standard version 17.0 (Chicago, IL, USA, 2007), and χ^2 criterion using 95% confidence interval. The level of significance for all analyses was set at P<0.05.

RESULTS

In our cohort, there were 167 females and 133 males, age range was from 18 to 93y (mean 47y). Altogether, 600 optic nerves were measured. For the TEM calculation, two measurements were obtained from each location of each nerve (n=1200 measurements for each of three locations). The difference between the first and second measurements were then determined and the relative TEM (expressed in %) was calculated to be 3.46 that was evaluated as acceptable. For inter-evaluator TEM, it varied from 3.18 to 3.49 for different locations (acceptable).

Table 1 Optic nerve sheath diameters measured by CT $\bar{x} \pm s$

Distance	Right ONSD	Max	Min	Left ONSD	Max	Min
Distal (A)	4.94±1.51	7.5	3.5	5.17±1.34	7.9	3.8
Middle (B)	4.35±0.76	5.8	3.3	4.45±0.62	5.9	3.3
Proximal (C)	3.55±0.82	5.5	2.7	3.65±0.70	4.8	2.9

A: 3 mm behind the globe; B: 8 mm behind the globe; C: 3 mm before entering the anterior opening of the optic canal.

The ethnic background of the patients was as follows: 1) Jews, half-Jews, and quarter-Jews of European, American, and Australian origin-59; 2) Jews, half-Jews, and quarter-Jews of Middle or Near Eastern, and Central Asian origin-58; 3) Jews, half-Jews, and quarter-Jews of Northern African origin-55; 4) Various European and American nationalities-66; 5) Palestinian Arabs-29; 6) Ethiopians and other African nationalities-21; 7) Other (India, Korea, China)-12.

Table 1 presents the results of the measurements. We did not find statistically significant differences correlated with gender of the patients (P=0.15), or their age (I *vs* II, P=0.25; I *vs* III, P=0.09; II *vs* III, P=0.36). In our cases, the right optic nerve was slightly smaller than the left one but this difference is also statistically insignificant (P=0.19). Finally, we did not find statistically significant differences of the ONSD sizes among the nationalities we dealt with in pair-wise comparisons, for example, ethnic group 1 *vs* ethnic group 2, P=0.40; ethnic group 1 *vs* ethnic group 4, P=0.28; ethnic group 2 *vs* ethnic group 4, P=0.33; *etc*. Figure 2 shows the measurement of the ONSD at its distal location, 3 mm behind the globe.

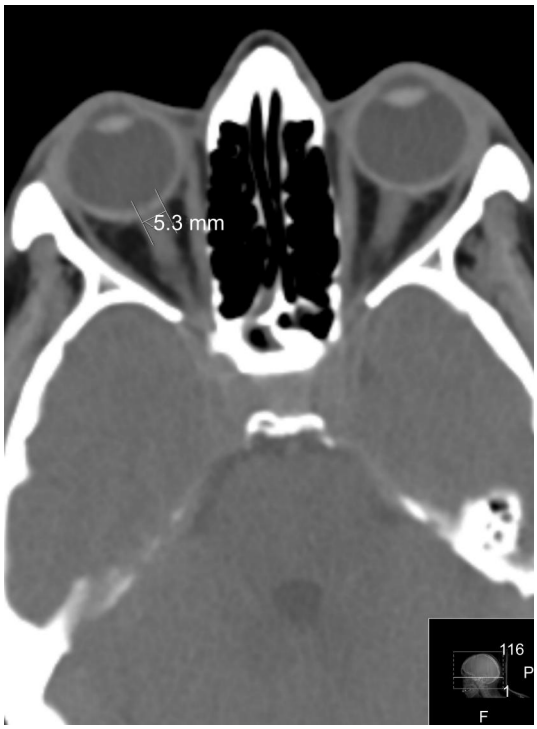

Figure 2 The measurement of the ONSD at its distal location, 3 mm behind the globe.

DISCUSSION

Analyzing the main body of the data obtained, we think the 3 mm distance from the globe is not the ideal location to measure ONSD for the sake of intracranial pressure monitoring. In 1984, when the ONSD method did not yet come to practice, it was found that the sheath is normally found to be loose near the eyeball, with a much bigger space between the optic nerve and the sheath than anywhere else in its course, consequently presenting bulbous appearance just behind the eyeball [16]. This fact is confirmed up-to-date [17]. Further histologic studies revealed a segment of the optic nerve in which maximal diameter fluctuations could be expected, namely the bulging dura mater region approximately 3 mm behind the papilla [5]. This position was recommended for the ONSD measurements for intracranial pressure monitoring and many researches used it [4-7,18]. All of the above said is correct but in our view this is rather disadvantage than advantage when we apply ONSD for intracranial pressure monitoring.

The dura mater is loose not without a purpose. The eyeball moves. Actually it moves constantly because in addition to human voluntary eye movements there are several involuntary movements (not necessarily nystagmus) such as constant physiological tremor at about 30-80 Hz, slow drifts, and flicking movements. These movements combined with voluntary and involuntary fixations, tracking movements, smooth pursuits, saccades, and some reflex movements do not give the eye even a second for a stand still[19,20]. While the optic nerve is much more elastic than dura mater, there should be a space between them closer to the globe because the optic nerve's head moves with the eye. Whatever method is used for the ONSD measurement-CT, MRI, or ultrasound-we take images from a constantly moving object even when a patient is given instruction to look straight forward, even when the eyes are closed, and even when the test is performed in a dark room. While we still lack the quantitative estimate of how the movements of the eyeball change shape and size of the bulging dura mater, we cannot recommend measuring the ONSD close to the globe.

Secondly, the enlargement of ONSD behind the globe at the position recommended for the ONSD measurements in cases of raised intracranial pressure was found also in papilledema, optic nerve lesions, optic atrophy, and endocrine orbitopathy[21,22].

Referring again to the Table 1, we can observe that SD of the mean ONSD, minimal, and maximal variations of the ONSD are the highest at 3 mm position while at 8 mm position they are the lowest. Variations of the proximal part of the ONSD that is close to the anterior opening of the optic canal are also less significant if compared with the distal 3 mm position but this location has its own disadvantage. Inside the optic canal, dura mater acts as the periosteum of the sphenoid bone and is firmly attached to the walls of the optic canal. If the canal itself and especially if its anterior opening is wide or narrow, the ONSD measurement could provide false positive or false negative results in some cases. The most stable results were obtained from the middle third of the intraorbital optic nerve path.

The most intriguing finding of our research is the lack of statistically significant differences of the ONSD between different age groups. We did not expect significant differences between the sexes in this matter but speaking of age changes, there are some data indicating that the optic nerves experience the age-dependent nerve fiber loss [7,23,24]. The question is not completely clear because the opposite opinion also exists [25]. However, even if this age-dependent loss of optic nerve axons occurs, there are at least two opposite processes that might lead to an increase of the ONSD. In theory, they can compensate its possible diminishing because of the axon loss. First, it was shown that while total axon count in the optic nerve decreases with age, mean axon diameter increases with age [25]. Second, the thickness of dura mater increases with age [26,27]. While all these processes take place at the same time, we might assume that the ONSD remains approximately the same during a lifetime.

In order to meet all the requirements of the Ethical Committee, we examined the CT images of the patients admitted to the Emergency Department because of various medical conditions that proved to be healthy in respect to their ophthalmological and neuro-ophthalmological anatomy. MRI has a much better spatial resolution on the optic nerve but it was very hard to obtain a sufficient number of MRI images of healthy persons.

Limitations of the Research We see the limitation of this research in view of possible differences in the eyeball and the optic nerve dimensions between ethnic groups. While in our series we did not find any significant differences in these dimensions among patients with various ethnic backgrounds that were hospitalized at our clinic, we cannot suggest generalization in this matter. The recent Chinese research suggests, for example, that Asian eyes had smaller anterior segments compared to Caucasian eyes [28]. We cannot completely rule out similar variations for the size of the optic nerve and additional research might clarify the picture.

In healthy persons, the ONSD varies from 5.17±1.34 mm to 3.55±0.82 mm in different locations within the intraorbital space with no significant difference between sexes and age groups. The most stable results with lesser SD can be obtained if the diameter is measured 8-10 mm from the globe. These data might be useful in ophthalmological and neurological practice. Specifically, we suggest to use this location when the ONSD is measured for the purpose of intracranial pressure monitoring.

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Conflicts of Interest: Vaiman M, None; **Abuita R,** None; **Bekerman I,** None.

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