Original paper

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Transorbital Sonography in the Evaluation of the Optic Nerve and Optic Nerve Sheath Diameter Considering Specific Demographic Features

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Abstract - Transorbital sonography is a reliable method for non-invasive assessment of optic nerve diameter (OND) and optic nerve sheath diameter (ONSD) in patients with increased intracranial pressure. A wide range of regular ONSD values has been reported in the literature. The aim of this study was to determine normal values for OND and ONSD, to determine differences between OND and ONSD considering sex, age, and body mass index (BMI), and to evaluate inter - and intra - examiner variability. The study included 100 healthy subjects, aged 22 - 87 years, who underwent transbulbar sonography by the two examiners, each examiner measuring OND and ONSD twice on both eyes at a depth of 3 mm behind the optic nerve papilla. Measurement and analysis of OND and ONSD was possible in all subjects. Mean OND was 2.39 +/- 0.28 mm and mean ONSD was 4.48 +/- 0.76 mm. In males, mean OND was 2.47 +/- 0.28 mm and in females 2.35 +/- 0.27 mm ($p = 0.042$). There was no statistically significant difference between mean ONSD values between sexes ($p > 0.001$). Correlation between age and mean OND and ONSD wasn`t observed. Positive correlation between mean OND and BMI ($p = 0.001$) was observed. Positive correlation within and between investigator measurements ($p < 0.01$) was shown. Men have a wider OND compared to women, but no difference in ONSD was observed. Age doesn`t effect on the width of OND and ONSD. BMI correlates positively with OND, but not with ONSD. Positive correlation within and between investigator measurements was shown.

Key words: sociodemographic factors; optic nerve; diameter; ultrasonography

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Introduction

Transorbital sonography is a reliable and non-invasive method for assessing optic nerve diameter (OND) and optic nerve sheath diameter (ONSD) in patients with elevated intracranial pressure (ICP) [1,2]. Elevated ICP is a common finding in patients with stroke, traumatic brain injury, meningoencephalitis, but, also in patients with non-neurologic emergencies, such as liver failure and post-resuscitation syndrome [3-5]. In addition, decreased levels of ONSD have been noted in patients with intracranial hypotension [6]. In general, elevated ICP is associated with high mortality, morbidity, and poor neurological outcomes. Therefore, early detection and treatment of elevated ICP is important, but often challenging because invasive ICP monitoring is often not routinely performed [7]. Magnetic resonance imaging

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(MRI) and transcranial doppler, as non-invasive methods, can provide the necessary information but are often impractical or impossible to implement in critically ill patients. The optic nerve is a part of the central nervous system surrounded by a subarachnoid space that is subject to the same pressure variations as the intracranial compartment of the subarachnoid space. The intraorbital portion of the sheath, particularly the retrobulbar segment, can expand with increased ICP due to communication between the dural sheath surrounding the optic nerve and the subarachnoid space [8,9]. Evaluation of ONSD with transbulbar sonography and MRI is a useful non-invasive evaluation of patients with elevated ICP, with cut-off values ranging from 5.7 +/- 0.5 mm to 5.9 mm +/- 0.5 mm, which has been assessed mainly in traumatic brain injury, infection, post-resuscitation syndrome, stroke, and other neurologic emergencies, also in brain death [10,11]. In some studies, ultrasound ONSD measurement showed high intra- and inter-observer reliability and high correlation between ultrasound and MRI assessment [12-14]. However, a relatively wide range of normal ONSD values has been observed in the literature, from 2.65 mm to 7.7 mm, with a mean ONSD of 5.95 mm reported as the cut-off value for elevated ICP above 20 mmHg [14,15,17]. Therefore, it is important to establish standards for OND and ONSD for the ultrasound laboratory so it can be applied in patients with elevated ICP.

The aim of this study was to investigate the relationships between OND and ONSD and certain demographic characteristics, such as sex, age, and BMI, and also to establish standards for these variables and to evaluate inter- and intra-observer variability.

Subjects and Methods

Study population

From January 1st to December 31st 2018, 100 volunteers aged 22 to 87 years were enrolled in the study population. The study population consisted of department staff and patients with cervical spine or low back pain, all without intracranial or ophthalmic pathology.

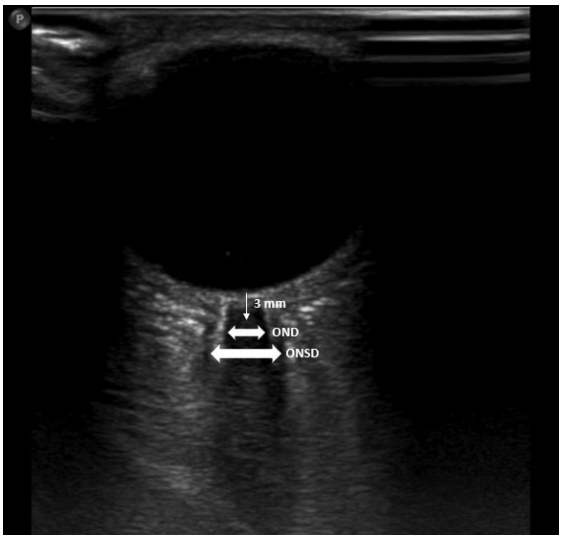

Figure 1. Measurement of optic nerve diameter (OND) and optic nerve sheath diameter (ONSD)

The study was approved by the Ethics Committee of the UHC Sestre milosrdnice and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki. All participants signed the informed consent before entering the study. Demographic data were collected.

Transorbital sonography

Ocular sonography was performed with a 12-MHz linear ultrasound probe (Terason T3000, Teratech Corporation, USA). OND and ONSD were measured by two trained investigators who examined both eyes of all subjects independently within 15 minutes without knowing each other's study results. Subjects were examined in the supine position with the chin slightly elevated. The probe was adjusted to provide a suitable angle for visualizing the entrance of the optic nerve into the eyeball. The anterior portion of the optic nerve was imaged in an axial plane showing the optic disc and optic nerve longitudinally. OND and ONSD were assessed at a depth of 3 mm posterior to the optic disc (Figure 1). Each bulb was examined twice by each investigator and the mean value of OND and ONSD was calculated.

Statistical analyses

Values are expressed as means and standard deviations (SD). Descriptive statistics was performed for

mean OND and mean ONSD for sex, age, and BMI. Linear regression analysis was performed to determine associations between sex, age, BMI, OND and ONSD. A two-tailed probability of $p < 0.05$ was used as the significance level. The maximum and minimum values of the OND and ONSD measures and the reference values for men and women were determined at a 95 % significance level. Correlation analysis was also performed using Pearson's correlation coefficient (r) to quantify the strength of agreement. All statistical analyses were performed using SPSS for Windows software.

Results

A total of 100 healthy volunteers between the ages of 22 and 87 were enrolled in the study. Thirty-nine were male (39 %) and sixty-one were female (61 %). All demographic and descriptive data are shown in Table 1, Figure 2, and Figure 3. ONSD and OND assessment was possible in all subjects. Signs of papilledema were not found. The mean OND, measured 3 mm posterior to the entrance of the nerve into the bulb, was 2.39 mm, SD 0.28 mm, and the mean ONSD at the same location was 4.48 mm, SD 0.76 mm. The overall mean values for OND, ONSD and SD in the general population, males and female are shown in Table 2. T-test for independent samples revealed a statistically significant difference between OND values in men and women ($p = 0.42$), but no statistically significant difference was found between ONSD values in men and women. Analysis of variance revealed no statistically significant correlations between the age of the subjects and the values of OND and ONSD ($p > 0.001$), as it`s shown in Table 3. A statistically significant difference ($p = 0.001$) was found for OND values considering BMI; study shown positive correlation between these two measures (Figure 4.), but not for ONSD values. The Pearson's coefficient showed a positive correlation within and between the examiners' measurements ($p < 0.01$) (Tables 4 and 5).

Table 1. Participant`s demographic data

		N	%
Sex	Male	39	39.0
	Female	61	61.0
	Total	100	100.0
Age	< 35 years	41	41.0
	36 – 70 years	45	45.0
	> 70 years	14	14.0
	Total	100	100.0
Body mass index (BMI)	< 18.5	3	3.0
	18,5 – 25	57	57.0
	25 – 30	28	28.0
	> 30	12	12.0
	Total	100	100.0

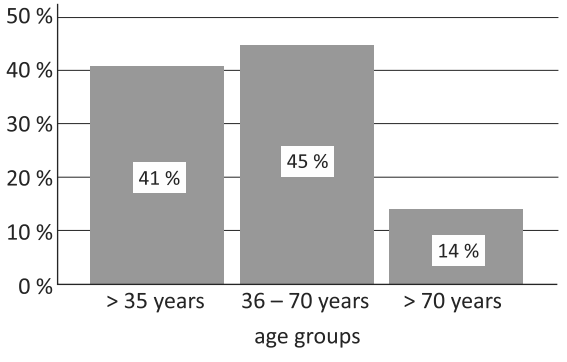

Figure 2. Participant`s age groups

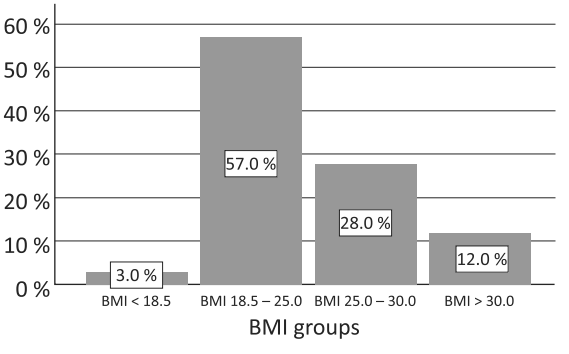

Figure 3. Participant`s body mass index (BMI) groups

Table 2. Mean values of optic nerve diameter (OND), optic nerve sheath diameter (ONSD) and standard deviation (SD) (total, for males and females)

	OND (mean + / - SD) mm	ONSD (mean + / -SD) mm
Total	2.39 + / - 0.28	4.48 + / - 0.75
Male	2.47 + / - 0.28**	4.57 + / - 0.89
Female	2.35 + / - 0.27**	4.42 + / - 0.66

** Statistically significant difference between mean OND values between sexes ($p = 0.042$)

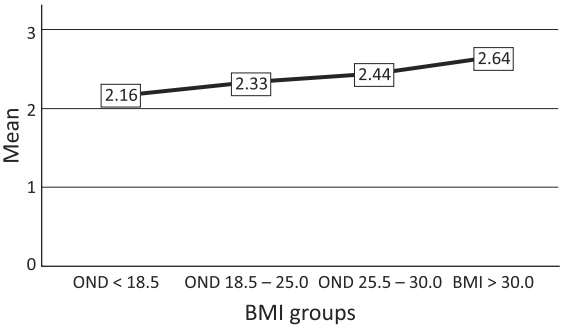

Figure 4. Linear increase in optic nerve diameter (OND) values with respect to body mass index (BMI) ($p < 0.01$)

Table 3. ANOVA for different age groups

		Sum of Squares	Degree of freedom	Mean Square	F value	Significance
Optic nerve diameter (OND)	Between Groups	0.161	2	0.080	1.018	0.365
	Within Groups	7.667	97	0.079		
	Total	7.828	99			
Optic nerve sheath Diameter (ONSD)	Between Groups	1.164	2	0.582	1.014	0.367
	Within Groups	55.662	97	0.574		
	Total	56.826	99			

Table 4. Pearson's correlation coefficient (r) for optic nerve diameter (OND) measures within and between examiners

	OND 1	OND 2	OND 3	OND 4
OND 1	1	0.854**	0.671**	0.638**
OND 2	0.854**	1	0.646**	0.618**
OND 3	0.671**	0.646**	1	0.865**
OND 4	0.638**	0.618**	0.865**	1

** Positive correlation within and between examiners for OND measures ($p < 0.01$)

Table 5. Pearson`s correlation coefficient (r) for optic nerve sheath diameter (ONSD) measures within and between examiners

	ONSD1	ONSD2	ONSD3	ONSD4
ONSD1	1	0.838**	0.141	0.697**
ONSD2	0.838**	1	0.076	0.691**
ONSD3	0.141	0.076	1	0.121
ONSD4	0.697**	0.691**	0.121	1

** Positive correlation within and between examiners for ONSD measures ($p < 0.01$)

Discussion

Our study, conducted on 100 healthy volunteers, provides the mean values for OND and ONSD. Previous results determined only values for ONSD in increased intracranial pressure, while OND didn't changed [18-21]. The mean values [95 % confidence interval (CI)] for OND and SD were 2.39 +/- 0.28 mm and for ONSD and SD were 4.48 +/- 0.75 mm. The mean values for ONSD obtained in our study are slightly lower than the results of studies by Bauerle (5.4 +/- 0.6 mm) and Lochner (5.95 +/- 0.68 mm) [14,17]. Results by Wang showed lower mean values for ONSD (3.46 +/- 0.28 mm), who emphasized the need for possible consideration of racial and ethnic characteristics when using ultrasonographic criteria to determine ONSD [16]. According to the previous studies, mean values of ONSD in patients with intracranial hypotension were from 2.96 +/- 0.15 mm [22] to 3.2 +/- 0.3 mm [23].

Mean values for OND, ONSD and demographic characteristics such as sex, age, and BMI were analysed. We didn't find correlation of OND or ONSD with age. However, linear regression analyses revealed that OND correlates with sex and body mass index; males have a wider OND and people with a higher BMI had also wider OND. When searching the literature, we haven`t found any studies that analysed OND values, for example; previously mentioned study by Wang and associates evaluated only ONSD in their study population [16]. Therefore, the cut-off values of OND and ONSD for each sex should be assessed for each neurosonologic laboratory. Further analysis and studies should be conducted to confirm our findings in a larger number of respondents. In our study, no correlation was found between ONSD and sex and BMI, as, for example, in a study of the Chinese population, in which sex and BMI were independently associated with ONSD, with underweight women having the smallest ONSD [16]. However, our results may be explained by the small proportion of the study population with a BMI < 18.5 (only 3 respondents) and a BMI < 30 (12 respondents), so a possible association cannot be completely excluded. However, the correlation between ONSD and BMI should be interpreted cautiously because obese individuals are prone to idiopathic intracranial hypertension, which may be in an asymptomatic phase during the conduct of the study [24]. Analysis of variance revealed no statistically significant correlations between age of the study population and OND and ONSD. Steinborn and associates showed that the mean ONSD in children (after 5 years) and young adolescents was 5.75 +/- 0.52 mm for transbulbar sonography and 5.69 +/- 0.31 for MRI [15]. This can be explained by the fact that after the completion of myelination of the optic nerve, there are no further significant change in the size of the nerve and nerve sheath in the healthy population [25].

Our study showed that the inter-observer and intra-observer correlation was positive and moderate, which is consistent with other studies previously performed by Bauerle and Lochner [14,17]. The data from tables 4 and 5 show that intra-observer and inter-observer agreement was higher for measure OND than for ONSD, which can be explained by the technical difficulties in distinguishing optic nerve sheath from surrounding tissue. Our results suggest that the boundary between the optic nerve and its sheath is easier to detect than the boundary between the optic nerve sheath and its surroundings. Overall, based on ours result and results from another studies, transorbital sonography is a useful tool in the assessment of OND and ONSD with moderate or high intra-observer and inter-observer reliability.

In conclusion, we would like to emphasize that the mean value of OND in a healthy population is 2.39 +/- 0.28 mm and the mean value of ONSD in a healthy population is 4.48 +/- 0.75 mm. According to our study, males have wider OND compared with females, whereas there is no difference in the width of ONSD between male and female sex. Moreover, there is no statistically significant correla-

tion between the age of the respondents and the values of OND and ONSD, but a positive correlation is observed between OND and BMI, while there is no correlation between ONSD and BMI. There is a positive correlation in the measurements between the examiners and between the individual measurements of the examiners.

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Conflict of interest

None to declare.

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