Erciyes Med J 2021; 43(6): 554–9 • DOI: 10.14744/etd.2021.43809
ORIGINAL ARTICLE – OPEN ACCESS

Diagnostic and Clinical Predictive Value of Optic Nerve Sheath Diameter Measurement in Children with Increased Intracranial Pressure

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ABSTRACT

Objective: In this study, we aimed to determine the diagnostic and clinical predictive value of optic nerve sheath diameter (ONSD) measurement in pediatric patients suspected of increased intracranial pressure (IICP) by comparing sonographic ONSD values with radiological parameters and controls.

Materials and Methods: In total, 57 pediatric patients with suspected IICP who underwent computed tomography (CT) scans were included in this prospective, observational study; meanwhile, 35 patients were included as controls. Measurements were obtained while the patients were in supine position with their eyes closed, and transbulbar images of both eyes were obtained via a 6–15 MHz linear probe. The CT scans were assessed by a radiologist blinded to sonographic measurements. Glasgow coma scale of patients, service where they were followed, clinical results, CT, and ONSD values were assessed in this study.

Results: In the patient group, 26 of the patients were girls (35.4%), and the mean age was 138±56 months (min-max: 82–194 months). Meanwhile, in the control group, 18 of the patients were girls (40.9%), and mean age was 151±45 months (min-max: 106–196 months). As per our findings, 31 patients (54.4%) presented with high-energy trauma. Mean ONSD was 0.5±0.07 cm in the patient group, whereas it was 0.3±0.02 cm in the control group (p=0.008). It was 0.55±0.07 cm in patients with cerebral edema (CE) on CT scan (p=0.013). Based on the presence of CE as detected via CT scan, cut-off value for measurement was determined to be 0.49 cm, with 83.33% sensitivity and 68.42% specificity (AUC: 0.784).

Conclusion: Optic nerve sheath measurement can be utilized to immediately support diagnosis and predict follow-up in the assessment of pediatric patients with ICP elevation.

Keywords: Optic nerve sheath measurement, increased intracranial pressure, cerebral edema

Cite this article as: Tolu Kendir Ö, Yılmaz HL, Ballı HT, Sarı Gökay S, Ünal İ, Özkaya AK. Diagnostic and Clinical Predictive Value of Optic Nerve Sheath Diameter Measurement in Children with Increased Intracranial Pressure. Erciyes Med J 2021; 43(6): 554-9.

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Submitted 30.09.2020

Accepted 19.03.2021

Available Online 28.09.2021

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INTRODUCTION

Increased intracranial pressure (IICP) has been described as a clinical entity associated with head trauma, mass, hemorrhage, and infection, which, in turn, can result in high morbidity and mortality (1, 2). The early diagnosis and timely treatment within acute period is deemed life-saving (3–5). Although neuroimaging modalities such as CT scan are preferred to support diagnosis in emergency departments, this method has some disadvantages such as ionizing radiation exposure and challenges in transport during critical time period. In the literature, invasive intracranial monitorization (IIM) has been suggested as the gold standard. However, adverse events such as hemorrhage, infection, and difficulties in feasibility in emergency practice have also been emphasized (4, 6). Lumbar puncture, which is another invasive technique, has also been used for diagnostic purposes in emergency department (4–9). Although fundoscopy has been used in routine practice, it has limited benefit in emergency management as papillae edema, which is a late finding in IICP (10–12). In previous studies, it was suggested that ONSD is consistent with IIM, which is the gold standard in the diagnosis of IICP (1, 2, 7, 10, 13).

The optic nerve is encased in three meninges; cerebrospinal fluid circulates in the intracranial and intra-orbital subarachnoid space, and intracranial pressure is simultaneously reflected to intra-orbital subarachnoid space when intracranial pressure (ICP) is increased, resulting in enlarged ONSD. This enlargement is best seen at 3 mm posterior to the globe of the eye (4, 5). In recent years, sonographic ONSD measurement has been introduced into clinical practice in both pediatric and adult patients, which is identified as a non-invasive, reproducible, easily applicable, inexpensive, sedation-free, operator-dependent method requiring experience (3–5, 7–14).

In this study, we aimed to determine the diagnostic and clinical predictive value of ONSD measurement in pediatric patients with suspected IICP according to symptoms and signs, comparing sonographic ONSD values with radiological parameters and healthy children.

MATERIALS and METHODS

This study included pediatric patients (aged 2–18 years) who presented to pediatric emergency department of Çukurova University, Medicine School, between June 2015 and August 2016 and underwent cranial imaging studies with suspected IICP. It was planned as a single-center, prospective, observational study. This study was approved by the Ethics Committee of Çukurova University (2015/44).

After initial assessment and acute vital interventions, optic nerve sheath diameter was measured by Sonosite Edge Ultrasound System (Sonosite Inc., Botwell, WA) using 6–15 MHz linear probe before cranial imaging. Informed consent was obtained from parents before sonography. Ocular sonography was performed by a pediatric emergency specialist who had sonography certificate and experience in pediatric sonography and blinded to CT. The patients with ocular anatomic defect, trauma, foreign body, optic glioma, retinoblastoma, or intracranial shunt were excluded from analysis. The hypo-echoic, double-sided, real-time, frozen images of optic nerve were obtained over the eyelid in the patient at neutral supine position with closed eyes. The measurement was made at 3 mm posterior to the globe of the eyes where enlargement is observed to be most prominent (8, 10, 14, 15). Overall, four measurements were performed from transverse and longitudinal images obtained over two eyelids, and the mean value was then calculated (Fig. 1). The cranial imaging was assessed with regard to the presence and severity of cerebral edema based on sulci effacement, collapse of ventricles, cisternal compression and shift by a radiologist blinded to sonographic measurements (9, 16). The demographic data, management setting, and duration of sonography were recorded in all patients. The patients were treated based on clinical, laboratory, and radiological data regardless of ONSD measurements. A group of children without suspected IICP who presented with several causes were employed as the control group, and ONSD measurements were performed using the same technique. The duration of the procedure was also recorded in both patient and control groups.

Statistical Analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and minimum-maximum where appropriate. Chi-square and Fisher's exact test were used to compare categorical variables between the groups. The normality of distribution for continuous variables was confirmed visually with histogram and probability plots and analytically with Shapiro-Wilk test. To compare the continuous variables between two groups, the Student's t-test was used. For comparison of more than two groups, one-way ANOVA was used. The "Levene's test" was applied to determine which groups are different from others. Regarding the homogeneity of variances, Bonferroni or Tamhane tests were used for multiple comparisons of groups. To evaluate the correlations between measurements, Pearson correlation coefficient was used. A receiver operator characteristic (ROC) curve analysis was performed in order to identify the optimal cut-off point of ONSD value. The mean values of the patients' right transverse, right sagittal, left transverse, and left sagittal measurements were examined under the ONSD value. Sensitivity and specificity values were calculated based on the ONSD values of the patients in terms of the presence of CT variable. All analyses were performed using IBM SPSS Statistics version 20.0 statistical software package. The statistical level of significance for all tests was considered to be 0.05.

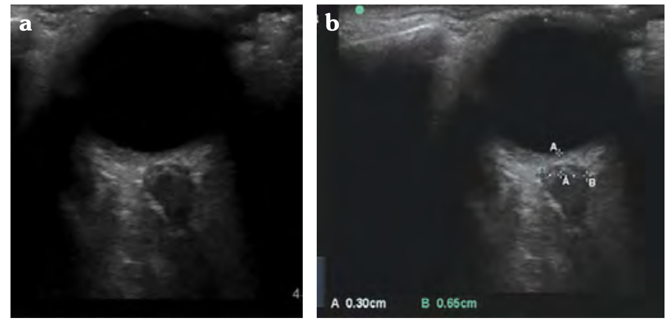

Figure 1. Images of optic nerve sheath diameter of the patients from this study

Table 1. Comparison of optic nerve sheath diameter (ONSD) and duration of procedure between patient and control groups

	n	ONSD (cm) Meana SD	p	Duration (min)	p
Patients	57	0.5±0.07	0.008	2.57±1.7	0.017
Controls	35	0.39±0.02		1.1±0.35	

SD: Standard deviation; ONSD: Optic nerve sheath diameter

Table 2. Comparison of brain edema with optic nerve sheath diameter (ONSD) values and duration of procedure

	CT n (%)	ONSD (cm) Mean±SD	p	Duration Mean±SD	p
No cerebral edema	38 (66.7%)	0.48±0.05	0.013	2.8±1	0.001
Cerebral edema	19 (33.3%)	0.55±0.07		2±1	

CT: Computed tomography; SD: Standard deviation; ONSD: Optic nerve sheath diameter

RESULTS

During the study period, 64 pediatric patients, who were suspected to have IICP and fulfilled the study criteria, presented to pediatric emergency department at the time period when a pediatric emergency specialist was present. Overall, 57 pediatric patients were included in this study (excluded were 2 patients due to noncompliance to sonographic measurements and 5 patients whom parents declined to give consent). In addition, 35 pediatric patients without suspected IICP were employed as controls. In the patient group, 26 were girls (35.4%), and mean age was 138±56 months (min–max: 82–194 months); meanwhile, in the control group, 18 were girls (40.9%), and mean age was 151±45 months (min-max: 106–196 months) (p>0.05). As per our findings, 31 patients (54.4%) presented with high-energy trauma, while the remaining patients presented with headache and/or nausea, vomiting, and altered mental status. Hematopoietic malignancy was noted in two patients, metabolic disorder in two patients, and neurological diseases in another two patients; in the remaining patients, no known disorder was observed. Table 1

Table 3. Comparison of GCS, CT scan, and ONSD values according to treatment setting

	Follow-up				
	Emergency department and clinic of pediatrics (n=40) (%) (ONSD-cm/description)	Intensive care unit (n=16) (%) (ONSD-cm/description)	Non-survivor (n=1) (%)	Total	p
GCS					
≤8	2 (5.0) (0.52–0.50)	5 (31.3)	1 (100.0)	8 (14.0)	
9–14	11 (27.5)	9 (56.3)	0 (0.0)	20 (35.1)	**0.001**
15	27 (67.5)	2 (12.5)	0 (0.0)	29 (50.9)	
Cerebral CT scan					
No cerebral edema	31 (77.5)	7 (43.8)	0 (0.0)	38 (66.87)	
Mild cerebral edema	8 (20.0)	6 (37.5)	0 (0.0)	14 (24.6)	**0.012**
Moderate-to-severe cerebral edema	1 (2.5) (transfered to another hospital)	3 (18.8) (0.55–0.50–0.73 and mean: 0.59)	1 (100.0)	5 (8.8)	
Mean ONSD (cm)±SD	0.49±0.06	0.54±0.07	0.56±0.0	0.50±0.07	0.000

SD: Standard deviation; CT: Computed tomography; ONSD: Optic nerve sheath diameter; GCS: Glasgow coma scale

presents the comparison of ONSD and procedure duration between patients with suspected IICP and controls.

Anti-edematous treatment was given to 28 patients with Glasgow coma scale (GCS) score ≤14 (GCS was ≤8 in 8 of the patients) at initial evaluation in pediatric emergency department. Two patients underwent surgical intervention in the neurosurgery department, while the remaining patients were treated with conservative approach. Table 2 presents relationships between presence of cerebral edema, ONSD values, and duration of procedure.

One patient was observed with pupillary anisocoria and negative pupil reflexes at presentation. The patient presented with out-of-vehicle traffic accident and died in the pediatric emergency department. Of the patients, 16 patients were treated at pediatric or neurosurgery intensive care unit, while the remaining patients were treated in the pediatric emergency department and pediatrics clinic. All patients were discharged after recovery. Table 3 presents the GCS score, CT scan results, and ONSD values according to treatment setting.

There was severe cerebral edema on the CT scan in the patient with fatal outcome. The OSND was noted to be larger in the patient (ONSD: 0.56 cm) when compared to those at the intensive care unit (ICU) setting. One patient with GCS score=7 and moderate-to-severe cerebral edema (CE) on CT scan in pediatric emergency department was transferred to another hospital (ONSD: 0.52 cm). In addition, there was no cerebral edema on CT scan in another patient with GCS score=8, and the patient was treated for drug intoxication (ONSD: 0.50 cm).

Of the five patients treated at the intensive care unit with GCS score ≤8, moderate and severe cerebral edema was detected in three patients, and their mean ONSD was 0.59 cm, whereas it was 0.52 cm in the two remaining patients. No cerebral edema was detected on CT scan of the two patients (GCS score: 15) who were initially admitted to the pediatrics clinic with diagnosis of meningitis

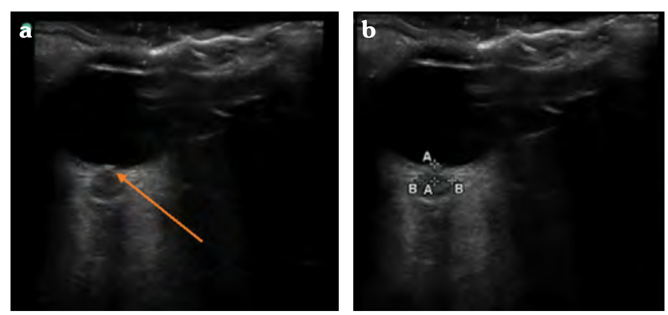

Figure 2. **Optic disc elevations of the patients**

and transferred to intensive care unit thereafter; however, ONSD was 0.50 cm in these patients. The mean ONSD value of those who were followed up in the intensive care unit was statistically significantly higher than those observed in the emergency observation-service.

Mean ONSD was noted to be higher in patients treated at intensive care unit when compared to those treated at pediatric emergency department or pediatrics clinic (p=0.03).

There was optic disc elevation (ODE) compatible with mild-moderate-severe CE on CT scan in three patients treated at ICU settings. Mean ONSD was 0.55, 0.50, and 0.73 cm in these patients, respectively. Some examples taken from the patients are presented on Figure 2.

A moderate, positive correlation was detected between ONSD and cerebral edema as detected via CT scan (r=0.45), while a moderate negative correlation between ONSD and GCS score was noted (r=0.32).

Based on cerebral edema as detected by CT scan, the cut-off value for mean ONSD values was determined to be 0.49 cm, with sensitivity of 83.33% (95% CI: 58.6–96.4) and specificity of 68.42%

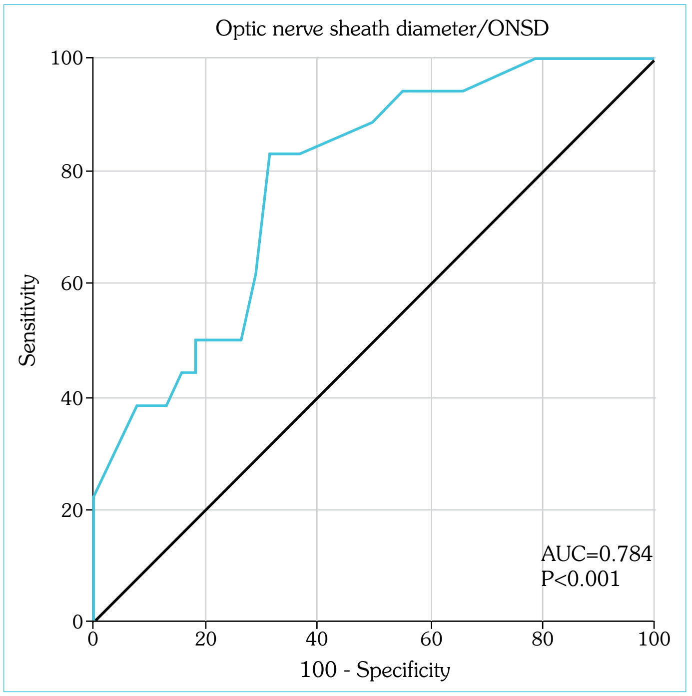

Figure 3. ROC analysis

Table 4. The results of ROC curve analysis for ONSD value and the diagnostic accuracy values of ONSD at the optimal cut-off value (0.49) defined in this study

Parameters	Values
AUC [95% Cl (%)]	0.784 (0.653–0.882)
Cut-off	>0.49
Sensitivity [%) (95% Cl (%)]	83.33 (58.6–96.4)
Specificity [95% Cl (%)]	68.42 (51.3–82.5)
PPV [95% Cl (%)]	55.6 (42.8–67.6)
NPV [95% Cl (%)]	89.7 (75.1–96.1)
+LR [95% Cl (%)]	2.64 (1.6–4.4)
-LR [95% Cl (%)]	0.24 (0.08–0.7)
p	<0.001

ROC: Receiver operator characteristic; ONSD: Optic nerve sheath diameter; AUC: Area under curve; CI: confidence interval; PPV: Positive predictive value; NPV: Negative predictive value; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio

(95% CI: 51.3–82.5) and AUC of 0.784 (95% CI: 0.653–0.882) (Fig. 3). The efficiency of ONSD value in distinguishing the presence of CT was found to be statistically significant (p<0.001). Also, statistical results were summarized in Table 4.

DISCUSSION

Increased ICP can have a fatal course if not diagnosed and treated early, and it can be difficult to arrive at a diagnosis without typical symptoms and findings in children. As per our findings, it was determined that ONSD measurement contributes to the diagnosis of IICP as soon as possible, thus reducing the ionizing radiation exposure in developing children and predicting the treatment course.

In the literature, it was shown that the intra-orbital subarachnoid space surrounding the optic nerve and intracranial subarachnoid space have identical pressures in cadaver studies. It was reported that intracranial pressure was simultaneously reflected to intra-orbital subarachnoid space when cerebral edema was developed and resulted in enlargement of the optic nerve sheath. This can be observed as hypo-echoic behind the globe of the eye on sonography (4, 6, 7). The finding that ONSD was higher in our cases predicted to have CE based on the cause of presentation and clinical findings when compared to controls supports the concept that acute alterations are reflected to optic nerve sheath diameter in exactly the same manner. The normal value for ONSD has been determined to be <0.4 cm in infants and <0.45 cm until adolescence. In this study, ONSD values in the control group were found to be consistent to literature (3, 13, 16).

At the early phases of cerebral edema, lacking prominent reduction in parenchymal density, sulci effacement, and other CE markers on CT scan have been associated to the presence of extra-axial space and compensation provided by this space. The immediate CT images can be inadequate at acute phase in patients with IICP. The diagnosis of cerebral edema via CT scan may be more difficult in pediatric patients as extra-axial space is greater in children compared to adults (17, 18).

In our study, which consists of patients who all have CE prediction with their presentation of symptoms and findings, ONSD values of our patients were noted to be higher than that in the control group. Among these patients, the ONSD value of those detected by CT with CE was higher than the others. This situation suggests that ONSD may be enlarged without CT findings associated with the compensation provided by the extra-axial space. This finding indicates that cerebral edema can be detected by enlargement in the optic nerve sheath earlier than CT findings of cerebral edema.

In previous studies using the presence of cerebral edema on CT scan as reference, it was found that ONSD has good sensitivity despite limited specificity (cut-off, 0.45–0.55 cm; sensitivity, 80%–100%; specificity, 60%–85%) (4, 7, 15, 16, 18). In agreement with literature, cut-off value was determined to be 0.49 cm for ONSD according to CT findings in our study (sensitivity, 83.33%; specificity, 68.42%; AUC, 0.784). It was suggested that ONSD is reliable in studies based on the definition of ICP elevation as cerebrospinal fluid pressure >20 cmH_2O on lumbar puncture (10, 19–22).

In previous studies, it was emphasized that ONSD could be used in monitorization (15, 16). On the other hand, it has been stated in the literature that the initial ONSD value is correlated with hospital mortality in post-cardiac arrest cases and that ONSD value of survivors is lower than that in non-survivors (23). Similarly, it has been reported that these values are associated with mortality in patients with traumatic brain injury and hypoxic-ischemic encephalopathy and may be a method to support clinical and radiological indicators (24, 25). On the other hand, our results show that the ONSD enlargement of patients with suspected CE in pediatric emergency services is compatible with intensive care admissions and that it was also higher in patients with cerebral edema detected via CT scan compared to those without cerebral edema among patients treated in ICU settings. To the best of our knowledge, this is the first study comparing ONSD value at initial assessment with treatment setting.

The optic nerve sheath values of patients have low GCS score at initial evaluation and without cerebral edema indicators by CT scan were striking. A moderate correlation between ONSD values and GCS score, cerebral edema on CT scan, and need for ICU admission suggests that ONSD measurement can be a predictive factor in the decision-making process in pediatric patients.

In our study, ODE compatible with papillary stasis, a late finding for cerebral edema, was detected in three patients. In their series, Marchese et al. and Teismann et al. emphasized that ODE indicates severe cases (22, 26). In support of these case series, ONSD values were above the cut-off value in patients with ODE in our study, which were measured as 0.55, 0.50, and 0.73 cm, respectively. There were mild, moderate, and severe cerebral edema cases noted on CT scan, while GCS scores were 8, 6, and 7 in these patients, respectively. Our results demonstrate that optic nerve sheath was enlarged before detection of cerebral edema by radiological findings; that the extent of optic nerve sheath enlargement was greater in severe cases; and that ONSD measurement could be predictive.

CONCLUSION

Our study indicates that optic nerve sheath measurement can be used as a readily available method that can support immediate diagnosis and predict follow-up in the assessment of pediatric patients with ICP elevation.

Limitation

The major limitation of this study is its smaller number of patients admitted to the intensive care unit with moderate-to-severe cerebral edema as detected via CT scan.

Ethics Committee Approval: The Çukurova University Clinical Research Ethics Committee granted approval for this study (date: 03.07.2015, number: 2015/44).

Informed Consent: Written or verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – ÖTK, HLY, HTB, SSG, İÜ, AKO; Design – ÖTK, HLY, HTB, SSG, İÜ, AKO; Supervision – ÖTK, HLY, HTB, SSG, İÜ, AKO; Materials – ÖTK, HLY, HTB, SSG, AKO; Data Collection and/or Processing – ÖTK, HLY, HTB, SSG, AKO; Analysis and/or Interpretation – OTK, HLY, İÜ; Literature Search – ÖTK; Writing – ÖTK, HLY; Critical Reviews – ÖTK, HLY.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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