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Research article

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The value of the optic nerve sheath diameter measured using computerized brain tomography in the evaluation of mortality status in patients admitted to the emergency department with intracranial hemorrhage

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Ethics Committee Approval
Approval for the study was granted by the Katip Çelebi University Medical Faculty clinical research ethical committee (decision no: 675, date: May 12, 2020).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The optic nerve sheath diameter (ONSD) measurement is a non-invasive method that can be obtained from computerized tomography (CT) images. It can therefore be a useful diagnostic tool in determining prognosis in the emergency department. The aim of this study was to investigate the relationship between ONSD and mortality status in patients with intracranial hemorrhage who presented to the emergency department by measuring ONSD on computerized brain tomography images taken during admission.

Methods: This retrospective cohort study was carried out in the emergency department of a tertiary hospital between December 1, 2018 and December 1, 2020 and included intracranial hemorrhage patients and patients with normal brain CT scans that had been obtained for any reason. Bilateral ONSDs were measured in both the intracranial hemorrhage and control groups. We first evaluated whether ONSD would differ between the two groups after which the relationship between ONSD and mortality was analyzed in the patient group who presented with bleeding.

Results: Intracranial hemorrhage was present in half the cases and midline shift in 21.5%. A statistically significant increase in ONSD was observed in cases with intracranial hemorrhage ($P < 0.001$). Similarly, a statistically significant increase in ONSD was found in cases with midline shifts and mortality ($P < 0.001$). A cut-off value of 4.19 mm for mean optic nerve diameter exhibited 100% sensitivity and 70% specificity in terms of hemorrhage detection (area under the curve [AUC]: 0.952; $P < 0.001$). A cut-off value of 6.03 mm for ONSD exhibited 76% sensitivity and 74% specificity in terms of hemorrhage detection (AUC: 0.730; $P = 0.001$). The odds ratio for prediction of mortality based on a regression analysis was 8.838 in cases with intracranial hemorrhage ($P < 0.001$).

Conclusion: ONSSD measured on CT images is a promising tool for prediction of intracranial hemorrhage, midline shift, and mortality status.

Keywords: Intracranial hemorrhage, Optic nerve sheath diameter, Computerized tomography, Mortality

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Introduction

The optic nerve is part of the central nervous system (CNS) and is surrounded by cerebrospinal fluid (CSF) and the dura mater. Changes in the optic nerve sheath diameter (ONSD) parallel changes in CSF pressure. An ONSD measurement is reliable method for showing increased intracranial pressure (ICP) [1]. Identifying an increase in ICP is as vitally important for the patient as it is difficult. An Increase in ICP following intracranial hemorrhage causes an increase in the ONSD. To date, clinical studies have observed high correlation between ONSD and symptoms, bedside ocular ultrasonography (USG), and computerized tomography (CT) scans of brain abnormalities with all three reported of being capable of indicating an increase in intracranial pressure (ICP) [2].

Patients presenting to the emergency department with traumatic or non-traumatic causes and in whom intracranial hemorrhage is suspected are diagnosed using a CT scan of the brain. Although ONSD can be measured with ultrasonography (USG), this procedure is not appropriate in patients with orbital trauma, and the fact that measurements may vary depending on individual operator performance leads to a reduction in the reliability of the procedure. Considering that tomography is performed on the majority of patients with head trauma in particular, ONSD measurement based on tomography results may be an appropriate diagnostic method since it is non-invasive and can be measured on the CT images of the brain that are obtained without any additional procedure.

The purpose of this study was to evaluate the effects of ONSD that was measured using computerized brain tomography on mortality and morbidity in patients with intracranial hemorrhage who presented to the emergency department.

Materials and methods

Study design and setting

This retrospective, observational study was performed in the emergency department of the Katip Çelebi University Training and Research Hospital in Izmir, Turkey, between December 1, 2018 and December 1, 2020. Approval for the study was granted by the Katip Çelebi University Medical Faculty Clinical Research Ethics committee (decision no: 675, date: May 12, 2020).

Study population

This study included the patients with intracranial hemorrhage and those who presented to the emergency department for any reason and obtained normal brain CT scans.

Inclusion criteria

- Age 18 or over

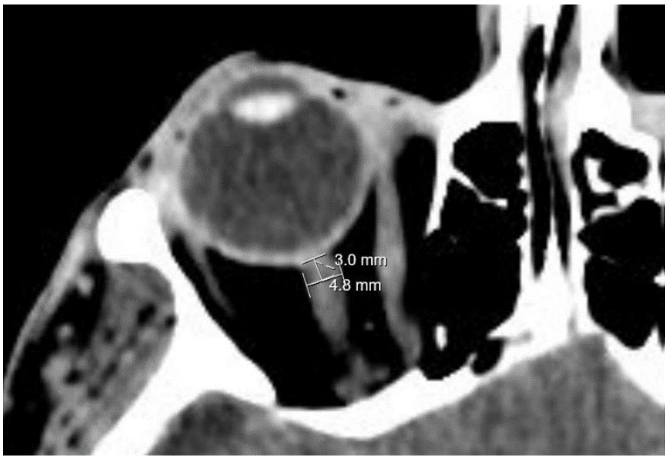
Exclusion criteria

- Age under 18
- Presence of glaucoma
- Presence of orbital trauma
- Presence of hydrocephaly
- Presence of intracranial space-occupying formations
- Diagnosis of intracranial hemorrhage
- Diagnosis of pseudotumor cerebri
- Presence of cerebral vein thrombosis

Study protocol and data collection

ONSD was measured by measuring transverse sections 3 mm distal to the point where the nerve exits from the globe (Figure 1) on the tomography images captured with a Toshiba Aquilion 64-Multislice system. All ONSD measurements were obtained separately for each eye with mean right and left eye diameters recorded for each patient. Statistical data were calculated using mean values. Patient information was retrieved by scanning electronic records in the hospital's data management system. Patient age, gender, chronic disease status, presence or absence of intracranial hemorrhage, history of trauma if applicable, hemorrhage site, and presence of midline shift were recorded by evaluating in-hospital mortality and morbidity records.

Figure 1: Optic nerve sheath diameter measurement from axial sections



Outcome measure

The primary outcome was the ONSD width.

Research sample

Vaiman et al. [3] examined the effectiveness of ONSD measurement for an evaluation of intracranial pressure in traumatic cerebral hemorrhage. Based on that study, a total sample size of 64 with 32 in each group was calculated using G-Power 3.1.9.2. software with mean and standard deviation values for the left ONSD that was measured 3 mm behind the globe. A study group consisting of 100 patients who developed intracranial hemorrhage for any reason and a control group of 100 patients who underwent brain CT for any indication and whose results were interpreted as normal were also included in the study.

Statistical analysis

The study data were analyzed on SPSS 20.0 software for Windows (IBM Corporation, Armonk, NY, USA). Numerical variables were subject to a normality of distribution test using parametric or non-parametric tests depending on the results. Categorical variables were expressed as frequency distribution (number and percentage) and numerical variables as descriptive statistics (mean, standard deviation, and interquartile range [IQR]). A type 1 error rate of $\alpha = 0.05$ was used to determine statistical significance. Descriptive statistics were expressed as frequency, percentage, mean, standard deviation, median, minimum, and maximum values. Numbers and percentages were calculated for categorical variables and as mean, standard deviation, minimum, maximum and IQR for numerical variables. Histogram curves, kurtosis and skewness values, and the Shapiro–Wilk test were used to determine whether data were normally distributed. Normally distributed parameters were expressed as mean plus standard deviation and non-normally distributed parameters as median and minimum-maximum values.

A Student's t-test was applied in two-group comparisons of means of normally distributed data normal and the Mann–Whitney U test in case of non-normally distributed data. A one way analysis of variance (ANOVA) was applied for the comparison of means between more than two groups since the data were normally distributed.

Results

Two hundred patients were included in the study, 57.5% (n = 115) were men, and 42.5% (n = 85) were women. The mean age of the total study group was 51.12 (18.65) years. Mean ages were 47.90 (19.86) in men and 55.48 (15.97) in women. Participants' demographic data are presented in Table 1.

Table 1: Patient demographic characteristics and clinical data

Parameter	ICH group (n = 100)	Control group (n = 100)
Gender		
Male	59 (59%)	NA
Female	41 (41%)	NA
History of Chronic Disease		
No	42 (42%)	67 (67%)
Yes	58 (58%)	33 (33%)
Intracranial Hemorrhage Type		
Subarachnoid hemorrhage	52 (52)	NA
Subdural hemorrhage	15 (15)	NA
Intraparenchymal hemorrhage	30 (30)	NA
Intraventricular hemorrhage	3 (3)	NA
Presence of midline Shift		
No	57 (57%)	100 (100%)
Yes	43 (43%)	0 (0%)
Mortality		
No	79 (79%)	95 (95%)
Yes	21 (21%)	5 (5%)
Morbidity		
No	80 (80%)	100 (100%)
Yes	20 (20%)	0 (0%)

NA: Not applicable, ICH: Intracranial hemorrhage

Examination of the effect of ONSD on intracranial hemorrhage showed that an increase in right- and left-side ONSD and in the mean value of the two was associated with intracranial hemorrhage independent of trauma ($P < 0.001$ for all) as shown in Table 2.

Table 2: Effect of ONSD on Intracranial Hemorrhage

Intracranial Hemorrhage	ONSD Mean (SD)	*P*-value	ONSD (Right) Mean (SD)	*P*-value	ONSD (Left) Mean (SD)	*P*-value
No	3.81 (0.86)	<0.001	3.73 (0.91)	<0.001	3.90 (0.98)	<0.001
Yes	5.76 (1.04)		5.66 (1.15)		5.91 (1.16)	

ONSD: optic nerve sheath diameter

When only the ICH group was evaluated, an increase in ONSD in patients with intracranial hemorrhage was found to be significant in terms of mortality and midline shift development ($P < 0.001$ and $P < 0.001$, respectively) but not of morbidity and ($P = 0.456$) as shown in Table 3.

Table 3: The effect of ONSD on morbidity, mortality, and midline shift development in the presence of intracranial hemorrhage

		ONSD Mean (SD)	*P*-value
Morbidity	No	5.72 (1.07)	0.456
	Yes	5.92 (0.91)	
Mortality	No	5.57 (0.92)	<0.001
	Yes	6.47 (1.18)	
Midline shift	No	5.38 (0.84)	<0.001
	Yes	6.26 (1.08)	

ONSD: optic nerve sheath diameter, SD: standard deviation

ROC analysis was performed in order to calculate the success of mean ONSD in determining intracranial hemorrhage and in determining mortality and midline shift development in patients with intracranial hemorrhage. Accordingly, a cut-off value of 4.19 mm (area under the curve [AUC]: 0.952) was determined for intracranial hemorrhage, a cut-off value of 5.67 mm (AUC: 0.737) for midline shift development in patients with intracranial hemorrhage, and a cut-off value of 6.03 mm (AUC: 0.730) for mortality (Table 4).

According to the cut-off values determined by the receiver operating characteristic (ROC) analysis, the odds ratio (OR) for ICH was 29.095, the OR for mortality was 8.838, and the OR for midline shift development was 6.078 based on the binary logistic regression analysis that was done to evaluate the relationship between ONSD and intracranial hemorrhage, mortality, and midline shift development (Table 5).

Table 4: Relationship between mean ONSD and mortality and morbidity ROC analysis

	Mean ONSD Cut-off	AUC	Sensitivity	Specificity	*P*-value	95% CI Lower Bound	Upper Bound
Intracranial hemorrhage	4.19	0.952	100	70	<0.001	0.907	0.997
Mortality	6.035	0.730	76	74	0.001	0.598	0.860
Midline Shift	5.675	0.737	72	70	<0.001	0.638	0.835

ONSD: optic nerve sheath diameter, ROC: receiver operating characteristic curve, AUC: area under the curve, CI: confidence interval

Table 5: Logistic regression analysis showing the relationship of ONSD with intracranial hemorrhage, mortality, and midline shift

	B	SE	Wald	*P*-value	Exp(B)	95% CI for EXP(B) Lower	Upper
Intracranial hemorrhage	3.371	0.470	51.346	<0.001	29.095	11.573	73.150
Mortality	2.179	0.572	14.505	<0.001	8.838	2.280	27.125
Midline shift	1.805	0.447	16.333	<0.001	6.078	2.533	14.585

SE: standard error, CI: confidence interval

Discussion

Despite developments in clinical approaches, intracranial hemorrhage is a disease with high morbidity and mortality. Mortality is observed at a rate of 50% in the first year after intracranial hemorrhage. The morbidity rate in the first six months after hemorrhage in non-fatal cases is 80% [4]. In the present study, ONSD was directly related to the presence of bleeding, independent of trauma, and to mortality and midline shift development in patients with bleeding.

ONSD has been associated with intracranial hemorrhage in most studies involving measurements performed with both USG and CT [5, 6]. However, in a study of intensive care patients, Zoerle et al. [7] reported no association between subarachnoid hemorrhage and ONSD measured based on USG. This finding may be attributable to the antiedema therapy administered to intensive care patients for a period; therefore, their intracranial pressures are not particularly high. In addition, since USG is an operator-dependent technique, measurements taken by different individuals may not be consistent. This difference may lead to inaccurate results. The increase in ONSD based on CT images in patients with intracranial hemorrhage in this study was found to be associated with the presence of bleeding. At a cut-off value of 4.19 for ONSD, every 3.371 unit increase in intracranial hemorrhage was associated with a 29.095-fold increase in ONSD.

Masquere et al. [8] reported that an increase in ONSD as viewed on the CT scan was associated with an increase in mortality following intracranial hemorrhage. Another study by

Zhao et al. [9] involving ischemic and hemorrhagic stroke patients reported a positive correlation between ONSD and mortality. In a study of patients admitted to intensive care unit (ICU) due to head trauma, Sekhon et al. [10] reported that a one unit increase in ONSD as measured on a CT scan led to a 2-fold increase in mortality. In the present study, at an ONSD cut-off value of 6.03, every 2.179 unit increase in mortality was associated with an 8.838-fold increase in ONSD.

In a study of patients presenting with head trauma and admitted to the ICU, Kazdal et al. [11] reported significantly higher ONSD in measurements that were obtained using USG in patients with intracranial hemorrhage with midline shift compared to a control group with intracranial hemorrhage without midline shift. Komut et al. [12] used USG measurements to investigate non-trauma patients who presented to the emergency department and reported that an increase in ONSD was associated with the presence of a midline shift. In that study, the authors determined an ONSD cut-off value of 5.3 mm for detecting the presence of midline shift (AUC: 0.728; 95% confidence interval [CI] 0.585–0.871). That cut-off point exhibited 70% sensitivity and 74% specificity. In the present study, an ONSD cut-off point of 5.67 mm was determined for the presence of a midline shift. That cut-off value exhibited 72% sensitivity and 71% specificity. Every 1.805 unit increase in midline shift was associated with a 6.078-fold increase in ONSD.

A number of limitations, including its retrospective nature and low patient number, can be found in this study. Its single-center nature also means that it cannot be generalized to the entire population. Further multi-center studies with larger patient groups are needed to further address this subject.

Conclusions

The findings of this study suggest that ONSD measurement is a non-invasive method that can be useful to clinicians for early detection of increased intracranial pressure and intracranial hemorrhage. It is also a promising method that could be used for predicting mortality in patients with intracranial hemorrhage. An increase in ONSD can also be added as a poor prognostic factor to newly developed scoring systems.

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