



Determination of Optic Nerve Sheath Diameter Cut-off after Cerebrospinal Fluid Drainage in Adults with Elevated Intracranial Pressure: A Prospective Study

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ABSTRACT

AIM: To evaluate the relationship between optic nerve sheath diameter (ONSD) and intracranial pressure (ICP) in patients with acute ICP elevation controlled through external ventricular drainage (EVD).

MATERIAL and METHODS: In this prospective observational study, simultaneous measurements of right and left ONSD, ICP, and cerebral perfusion pressure (CPP) were recorded in 46 adult patients undergoing EVD. Two patients were excluded due to ophthalmic pathology and missing data, resulting in a final cohort of N = 44 patients. After we obtained the baseline measurements, 5 mL of cerebrospinal fluid (CSF) were drained, and the measurements were repeated 2 minutes (min) later.

RESULTS: CSF drainage led to significant reductions in both ICP and bilateral ONSD ($p = .001$ for all), while CPP significantly increased ($p = .038$). We identified an ONSD cut-off of 5.35 mm for detecting ICP values ≥ 15 mmHg, and this cut-off had 53% sensitivity and 86% specificity (Youden index: 0.395). However, we could not determine a reliable cut-off for detecting ICP values ≥ 20 mmHg ($p = .076$).

CONCLUSION: When ICP is controlled through EVD, the linear relationship between ONSD and ICP observed during acute pressure elevations may be disrupted, particularly at higher ICP values (≥ 20 mmHg). Although we identified a cut-off ONSD value of 5.35 mm for detecting ICP values ≥ 15 mmHg, the low sensitivity of this cut-off significantly limits its clinical utility. Additionally, since no reliable cut-off could be established for ICP values ≥ 20 mmHg, ONSD may have limited value for monitoring pressure following CSF drainage.

KEYWORDS: Cerebral perfusion pressure, Intracranial pathology, Intracranial pressure, Elevated, Normal, Optic nerve sheath

INTRODUCTION

The rapid detection of elevated intracranial pressure (ICP) is essential when managing critically ill patients with brain pathology (3). The optic nerve sheath is essentially an extension of the dura mater, and as it can stretch, the optic nerve sheath diameter (ONSD) changes when ICP changes (12). Measuring the ONSD using ultrasound offers a practical approach, as it is non-invasive, cost-effective, and can be carried out at the bedside. A meta-analysis by Berhanu et al. involving 2,824 patients found that ONSD cut-off values

between 5.6–6.3 mm were effective for detecting ICP values around 20–22 mmHg. These ONSD cut-off values had good specificity and maintained reasonable sensitivity compared to lower thresholds in the 4.9–5.5 mm range (2).

However, most previous studies have focused on patients during the acute illness phase when ICP values were actively increasing. Moreover, there is limited information on how ONSD relates to ICP in patients whose ICP is being controlled using CSF drainage via the external ventricular drainage (EVD) method. Consequently, our main goal in this study was to

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identify the best ONSD cut-off values for detecting ICP values ≥ 15 mmHg and ≥ 20 mmHg in patients undergoing EVD. Additionally, we aimed to explore the correlation between ONSD measurements and actual ICP from intraventricular catheter monitoring.

MATERIAL and METHODS

Study Design and Ethical Approval

This prospective observational study was performed over a 13-month period at the Neurosurgical Intensive Care Unit, Cerrahpasa School of Medicine, Istanbul University-Cerrahpasa, following ethics committee approval. The Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine, Istanbul, Türkiye (Chairperson Prof Ozgur Kasapcopur) provided ethical approval on September 7, 2021 (Ethical Committee Approval No: 179951, ClinicalTrials.gov identifier: NCT06367868).

Participants

This study was performed with 46 adult patients who had intraventricular drainage catheters due to intracranial pathology. To participate in the study, written informed consent had to be given by the patients or their relatives. Patients with orbital tumors, Graves' disease, exophthalmos, sarcoidosis, optic neuropathy, meningitis, ocular trauma, and severe lung disease with ventilation requirements greater than 5 cm H₂O PEEP were excluded from the study (4). Two patients were excluded due to ophthalmic pathology and missing data, resulting in a final cohort of 44 patients.

Data Collection and Measurements

In the intensive care unit, with routine ASA monitoring, ICP and cerebral perfusion pressure (CPP) were continuously monitored using an intraventricular catheter, with transducers placed at the level of the tragus.

All patients underwent continuous ICP monitoring using an EVD catheter, with the transducer placed at the level of the tragus, and cerebral perfusion pressure (CPP) monitoring following the standard protocols of the American Society of Anesthesiologists (ASA). ONSD measurements were performed using an ARIETTA 65 ultrasound system (Hitachi, Japan) with an L64 high-frequency linear probe (5–18 MHz). A transbulbar approach was applied in the transverse plane, with the probe angled medially and superiorly, thus ensuring that no pressure was applied to the globe. This technique allowed for clear visualization of the globe, the hyperechoic retrobulbar fat, and the hypoechoic optic nerve. After obtaining the clearest image of the optic nerve at its thickest point, the ONSD was measured 3 mm posterior to the globe. To minimize inter-observer variability, all of the measurements were performed bilaterally by a single experienced sonographer.

The baseline measurements included the bilateral ONSD, ICP, and CPP, which were recorded simultaneously. Subsequently, 5 mL of CSF were drained through the EVD catheter over 30–60 seconds under sterile conditions. At 2 minutes (min) after drainage, repeated measurements of the bilateral ONSD, ICP, and CPP were made to assess acute changes in these

variables. The 2 min interval was chosen based on previous studies suggesting that the ONSD rapidly adapts to changes in the ICP (12). All of the measurements were performed under standard conditions with patients maintained in a neutral head position and with stable ventilation settings.

Power Analysis

The minimum sample size of (n=44) was based on the detection of a Cohen's d effect size of 0.5 with a type I error of 0.05 and power of 0.8.

Statistical Analysis

Descriptive statistics for the continuous variables were expressed as the mean $\pm$ standard deviation (SD) for normally distributed data and as the median, minimum, and maximum for non-normally distributed data. The categorical data were presented as frequency and percentage values. Normality was assessed using the Shapiro-Wilk test ($n < 50$) and skewness-kurtosis tests. Paired t-tests were used to compare the pre- and post-CSF drainage measurements for normally distributed variables, while the Wilcoxon signed-rank test was used for non-normal data. Between-group comparisons for non-normal data were carried out using the Mann-Whitney U test (two groups) or Kruskal-Wallis test (multiple groups), and post-hoc corrected p-values were used to identify significant differences. Categorical variables were compared using the Chi-square test, whereas Pearson or Spearman correlation tests were used to evaluate the relationships between the continuous variables (i.e., ONSD, ICP, and CPP). A receiver operating characteristic (ROC) analysis was used to determine the ONSD cut-off values for detecting ICP ≥ 15 mmHg and ≥ 20 mmHg, and the sensitivity, specificity, and Youden index were calculated. All of the statistical analyses were conducted using SPSS (version 26.0, IBM Corp.), and $p < 0.05$ was considered significant.

RESULTS

Of the 46 enrolled patients, 44 were included in the final analysis (Figure 1). The patient's demographic characteristics, diagnoses, and Glasgow coma scale (GCS) scores are presented in Table I. CSF drainage significantly reduced ICP values ($p = 0.001$), right ONSD ($p = 0.001$), and left ONSD ($p = 0.001$) and increased CPP ($p = 0.038$) (Table II, Figures 2–4). A significant correlation was observed between bilateral ONSD and ICP before and after CSF drainage (Table III).

The ROC analysis identified an ONSD cut-off of 5.35 mm for identifying ICP values ≥ 15 mmHg (sensitivity: 53%; specificity: 86%; Youden index: 0.395; Table IV, V, Figure 5). However, no significant ONSD cut-off was identified for ICP values ≥ 20 mmHg ($p = 0.076$; Table VI). No differences in ONSD measurements were observed based on patient diagnosis or GCS scores (Tables VII, VIII).

DISCUSSION

This study aimed to investigate the relationship between ONSD and ICP in patients with ICP controlled via EVD and revealed a significant reduction in both ICP and bilateral ONSD

following CSF drainage, alongside increased CPP. We also identified an ONSD cut-off value of 5.35 mm for detecting ICP values ≥ 15 mmHg, and this cut-off had 53% sensitivity and 86% specificity. However, no cut-off could be determined for ICP values ≥ 20 mmHg, which suggests that the linear ONSD-ICP relationship may be disrupted at higher ICP levels following CSF drainage.

The ONSD cut-off of 5.35 mm for ICP values ≥ 15 mmHg is relatively similar to the cut-off of 5.49 mm reported by Padayachy et al. in their pediatric work with children over 4 years

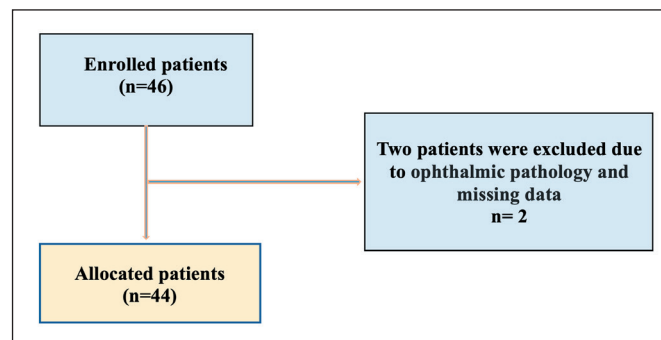


Figure 1: The flowchart.

Table I: Patient's demographic values, diagnosis and Glasgow Coma Scores

Variables	Values	
Age, mean $\pm$ SD (years)	51.55 $\pm$ 17.66	
Body mass index, mean $\pm$ SD (kg/m ²)	25.71 $\pm$ 4.99	
Gender	n	%
Female	15	34.1
Male	29	65.9
Diagnosis	n	%
Intracranial haemorrhage	19	43.2
Vascular	7	15.9
Tumor	18	40.9
GCS score	n	%
3-8	12	27.3
9-13	14	31.8
14-15	18	40.9

Data are presented as mean $\pm$ standard deviation (SD) for continuous variables and as number (n) and percentage (%) for categorical variables. **GCS:** Glasgow Coma Scale.

Table II: Intracranial Pressure, Right and Left Optic Nerve Sheath Diameters and Cerebral Perfusion Pressure Before and After Cerebrospinal Fluid Drainage

	ICP (mmHg)		R-ONSD (mm)		L-ONSD (mm)		CPP	
	mean $\pm$ SD	p-value	mean $\pm$ SD	p-value	mean $\pm$ SD	p-value	mean $\pm$ SD	p-value
Before CSF drainage	14.68 $\pm$ 9.31	0.001*	5.12 $\pm$ 0.55	0.001*	5.18 $\pm$ 0.53	0.001*	77.82 $\pm$ 19.05	0.038*
After CSF drainage	9.89 $\pm$ 7.86		4.52 $\pm$ 0.53		4.54 $\pm$ 0.53		80.32 $\pm$ 16.50	

Values expressed as mean $\pm$ SD (standard deviation). **ICP:** Intracranial Pressure, **CPP:** Cerebral perfusion pressure, **R-ONSD:** Right optic nerve sheath diameter, **L-ONSD:** Left optic nerve sheath diameter, **CSF:** Cerebrospinal fluid. * Paired t-test, statistically significant values ($p < 0.05$)

Table III: The Correlation between the Right and Left Optic Nerve Sheath Diameters as well as Intracranial Pressure Before and After Cerebrospinal Fluid Drainage

	R-ONSD (mm)		L-ONSD (mm)		Mean-ONSD (mm)	
	mean ± SD	p-value	mean ± SD	p-value	mean ± SD	p-value
Before CSF drainage	5.12±0.55	0.001*	5.18±0.53	0.001*	5.16±0.49	0.001*
After CSF drainage	4.52±0.53		4.54±0.53		4.53±0.48	
	R-ONSD-1		L-ONSD-1		Mean-ONSD-1	
	p-value	r	p-value	r	p-value	r
ICP-1	0.002*	0.463	0.028*	0.332	0.003*	0.442
	R-ONSD-2		L-ONSD-2		Mean-ONSD-2	
	p-value	r	p-value	r	p-value	r
ICP-2	0.029*	0.329	0.095	0.255	0.032*	0.325

Spearman's rank correlation and Paired t test, r: correlation coefficient. **ICP-1:** Intracranial pressure before cerebrospinal fluid (CSF) drainage, **ICP-2:** Intracranial pressure after CSF drainage, **ONSD-1:** Optic Nerve Sheath Diameter before CSF drainage, **ONSD-2:** Optic Nerve Sheath Diameter after CSF drainage

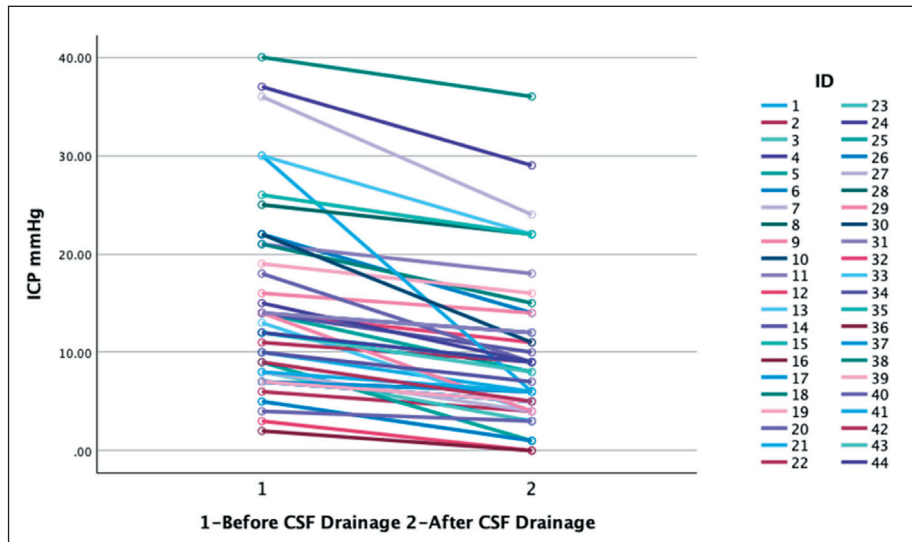


Figure 2: Changes in intracranial pressure after cerebrospinal fluid drainage.

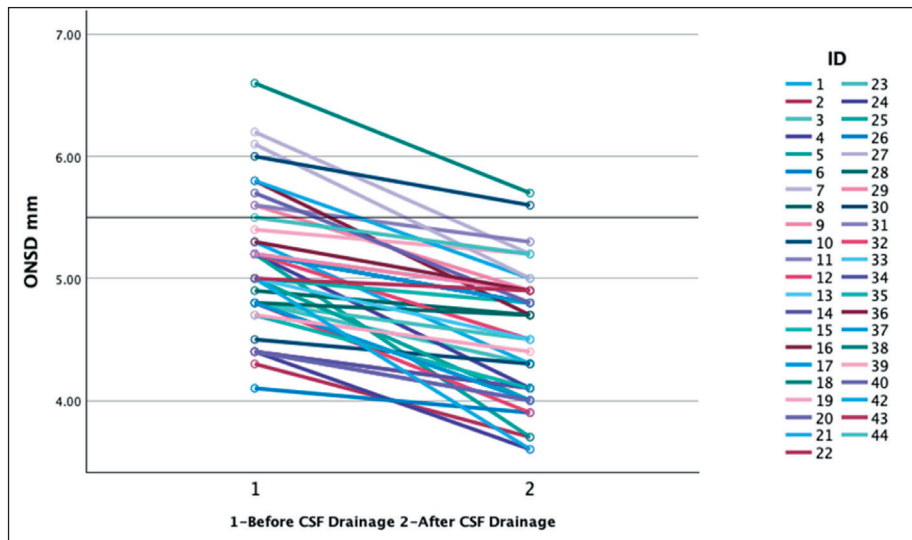


Figure 3: Changes in right optic nerve sheath diameters after cerebrospinal fluid drainage.

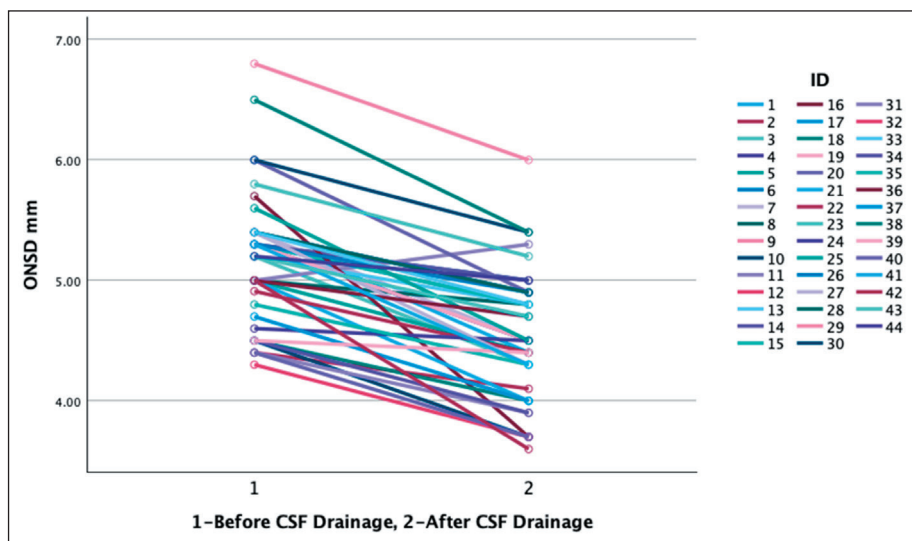


Figure 4: Changes in left optic nerve sheath diameters after cerebrospinal fluid drainage.

Table IV: The Number of patients with Intracranial Pressure ≥ 15 mmHg and < 15 mmHg Before Cerebrospinal Fluid Drainage

ICP-1	n (number)
≥ 15 mmHg	15
< 15 mmHg	29

ICP-1: Intracranial pressure before cerebrospinal fluid drainage

old. Notably though, the sensitivity of 53% in this study is considerably lower than the sensitivity values reported previously in acute ICP elevation scenarios (13). For example, Berhanu et al. (2) achieved sensitivities ranging from 70% to 90% using ONSD cut-offs between 5.6 and 6.3 mm (2).

This discrepancy between the present study and the previous literature warrants closer examination, and several factors may be involved.

Table V: ROC Analyses for Intracranial Pressure ≥ 15 mmHg before Cerebrospinal Fluid Drainage and Right Optic Nerve Sheath Diameter before Cerebrospinal Fluid Drainage

Variable	AUC	Std.Error	p-value	Cut-off	Specificity	Sensitivity	Youden Index	95% Confidence Interval	
								Upper limit	Lower limit
R-ONSD-1	0.701	0.087	0.030*	5.35	0.862	0.533	0.395	0.530	0.872

ROC (Receiver operating characteristic) Curve Analyses. **R- ONSD-1:** Right optic nerve sheath diameter before CSF drainage, **AUC:** Area Under Curve

Table VI: ROC Analyses for Intracranial Pressure ≥ 20 mmHg before Cerebrospinal Fluid Drainage and Right Optic Nerve Sheath Diameter before Cerebrospinal Fluid Drainage

Variable	AUC	Std.Error	p-value	95% Confidence Interval	
				Upper limit	Lower limit
R-ONSD-1	0.680	0.096	0.076	0.492	0.869

ROC (Receiver operating characteristic) Curve Analyses. **R- ONSD-1:** Right optic nerve sheath diameter before CSF drainage, **AUC:** Area Under Curve

Table VII: Relationship among Right and Left Optic Nerve Sheath Diameters Before and After Cerebrospinal Fluid Drainage with Patients Diagnosis

	Diagnosis	n	mean $\pm$ SD	p-value
R-ONSD-1	Intracranial Haemorrhage	19	5.02 $\pm$ 0.65	0.578
	Tumor	18	5.16 $\pm$ 0.45	
	Vascular	7	5.25 $\pm$ 0.49	
L-ONSD-1	Intracranial Haemorrhage	19	5.15 $\pm$ 0.55	0.854
	Tumor	18	5.23 $\pm$ 0.55	
	Vascular	7	5.11 $\pm$ 0.50	
R-ONSD-2	Intracranial Haemorrhage	19	4.49 $\pm$ 0.56	0.639
	Tumor	18	4.59 $\pm$ 0.52	
	Vascular	7	4.37 $\pm$ 0.50	
L-ONSD-2	Intracranial Haemorrhage	19	4.43 $\pm$ 0.52	0.261
	Tumor	18	4.70 $\pm$ 0.56	
	Vascular	7	4.41 $\pm$ 0.42	

Independent t-test. **ONSD-1:** Optic nerve sheath diameter before CSF drainage, **ONSD-2:** Optic nerve sheath diameter after CSF drainage, **R:** Right, **L:** Left, **n:** number, **SD:** Standard deviation

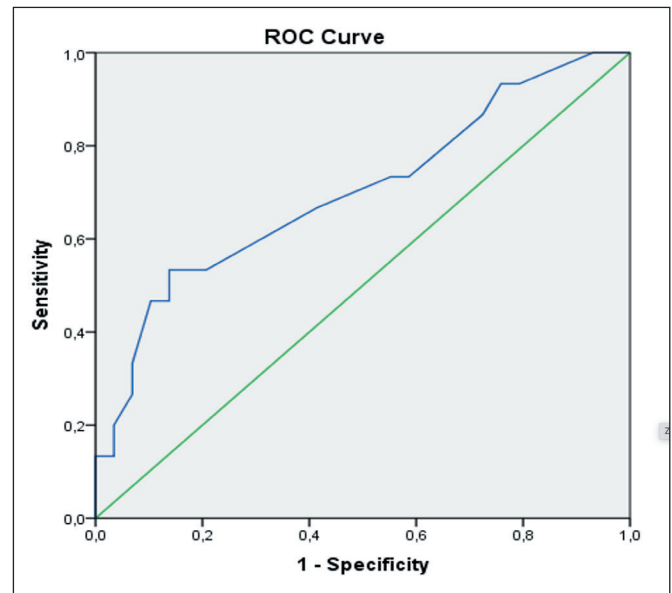
**Figure 5:** ROC Analyses for intracranial pressure ≥ 15 mmHg before cerebrospinal fluid drainage and right optic nerve sheath diameter before cerebrospinal fluid drainage.

Table VIII: Relationship among Intracranial Pressure, Right and Left Optic Nerve Sheath Diameters Before and After Cerebrospinal Fluid Drainage with Patients Glasgow Coma Score

	GCS	n	mean± SD	p-value
ICP-1	3-8	12	13.67±10.65	0.881
	9-13	14	14.57±9.56	
	14-15	18	15.44±8.65	
R-ONSD-1	3-8	12	4.97±0.71	0.168
	9-13	14	4.99±0.43	
	14-15	18	5.30±0.48	
L-ONSD-1	3-8	12	5.20±0.61	0.542
	9-13	14	5.05±0.46	
	14-15	18	5.26±0.54	
ICP-2	3-8	12	10.50±10.15	0.911
	9-13	14	10.14±7.78	
	14-15	18	9.28±6.54	
R-ONSD-2	3-8	12	4.58±0.57	0.414
	9-13	14	4.35±0.47	
	14-15	18	4.59±0.55	
L-ONSD-2	3-8	12	4.59±0.49	0.494
	9-13	14	4.40±0.50	
	14-15	18	4.61±0.58	

One-way analysis of variance (or one-way ANOVA)

GCS: Glasgow Coma Scale, **ICP-1:** Intracranial pressure before cerebrospinal fluid (CSF) drainage, **ICP-2:** Intracranial pressure after CSF drainage, **ONSD-1:** Optic nerve sheath diameter before CSF drainage, **ONSD-2:** Optic nerve sheath diameter after CSF drainage, **R:** Right, **L:** Left, **n:** number, **SD:** Standard deviation

Firstly, CSF drainage could be changing the mechanical properties of the optic nerve sheath itself, making it less responsive to fluctuations in ICP. Additionally, our measurement timing (2 min after drainage) may not have been optimal for capturing the full dynamic range of ONSD changes; for example, Moretti et al. used a shorter 1 min interval, which may have elicited different results (12). Biological variability between patients may also be involved; indeed, the elasticity of the optic nerve sheath varies among individuals and can be affected by factors such as age or how long they have experienced increased intracranial pressure (14). Taken together, these findings indicate that relying on a single ONSD measurement for clinical decisions may not be sufficient. Instead, patient-specific calibration of the ONSD-ICP relationship may be necessary to improve sensitivity and make this technique more clinically reliable.

The most significant finding in this study is that we could not establish a reliable ONSD cut-off for ICP values ≥ 20 mmHg. This issue is notable because previous studies on acute ICP

elevation have consistently reported that ONSD cut-offs between 5.6–6.3 mm are effective for detecting these higher ICP values (2). However, the patients differed from those in previous studies in an important way, as they all had functioning EVDs, meaning their ICP was being actively managed. As such, this controlled environment seems to change how ONSD relates to ICP, which needs more investigation.

Our findings are in line with observations from other groups who studied patients with managed ICP. For example, Kersch et al. found non-linear correlations between ONSD and ICP in children, which suggests the optic nerve sheath might hit biomechanical limits at very high ICP values (8). Lochner et al. also reported that ONSD values became less sensitive when the ICP values exceeded 20 mmHg in patients whose ICP had been stabilized (11). The authors suggested that this reduced sensitivity may occur due to sheath fibrosis or decreased compliance after repeated pressure fluctuations, which aligns with the fact that many of these brain conditions are chronic.

Further to the control of ICP in this work, the patients were in a post-drainage state, which likely complicated the situation. When CSF drains through an EVD, the ICP drops quickly, sometimes within minutes. In these cases, the ONSD might need longer to respond to these rapid changes. Individual variation in how elastic each person's optic nerve sheath is should also be considered. Indeed, factors such as age and how long someone has had elevated ICP may affect the compliance of the tissue (14).

Another consideration is hysteresis, which researchers have described in patients with long-standing intracranial hypertension (6,8). In hysteresis, the optic nerve head undergoes structural changes, as does the trabecular structure inside the sheath, and these changes may limit how well the tissue can respond to pressure shifts in real time. As such, hysteresis could explain why ONSD is not always a reliable indicator for monitoring ICP.

In terms of future research, future studies need to track ONSD measurements over longer periods after procedures such as EVD. We measured at 2 min post-drainage, but ONSD may continue adapting for hours afterward. Obtaining longitudinal data would support the current understanding of this timeline and help to identify the best time for taking measurements.

Even though there were issues with using ONSD measurements at higher ICP levels, we did confirm an important finding that others have reported before (1,7,8,9); specifically, ONSD measurements from both eyes correlated well with ICP. This outcome supports measuring just one side in clinical practice, which is both more practical and faster.

Finally, it should be noted that our results did not match with those of Komut et al., who reported higher ONSD in patients with GCS scores ≤ 13 in acute settings (10). Conversely, in this work, we did not identify any connection between GCS and ONSD. The difference in findings is likely due to patient condition, as the patients in the work of Komut et al. were acutely deteriorating (10), whereas ours had already undergone drainage and were hemodynamically stable. This comparison

highlights the significance of the clinical situation when using ONSD to assess ICP.

Limitations

Several limitations should be acknowledged in this study. All of the patients had controlled ICP through the use of functioning EVD, which limits the generalizability of these findings to patients with acute, unmanaged intracranial hypertension. Our cohort was also heterogeneous in terms of underlying pathology, as the patients presented with different diagnoses, and this variation may have influenced the relationship between ONSD and ICP in ways that we did not fully account for. We chose to measure ONSD at 2 min post-drainage, but this timepoint may not capture the complete adaptation process. As such, longer observation periods are needed to determine when the ONSD stabilizes after acute pressure changes. Finally, we used a single sonographer for all measurements to minimize inter-observer variability. While this improved consistency in our data, the outcomes may not reflect the measurement variability that occurs in routine clinical settings where multiple operators perform ultrasound examinations (5).

CONCLUSION

We found an ONSD cut-off of 5.35 mm for identifying ICP values ≥ 15 mmHg, but the sensitivity of this cut-off was only 53%, which limits its utility in clinical practice. There are several possible explanations for this low sensitivity. CSF drainage likely changes how compliant the optic nerve sheath is, potentially making it less responsive to pressure shifts. The timing of our measurements may also have been influential; we measured at 2 min after drainage, but the ONSD could be adjusting either faster or slower than that, and the timeline of these changes is unclear from the literature. There is also natural variation among patients in the elasticity of their optic nerve sheath, and the nerve sheaths of individuals with chronic brain problems may respond differently from others.

Another key finding is that we could not find a reliable cut-off value for ICP ≥ 20 mmHg, which suggests ONSD may plateau or simply become unreliable once pressures become high, at least after CSF drainage. A potential solution to this issue would be taking multiple ONSD measurements over time rather than relying on a single value. Indeed, having multiple measurements might also help to calibrate the measurement to each individual patient rather than using universal cut-offs.

Overall, more research is needed to understand the timing and biomechanical aspects of how ONSD responds to ICP when the pressure is being actively managed. Indeed, controlling the ICP environment appears to change the relationship in ways that are, as yet, not fully clear.

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Declarations

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Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: GO, YT

Data collection: GO

Analysis and interpretation of results: GO

Draft manuscript preparation: OKD

Critical revision of the article: GO, EFA, YT

Other (study supervision, fundings, materials, etc...): n/a

All authors (GO, OKD, EFA, YT) reviewed the results and approved the final version of the manuscript.

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