The Egyptian Journal of Hospital Medicine (January 2025) Vol. 98, Page 379- 384

Reliability of Optic Nerve Ultrasound Compared with Ophthalmoscopy and Computed Tomography in Prediction and Follow up of Elevated Intracerebral Pressure

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ABSTRACT

Background: Cerebral oedema and elevated intracranial pressure are frequent neurologic complications of a variety of cerebral disorders. Though it carries a risk of complications, invasive intracranial pressure monitoring is the gold-standard method for monitoring intracranial pressure. **Objective:** Our goal was to study the reliability of ophthalmoscopy and ultrasound evaluation of optic nerve sheath diameter in relation to computed tomography brain imaging as tools for monitoring increased intracranial pressure. **Methods:** This prospective observational study was conducted on 57 patients with traumatic or non-traumatic brain insult admitted to the intensive care unit (ICU) at Menoufia University Hospitals. All patients underwent clinical examination, routine daily laboratory investigations, and radiological investigations (computed tomography brain, ocular ultrasound, and ophthalmoscopy). **Results:** There was a statistically significant association between computed tomography brain findings & optic nerve sheath diameter measurement by the ultrasound. With a sensitivity of 94%, specificity of 88%, positive predictive value of 93%, negative predictive value of 70%, and an optic nerve sheath diameter at a cut-off point of 6.55 mm on day 1, the results are impressive. The results of the ophthalmoscopic examination and the computed tomography scan of the brain showed a strong correlation on day 3.**Conclusions:** Clinically, optic nerve sheath diameter (ONSD) measurement is an effective, rapid, bedside, and non-invasive tool for intracranial pressure monitoring, that guides early intervention, particularly in critical settings where immediate computed tomography access may be limited.

Keywords: Optic nerve ultrasound, Ophthalmoscopy, Computed tomography, Elevated intracerebral pressure.

INTRODUCTION

Intracerebral haemorrhage (ICH), subarachnoid haemorrhage (SAH), and traumatic brain injury (TBI) are among the many cerebral disorders that can lead to cerebral oedema and increased intracranial pressure (ICP**)** [1]. ICP monitoring is considered the gold standard, but it is not universally available or easy to perform without specialised expertise, and it carries risks such as haemorrhage and infection. For better results in patients with traumatic brain injuries, it is essential to identify, assess, and treat elevated intracranial pressure (ICP) as soon as possible. Other than invasive procedures, non-invasive methods of monitoring intracranial pressure (ICP) include ophthalmoscopy, computed tomography (CT), and transcranial Doppler [2] However, CT and MRI are time-consuming, costly, and often require patient transport, which may not be feasible for critically ill patients. In contrast, ultrasound and ophthalmoscopy are more accessible, cost-effective, and can be performed quickly at the bedside without radiation exposure. This makes them particularly useful for real-time ICP monitoring in unstable patients, especially in the intensive care unit (ICU) [4]**.** Cerebrospinal fluid (CSF) accumulates in the subarachnoid space as ICP increases, resulting in the enlargement of the optic nerve sheath (ONS), which is contiguous with the brain's meninges. This expansion can be identified through imaging methods [5]**.** We aimed to assess the reliability of ultrasound assessment of ONSD and ophthalmoscopy as monitoring tools of increased ICP in correlation with CT brain.

PATIENTS AND METHODS

This prospective observational study was conducted on 57 adult patients admitted to the ICU, Menoufia University Hospitals during the period from January to August 2024, after approval of The Local Ethics Committee. Written informed consent was obtained from the participants or their legal surrogates.

Inclusion criteria: Patients above 18 years old, both sexes, with traumatic or non-traumatic brain insult who were transferred to ICU with signs of increased ICP in the initial CT scan of the brain.

Exclusion criteria: Any patient with a preexisting condition that increases the risk of ONSD, including arachnoid cysts of the optic nerve, optic nerve trauma, cataracts, ocular surgeries and eye globe trauma, or oedematous eyelids. Additionally, any patient planning decompressive cranial surgery, patients who received any brain dehydrating measures before the initial CT brain, and patients who had prior ICU admission for elevated ICP.

In addition to routine daily laboratory and radiological investigations, all patients underwent a comprehensive history recording, clinical examination, which included vital data and Glasgow Coma Scale (GCS).On admittance, a CT brain was conducted to identify brain injury and elevated ICP. A follow-up CT brain was conducted on the third day after the patient had received all prescribed dehydrating measures. On an image that has not been enhanced, oedema is manifested as regions of low density and a loss of gray/white matter differentiation. In addition, the cisterns and sulcal spaces may be destroyed. Flattened gyri, restricted sulci, or compression of the ventricles are indicative of elevated ICP. Our assessment of the presence or absence of cerebral oedema is contingent upon the radiology specialist's assessment, which is represented by either positive or negative values.

For the purpose of assessing ONSD in every eye, a linear ultrasonic probe operating between 7.5 and 10

Received: 04/08/2024
Accepted: 02/10/2024

MHz was employed in an ocular ultrasound. While the patient was lying face down on the table, conductive ultrasound gel was gently placed over their closed upper eyelid. According to the protocol, the probe should be placed on the upper and outer parts of the orbit. The optical nerve was shown as a hypoechoic, linear structure with clearly defined borders, situated behind the eyeball. In order to record the ONSD, it was transversely measured, three millimeters behind the eye globe, as shown in images A and B **(Figure 1).** Increased ICP causes swelling in the part of the optic nerve inside the eye globe. Fundus examination assesses the grade of papilledema by direct or indirect ophthalmoscope using the papilledema grading system (Frisén Scale) [6].

The primary outcome was the assessment of the accuracy of ultrasound assessment of ONSD and ophthalmoscope as monitoring tools of increased ICP in correlation with CT brain. The secondary outcome was the reliability of ONSD compared to CT brain

Ethical approval: Ethical approval was obtained from Menoufia University Faculty of Medicine Research Ethics Committee Institutional Review Board with number and date 6/2023 ANET45. All individuals provided written informed consents. The study adhered to the principles outlined in the Declaration of Helsinki.

Statistical analysis: The SPSS version 25 statistical program, developed by IBM and located in Chicago, IL, USA, was used for the study. The quantitative values were presented using the standard deviation (SD) and the mean. For the qualitative characteristics, were expressed as frequency and percentage. We used the Fisher exact test to look for correlations between qualitative variables when any of the predicted cells were fewer than five. For paired categorical data with just two outcomes and two measurements, the Mcnemar test was used to evaluate multiple testing. For paired categorical data with more than two outcomes and only two measurements, a marginal homogeneity test was used to evaluate multiple testing. To compare quantitative variables between two sets of normally distributed data, the t-test (t) was used. To compare different ways of looking at the same set of normally distributed data, we used a paired t-test. To compare the different readings of non-normally distributed data within the same group, we used the Wilcoxon signed-rank test. We created receiver operator characteristics (ROC) with maximum sensitivity and specificity values to assess the instrument's performance. The AUROC, or area under the ROC curve, is a way to measure how accurate the test is. We defined statistical significance as a P-value ≤ 0.05.

RESULTS

Table (1) outlined the demographic characteristics of the study participants. The average age of the patients was 47.68 ± 13.74 years, and the average weight was 82.02 ± 12.87 kg. The sample consisted primarily of males (66.7%), with females accounting for 33.3%. Notably, over half of the patients (54.4%) had neurological disorders, which were directly relevant to brain edema and intracranial pressure. A range of medical conditions was reported, with hypertension (38.6%), followed by diabetes mellitus (22.8%) and cardiac conditions (19.3%). All patients (100%) exhibited brain edema, with the majority showing moderate edema (54.4%), followed by massive edema in 35.1% and mild edema in 10.5%.

Table (1): Demographic characteristics of studied patients

Variable		No.=57
Age (years)		47.68 ± 13.74
Weight (Kg)		82.02 ± 12.87
Sex	**Male**	38 (66.7%)
	Female	19 (33.3%)
Medical history	**Free Medical history**	10 (17.5%)
	Hypertension	22 (38.6%)
	DM	13 (22.8%)
	Cardiac	11 (19.3%)
	Smoker	8 (14%)
	Urogenital system	12 (21.1%)
	Neurological diseases	31 (54.4%)
	Malignancy	14 (24.6%)
	Autoimmune diseases	2 (3.6%)
	Trauma	12 (21.1%)
	Asthma	1 (1.8%)
	Toxicology	3 (5.3%)
Initial CT brain findings	**Brain edema** **Mild** **Moderate** **Massive**	57 (100%) 6 (10.5%) 31 (54.4%) 20 (35.1%)
	ICH	17 (29.8%)
	IVH	6 (10.5%)
	SAH	5 (8.8%)
	SDH	3 (5.3%)
	Hydrocephalus	5 (8.8%)
	Contusion	2 (3.5%)
	Stroke	14 (24.6%)
	Mass	15 (26.3%)
	Skull fracture	4 (7%)
	Brain abscess	2 (3.5%)

Data presents as mean ± SD or frequency (%), ICH: Intracerebral hemorrhage, IVH: Interventricular hemorrhage, SAH: Subarachnoid hemorrhage, SDH: Subdural hemorrhage.

Table (2) showed that there were significant changes in clinical indicators from day one to day three. In comparison with day 1, SBP, DBP, HR, RR, and temperature all decreased significantly on day 3. Furthermore, there was a significant improvement in the GCS on day 3 ($P < 0.05$). Significant increases were seen in sodium (Na) levels. On the other hand, parameters including RBS, Hb, TLC, pH, PCO_2, PO_2, HCO_3, K, creatinine, urea, INR, AST, and ALT did not undergo any notable changes from day 1 to day 3. In addition, there was a significant decline in ultrasound-guided binocular ONSD values on day 3 ($P < 0.001$). No significant differences were found in the incidence of CT findings between day 1 and day 3, but a significant improvement in brain edema was detected on day 3 ($P < 0.001$). Additionally, grades of papilledema observed via ophthalmoscopy showed significant improvement on day 3 compared to day 1 ($P < 0.001$).

Table (2): Vital, laboratory data, ONSD and CT evidence of brain edema, CT brain edema grading and ophthalmoscope follow up among studied patients

		Day 1 (N=57)	Day 3 (N=57)	Test of significance	P value
Vital data					
SBP (mmHg)		144.65 ±34.51	133.51 ±17.78	t=3.03	**0.004***
DBP (mmHg)		93.42 ±22.62	86.49 ±11.42	t=2.49	**0.016***
HR (Beat/min)		88.44 ±14.44	77.86 ±12.03	t=6.13	**<0.001***
RR (Breath/min)		18.00 ±2.95	16.72 ±1.32	t=3.23	**0.002***
Temperature (C°)		37.34 ±0.54	37.16 ±0.37	t=2.93	**0.005***
GCS		10.30 ±2.46	11.96±3.24	t=5.09	**<0.001***
Laboratory data					
RBS (mg/dL)		147.19 ± 5.11	142.12 ± 25.07	W=0.09	0.929
Hemoglobin (g/dl)		11.53 ± 1.68	11.50 ± 1.62	t=1.43	0.159
TLC ($\times 10^3$/cm)		10.33 ± 2.61	10.09 ± 2.16	W=0.09	0.926
Platelets($\times 10^3$/cm)		274.9 ± 11.65	277.09 ±9.64	W=1.69	0.091
PH		7.39 ± 0.05	7.39 ± 0.03	t=0.16	0.876
PCO_2 (mmHg)		38.32 ± 5.20	38.68 ± 2.59	t=0.44	0.662
PO_2 (mmHg)		68.14 ± 9.52	62.60 ± 7.49	t=1.22	0.230
HCO_3 (mEq/L)		22.12 ± 3.01	21.97 ±1.60	t=0.46	0.649
Na^+ (mmol/L)		138.77 ± 6.55	140.39 ± 4.14	t=2.61	**0.012***
K^+ (mmol/L)		4.11 ± 0.58	4.09 ± 0.39	t=0.26	0.798
Creatinine (mg/dl)		1.34 ± 0.46	1.28 ± 0.01	W=0.53	0.597
Urea (mg/dl)		40.96 ± 4.66	36.96 ± 9.59	W=0.59	0.559
INR		1.08 ± 0.15	1.05 ± 0.14	t=1.21	0.231
AST (U/L)		44.16 ± 6.29	42.04 ± 5.28	W=1.12	0.234
ALT (U/L)		33.30 ± 4.81	29.72 ± 3.55	W=1.03	0.302
ONSD in millimeter					
Both eyes		7.21± 0.74	5.89±0.53	t=14.78	**<0.001***
< 5.8 mm		0(0%)	2(3.6%)	MH=6.65	**<0.001***
≥ 5.8-5.99 mm		4(7%)	32(56%)		
6 – 6.99 mm		21(36.8%)	21(36.8%)		
7 – 7.99 mm		20(35.1%)	2(3.6%)		
≥ 8 mm		12(21.1%)	0(0%)		
CT brain					
Positive		57 (100 %)	49 (94.7 %)	Mc=1.33	0.250
Negative		0(0%)	8(5.3%)		
CT brain edema	**Absent**	0(0%)	8 (14 %)	MH=6.27	**<0.001***
	Mild	6 (10.5 %)	25 (43.9%)		
	Moderate	31 (54.4 %)	18 (31.6 %)		
	Massive	20 (35.1%)	6 (10.5%)		
Ophthalmoscope	**Absent**	3(5.3%)	5 (8.7%)	MH=5.33	**<0.001***
	Grade 1	2(3.6%)	10 (17.5%)		
	Grade 2	10(17.5%)	19 (33.3%)		
	Grade 3	24(42.1%)	14 (24.6 %)		
	Grade 4	18(31.6%)	7 (12.3 %)		
	Grade 5	0(0%)	2(3.6%)		

Data presents as mean ± SD or frequency (%), *: Statistically significant, t: Paired t test, : Wilcoxon signed rank test, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, RR: Respiratory rate, GCS: Glasgow coma scale , RBS: Random blood sugar, TLC: Total leukocytic count, INR: International normalized ratio, AST: Aspartate Aminotransferase, ALT: Alanine transaminase, *: Statistically significant, t: Paired t test, , MH: Marginal homogeneity test.

Table (3) showed a statistically significant association between CT brain findings and ultrasound-measured ONSD.

Table (3): Relation between ONSD and CT brain among studied patients

Parameter	Positive CT brain edema (N=49)	Negative CT brain edema (N=8)	Test of significance	P value
ONSD in Day1	7.39 ±0.63	6.13 ±0.31	t= 5.52	**<0.001***
ONSD in Day 3	5.95 ±0.53	5.49 ±0.35	t= 3.23	**0.007***

*: Statistically significant, SD: Standard deviation, t: Student t test

Table (4) showed that on day 1, no significant association was found between ophthalmoscopic findings and CT brain results. On the third day, nevertheless, a statistically significant correlation emerged with sensitivity of 98%, specificity of 50%, accuracy of 91%, PPV of 92%, and NPV of 80% correspondingly.

Table (4): Diagnostic accuracy of ophthalmoscope in relation to CT brain in prediction of brain edema in Day 1

Ophthalmoscope	Day 1			Day 3		
	Positive CT brain edema (n=49)	Negative CT brain edema (n=8)	P value	Positive CT brain edema (n=49)	Negative CT brain edema (n=8)	P value
Positive	47 (95.9%)	7 (87.5%)	0.370	48 (98%)	4 (50%)	**<0.001***
Negative	2 (4.1%)	1 (12.5%)		1 (2%)	4 (50%)	
Sensitivity	96%			98%		
Specificity	13%			50%		
Accuracy	84%			91%		
PPV	87%			92%		
NPV	33%			80%		

FE: Fisher exact test, PPV: Positive predictive value, NPV: Negative predictive value, *: Statistically significant.

Table (5) presented the diagnostic performance of ONSD measurements. On day 1, a cut-off point of ≥ 6.55 mm for ONSD yielded sensitivity of 94%, specificity of 88%, accuracy of 93%, PPV of 98%, and NPV of 70%. On day 3, using a cut-off point of ≥ 5.675 mm, the sensitivity decreased to 76%, specificity to 75%, and accuracy to 75%, while the PPV increased to 95%, and the NPV decreased to 33%.

Table (5): Diagnostic accuracy of ONSD in relation to CT brain (n=57)

Diagnostic accuracy	ONSD (mm)	
	D1	D3
AUC	0.977	0.788
95% CI	0.942-1.000	0.664-0.913
P value	**<0.001***	**<0.009***
Cut off point	≥ 6.55	≥5.675
Sensitivity	94%	76%
Specificity	88%	75%
Accuracy	93%	75%
PPV	98%	95%
NPV	70%	33%

*: Statistically significant, AUC: Area under curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value.

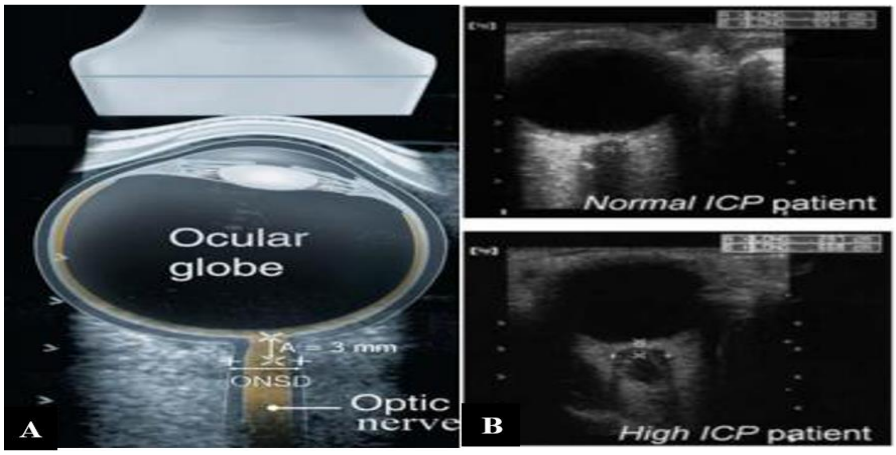

Figure 1: A) show how to measure ONSD, B) show difference between normal and increasing ICP

DISCUSSION

CT and MRI are widely used for noninvasive detection of elevated intracranial pressure (ICP). However, their availability can be limited, and the time required for patient transfer poses challenges, particularly for critically ill patients who depend on intensive inotropic or ventilatory support [7] .

In our study, males comprised 66.7% of total participants. Neurological conditions like stroke, traumatic brain injury, and variations in ICP may be more prevalent in males due to biological factors such as hormonal differences and brain structure. Differences in anatomy, physiology, and responses to stress or injury could influence the manifestation of brain edema and elevated ICP, affecting how these conditions present and how patients respond to treatment, potentially leading to variations in the severity of brain edema. In our study, all patients diagnosed with brain edema via CT scans had a range of underlying conditions. The most common were intracerebral hemorrhage (29.8%), brain masses (26.3%), and stroke (24.6%). Other causes included interventricular hemorrhage (10.5%), subarachnoid hemorrhage and hydrocephalus (8.8% each), skull fractures (7%), subdural hemorrhage (5.3%), brain contusions (3.5%), and brain abscesses (3.5%). These findings align with the study by **Pansell *et al.* [8]**, which also confirmed brain edema in all cases using CT scans. Their study reported subarachnoid hemorrhage in 47% of patients, traumatic brain injuries in 29%, intracerebral hematoma in 12%, and other conditions accounting for 12% of cases.

Systolic and diastolic blood pressure, heart rate, respiration rate, and temperature all showed a statistically significant decline from day 1 to day 3 according to vital sign monitoring in this study. Additionally, Glasgow Coma Scale (GCS) scores showed significant improvement by day 3, indicating better consciousness and neurological function ($P < 0.05$). These changes likely reflect the stabilization of vital signs and reduced physiological stress as initial treatments took effect. This surveillance is consistent with findings of **Liu *et al.* [9]**, where in their analysis of 2,848 patients who had suffered severe intracerebral haemorrhage (ICH), they found comparable patterns, including improvements in GCS scores and significant reductions in blood pressure, heart rate, respiratory rate, and temperature. Sodium levels showed a significant increase by day 3 ($P = 0.012$), possibly indicating mild dehydration or fluid balance alterations commonly seen in critical care settings. However, no statistically significant changes were observed in other laboratory parameters, including random blood sugar (RBS), hemoglobin, total leukocyte count (TLC), pH, PCO_2, PO_2, bicarbonate (HCO_3), potassium (K), creatinine, urea, international normalized ratio (INR) and AST, or ALT ($P > 0.05$). This suggests that the treatment regimen effectively maintained electrolyte and metabolic stability. These findings are consistent with studies by **Luo *et al* [10]** and **Zheng *et al.* [11]**, which also reported significant increases in sodium levels and PCO_2 among patients with elevated intracranial pressure (ICP), while other laboratory values remained largely unchanged. In our study, follow-up CT scans on day 3 revealed no statistically significant change in the number of patients showing improvement in brain edema compared to day 1 ($P > 0.05$). However, there was a significant reduction in the severity of brain edema ($P < 0.001$). This aligns with findings by **Steffen *et al.* [12]** who reported a significant decrease in brain edema on follow-up CT scans within 48–72 hours after successful recanalization in stroke patients ($P < 0.001$).

In the present study, ultrasound-guided binocular ONSD measurements significantly decreased on day 3 compared to day 1 (5.89 ± 0.53 mm vs. 7.21 ± 0.74 mm; $P < 0.001$). This finding is consistent with results from **Lioi *et al*. [13]** who reported a significant decrease in ONSD from baseline to follow-up in 20 adult patients with severe traumatic brain injury (TBI). Similarly, **Schuchardt *et al.* [14]** noticed that patients suffering from acute cerebral venous thrombosis experienced a significant decrease in ONSD following successful recanalisation, indicating a possible relationship between the lowering of intracranial pressure (ICP) and the regression of ONSD.

In our study, ophthalmoscopic follow-up on day 3 demonstrated a statistically significant improvement in papilledema grades compared to day 1 ($P < 0.001$). Similarly, **Pruckner *et al.* [15]** reported significant improvements in papilledema grades among 113 patients with idiopathic intracranial hypertension following treatment. In contrast, **Schuchardt *et al.* [14]** observed improvements in papilledema grades during follow-up, but these changes did not reach statistical significance ($P = 0.152$). Additionally, a statistically significant association was identified between CT findings of brain edema and ultrasound-derived ONSD measurements in our study. This aligns with previous research indicating a strong correlation between elevated ONSD measurements and increased intracranial pressure (ICP) markers on CT imaging ($P < 0.001$). These findings highlight the reliability of ONSD measurements in reflecting changes in ICP as observed on CT scans. Furthermore, they underscore the potential of ONSD as a rapid, bedside alternative to CT imaging for both initial diagnostics and follow-up care, particularly in critical care settings **[16-18].**

In our study, no significant association was observed between ophthalmoscopic findings and CT scans for detecting brain edema on day 1. However, by day 3, a significant association emerged. Ophthalmoscopy demonstrated a sensitivity of 98%, specificity of 50%, accuracy of 91%, positive predictive value (PPV) of 92%, and negative predictive value (NPV) of 80% for detecting brain edema. These results suggest that early ophthalmoscopic findings may not reliably predict CT-detected edema, likely due to a delay in visible optic nerve changes following ICP elevation. In contrast, **Schuchardt *et al.* [14]** reported lower sensitivity (63.6%) and specificity (76.9%) for ophthalmoscopy in predicting brain edema, with a PPV

of 43.8% and NPV of 88.2%. Similarly, **K *et al.*** [19] found that while ophthalmoscopic detection of papilledema had 100% specificity, its sensitivity was only 46%. **Mitchell *et al.*** [20] also noted that confirmed papilledema on ophthalmoscopy had a sensitivity of 48%, specificity of 100%, PPV of 100%, and NPV of 64% for elevated ICP, with no significant correlation to neuroimaging findings. These discrepancies highlight the variability in ophthalmoscopy's diagnostic accuracy and its limitations in early detection compared to imaging techniques. We found that ONSD measurements consistently showed higher intracranial pressure (ICP) than CT results did in this study. The specificity, accuracy, and sensitivity of a first-day ONSD cutoff of ≥ 6.55 mm were 98%, 88%, and 94% respectively. Due to an increase in intracranial pressure (ICP), the ideal threshold likely decreased to ≥ 5.675 mm by day 3 exhibiting a sensitivity of 76% and specificity of 75%. These findings are consistent with prior research. **Kerscher *et al***. [19] discovered that a negative predictive value (NPV) of 82.6%, a sensitivity of 92%, a specificity of 86.4%, and an ONSD cut-off of ≥5.73 mm yielded a total of 93.9%. **Schuchardt *et al.*** [14] reported the following results: Sensitivity of 88.9%, specificity of 61.5%, and NPV of 96% when the ONSD was greater than 5.8 mm at baseline. Similarly, **Kerscher *et al.*** [19] observed that an ONSD cutoff of ≥5.0 mm achieved 86.42% sensitivity, 64.29% specificity, a PPV of 93.33%, NPV of 45.00%, and an overall accuracy of 83.16%.

The diagnostic ONSD cutoff values in our study and comparative studies ranged from 5.0 mm to 6.55 mm, likely reflecting differences in patient demographics, ultrasound techniques, and the timing of ICP assessment. These variations underscore the importance of tailoring ONSD thresholds to specific clinical contexts.

LIMITATIONS

This study was conducted based on medical data from a single medical center. The number of patients included in the study was a little bit limited. This study was totally self-funded.

CONCLUSION

Clinically, optic nerve sheath diameter measurement is an effective, rapid, bedside, and non-invasive tool for ICP monitoring that guides early intervention, particularly in critical settings where immediate CT access may be limited.

Financial support and sponsorship: Nil.
Conflict of Interest: Nil.

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