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Accuracy of Optic Nerve Sheath Diameter Measurement as a Predictor of Intracranial Pressure in Traumatic Brain Injury

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ABSTRACT

Background: Ultrasound assessment of optic nerve sheath diameter (ONSD) has been used as a promising tool to aid in the diagnosis of elevated intracranial pressure (ICP). Optic nerve sheath is contiguous with the dura matter surrounding the brain and contains cerebrospinal fluid, which allows transmission of pressure from the cranium.

Objective: To determine the diagnostic accuracy of measurement of ONSD by using ocular ultrasonography to detect elevated ICP in patients with TBI in Emergency Department.

Patients and methods: This prospective cross-sectional observational study that was carried out on 99 patients presented and admitted to Mansoura University Emergency Hospital with traumatic brain injury (TBI) over a year from June 2020 to June 2021.

Results: The clinical features of raised ICP had low specificity (38%), positive predictive value (PPV) (61.7%), and accuracy (69%) for diagnosis of raised ICP with high significant statistical difference (62% vs 100%) towards group 2. The ONSD were much higher (P <0.01) in group 2 (6.493 ± 0.586 mm) than group 1 (3.93 ± 0.976 mm). The cutoff value of binocular mean ONSD for diagnosing raised ICP was > 5 mm with sensitivity of 100 %, specificity of 96%, and accuracy of 99%. The optimal cutoff value to predict mortality rate was >6.8 mm with modest sensitivity and accuracy. While the optimal value to predict unfavorable Glasgow Outcome Scale (GOS) was >6.05 mm with high sensitivity and accuracy.

Conclusion: ONSD measurement via bedside ocular ultrasound is a useful, non-invasive method for early diagnosis of elevated ICP in adult patients with TBI in the Emergency Department.

Keywords: Intracranial Pressure, Optic Nerve Sheath Diameter Measurement, Traumatic Brain Injury

INTRODUCTION

Traumatic brain injury (TBI) is defined as brain damage resulting from external mechanical force leading to physical, cognitive, emotional and behavioral symptoms and outcome can range from complete recovery to permanent disability or death. TBI is a major cause of morbidity and mortality worldwide, mainly in children and young adults [(1)]. Timely diagnosis of post-traumatic elevated ICP can allow for early momentary procedures and definitive treatment in the neurologically compromised patient and is associated with improved outcomes. Invasive ICP monitoring is the gold standard for demonstrating ICP increase but can lead to complications as hemorrhage, infection, malposition and device malfunction. Also, it is not always available in many healthcare facilities [(2)].

Hence, noninvasive methods have been developed for detection of elevated ICP. CT is considered as the noninvasive method of choice in this concern, but several limitations for its use exist as transport of critically ill patient, excessive radiation hazards exposure, being time-consuming and high cost, which has urged researchers to find other alternatives [(3)]. Fundoscopy allows detection of papilledema which may take hours to days to develop after sustained elevation of CSF pressure, which stands for increased ICP. Transcranial Doppler pulsatility index has been shown to reflect decreases in cerebral perfusion pressure due to increases in ICP. However, both maneuvers are not always easy to perform even in expert hands [(4)].

Ultrasonography has become an indispensable component of the emergency department as a result of being an easy-to-learn, bedside, fast, noninvasive, and reproducible method. Use of the focused assessment with sonography in trauma (FAST) examination has already gained wide acceptance as an adjunct in evaluating patients with major trauma to the chest and abdomen. However, the role of ultrasonography in assessing ICP remains unclear [(5)].

The optic nerve is a tubular structure surrounded by the same meningeal layers as the brain with its intraorbital segment is evaluable sonographically. It appears as a hypoechoic linear structure located inside the optic nerve sheath. Between the optic nerve and the sheath is situated the subarachnoid space which experiences the same pressure change as the intracranial compartment. Thus, the use of bedside ocular ultrasonography in measuring optic nerve sheath diameter (ONSD) may be a useful method for detecting raised ICP [(5)].

The objectives of the current study are to determine the diagnostic accuracy of measurement of ONSD by using ocular ultrasonography to detect elevated ICP in patients with TBI in Emergency Department (ED). Also, to determine the prognostic value of ONSD measurement by ultrasonography for outcome.

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PATIENTS AND METHODS

This prospective cross-sectional observational study that was carried out on 99 patients presented and admitted to Mansoura University Emergency Hospital (a level one trauma center with about 250,000 visit and 25,000 trauma cases per year) with TBI over a year from June 2020 to June 2021. The studied patients were divided into 2 groups: group 1 (patients with no findings of increased ICP on CT brain); 41 patients and group 2 (patients with findings of increased ICP on CT brain); 58 patients.

Inclusion criteria: Patients with TBI, age group above 18 years old, and both genders.

Exclusion criteria: Age group less than 18 years old, ocular trauma, history of ocular pathology, history of a previous operation to the eye, treatment with medications affecting the intracranial pressure, and patients who refused to participate in the study.

The primary survey:

The initial resuscitation occurred concurrently with primary assessment. When a life-threatening condition was found, immediate corrective actions were taken, and its effects were evaluated before moving on to the next step. The primary assessment was proceed with using the "ABCDE" approach.

A. Airway and cervical Spine.
B. Breathing and ventilation.
C. Circulation and bleeding control.
D. Disability and neurologic assessment.
E. Exposure and environment control.

To complete the primary survey, all polytrauma unstable patients were exposed in the resuscitation room to the following: (1) FAST (Focused assessment sonography for trauma patient): in polytrauma patients for possible internal hemorrhage. (2) Portable chest and pelvis X-ray: Anteroposterior supine view for unstable patients using Shimadzu Collimator r-20c portable X–ray device.

The secondary survey:

I. After initial resuscitation effort, all patients were subjected to full history taking including age, gender, mode and time of trauma, time of arrival and resuscitation.

II. Clinical Examination including:
1) Vital signs.
2) Local examination.
3) Neurological examination.
4) Complete general examination: head-to-toe examination to define other associated or occult injuries.

III. Investigations:

A. Laboratory tests:
- Complete blood count, blood grouping and cross matching.
- Coagulation profile (PT, PTT, INR).
- Liver functions test (ALT, AST, Albumin, Bilirubin).
- Kidney functions test (serum creatinine, Blood Urea Nitrogen).

B. CT brain:
- By using Toshiba scanner Aquilion Prime TSX-303A (164-MCCT scanner) with reconstruction at 0.5 mm slice thickness.
- Looking for signs of elevated ICP: Basal cisterns compression/absence, ventricles compression/absence, effacement of sulci, midline shift, and loss of grey/white matter differentiation.

C. ONSD measurement by ultrasound: By using LOGIQ P5 ultrasound machine. It was performed within 15 minutes after brain CT scans. The ONSD was measured bilaterally at 3 mm before entrance of the optic nerve to the globe. The mean ONSD measurements from each eye were averaged to create a binocular ONSD measurement.

Ethical considerations:

Study protocol was submitted for approval by Institutional Review Board (IRB). The research objectives were explained to the participants' relatives individually and in groups. The researcher was available throughout the study. Informed written consent was obtained from each participant's relatives sharing in the study. Confidentiality and personal privacy were respected in all levels of the study. Collected data were not used for any other purpose. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0**.** Qualitative data were expressed as number and percentage. Quantitative data were expressed as mean, standard deviation for parametric data and median (minimum and maximum) for non-parametric data after testing normality using Kolmogorov-Smirnov test. Significance of the obtained results was judged at the 5% level. All tests were 2 tailed. Independent t-test was used to compare means of the 2 groups, while the paired (T) test was used to compare the means of 2 variables for a single group.

Chi-square (χ^2) test was used for comparison between groups as regards qualitative data. Receiver Operating Characteristic (ROC) curve analysis was used to obtain a ROC plot and a complete

sensitivity/specificity report. P < 0.05 was considered significant.

RESULTS

Most of the studied patients in group 1 and group 2 were males of middle age. There were no significant statistical differences in the demographic parameters and different modes of trauma between both groups (Table 1).

Table (1): Demographic data and modes of trauma of the studied cases

	Group 1 (N=41)	Group 2 (N=58)	P value
Age:			
Mean ± SD	35.7± 9.4	34.1 ± 10.1	0.4142
Median (Min-Max)	31 (19-79)	29 (19-75)	
Gender:			
Male	32 (78%)	39 (68%)	0.240
Female	9 (22%)	19 (32%)	
Mode of trauma:			
MVC	14 (34%)	23 (40%)	0.577
RTA	11 (26%)	13 (22%)	0.614
FFH	7 (18%)	14 (24%)	0.482
Struggle	9 (22%)	8 (14%)	0.289

There was a high significant statistical difference between both groups as regard means and grades of GCS (Table 2).

Table (2): Classification of TBI in the studied cases

	Group 1 (N=41)	Group 2 (N=58)	P value
Glasgow Outcome Scale			
Mean ± SD	12.3 ± 3.11	8.1 ± 2.79	<0.001**
Median (Min-Max)	11 (7-15)	6 (3-12)	
Grading of traumatic brain injury			
Mild (13-15)	30 (74%)	2 (4%)	< 0.001**
Moderate (9-12)	8 (20%)	15 (26%)	
Severe (3-8)	3 (6%)	41 (70%)	

** High statistically significant difference

The CT brain findings in the patients of group 2 are shown inn table 3.

Table (3): CT findings of raised ICP in group 2

Group 2 (N=58)		
CT findings of raised ICP	**Frequency**	**Percentage**
Cisterns compression	32	55%
Ventricles compression	45	78%
Loss of grey/white matter differentiation	31	53%
Sulci effacement	36	62%
Midline shift	29	50%

[#] Clinical features of raised ICP are not mutually exclusive, so totals can be >100%

The mean values of ONSD showed high significant statistical difference between both groups. While, the mean values of ONSD were closely related to each other in right and left sides of group 1 and also in group 2.

Table (4): ONSD estimation in the studied patients

ONSD	Group 1 (N=41)	Group 2 (N=58)	P value
Right Side:			
Mean ± SD	3.99 ± 0.765	6.455 ± 0.761	< 0.001 **
Median (Min-Max)	4 (2.56 - 5)	6.54 (4.98 - 7.45)	
Left Side:			
Mean ± SD	3.87 ± 0.771	6.465 ± 0.744	< 0.001 **
Median (Min-Max)	4.06 (2.5 – 4.99)	6.55 (5 - 7.49)	
	P= 0.5406	P= 0.8715	
Mean (Binocular):			
Mean ± SD	3.92 ± 0.767	6.459 ± 0.750	< 0.001 **
Median(Min-Max)	4.02 (2.5 - 5)	6.6 (4.98-7.49)	

** High statistically significant difference

The cutoff value of binocular mean ONSD for diagnosing increased ICP was > 5 mm (Table 5).

Table (5): Comparison of ONSD and clinical features of raised ICP

	Cut-off value	Sensitivity	Specificity	PPV	NPV	AUC	Accuracy
ONSD	> 5 mm	96%	100%	100%	96.1%	0.999	98%
Clinical features		100%	38%	61.7%	100%	0.69	69%

PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under curve

The outcome assessment parameters showed high significant statistical differences in favor of group 1 regarding mortality rate and poor neurological outcome (unfavorable Glasgow Outcome Scale "GOS") of survived patients (Table 6).

Table (6): Outcome of the studied cases

	Group 1 (N=41)	Group 2 (N=58)	P value
Mortality rate:			
Died	2 (4%)	30 (52%)	< 0.0001**
Survived	39 (96%)	28 (48%)	
Unfavorable Outcome (GOS) of survival at discharge:			
Total	N=39	N=28	
N (%)	4 (10.5%)	18 (64.3%)	< 0.0001**

** High statistically significant difference

Regarding to the outcome, the cutoff value of ONSD > 6.8 for mortality rate prediction and > 6.05 mm for unfavorable GOS prediction. The sensitivity and diagnostic accuracy for unfavorable GOS appeared to be obviously higher than for mortality rate (Table 7).

Table (7): ONSD in relation to outcome in group 2

ONSD	Cutoff value	Sensitivity	Specificity	AUC	Accuracy
Mortality rate	> 6.8 mm	46.15%	100%	0.675	72%
Unfavorable GOS	> 6.05 mm	80%	100%	0.96	87.5%

DISCUSSION

In this study, most of the studied patients were of middle age. Male gender predominated in group 1 and group 2. The differences in demographic data between both groups were not statistically significant. The reason why middle-aged males are the most frequently involved patients in trauma because they have a tendency to share in high risk activities as over-speed and drive without wearing any protective devices leading to high incidence exposure to motorcycle crashes, which add further economic burden over the community [(6)].

In the present study, the modes of trauma in both groups were closely approximated without significant differences. The most common mode of trauma was MVC in 34% and 40%; followed by RTA in 26% and 22%, FFH in 18% and 24%, and struggle in 22% and 14% in group 1 and group 2 respectively. In concordance, **Agrawal *et al.*** [(7)] informed that the modes of trauma were not significantly different between the group with no ICP elevation and the other with ICP elevation (P= 0.28). The most common mode of trauma was MVC (76% and 81%) followed by FFH (15% and 19%) in both groups respectively and other modes in 9% of the 1st group.

In the current study, the mean values of GCS were much higher in group 1 (12.3± 3.11) than in group 2 (8.1±2.79). In group 1; mild TBI was prevalent in 74%. While in group 2; severe TBI was the predominant form in 70% with a high significant statistical difference between both groups regarding the severity. Likewise, **Altayar *et al.*** [(8)] reported that GCS values were lower in patients with positive CT criteria for high ICP than negative criteria for high ICP (6.79 ± 3.3 vs 8.3 ± 2.49 respectively) but without significant statistical difference between both groups. We are in agreement with **Mabrouk *et al.*** [(9)] who found that significant lower GCS values in patients of group B compared with group A (P < 0.01). Mild TBI was found in 67.5% of group A, while most of patients in group B (65%) had severe TBI with a significant statistical difference between the two groups in this regard (P < 0.01). There was a significant inverse correlation between the mean ONSD and the GCS of patients. Also **Canakci *et al.*** [(10)] who performed a study to investigate the value of the measurement of ONSD by ultrasound in patients presenting to the ED with headache; stated that significant drop in GCS was seen in patients with increased ICP. Moreover, there was a significant inverse correlation between the mean ONSD and the GCS of patients.

In this study, CT brain was used as gold standard for diagnosis of elevated ICP. The findings of raised ICP (group 2) were ventricles compression or absence in 78%; sulci effacement in 62%; cisterns compression or absence in 56%; loss of grey/white matter differentiation in 54% and midline shift in 50%. In the same way, **Mabrouk *et al.*** [(9)] listed CT findings of elevated ICP as loss of grey-white matter differentiation (80%), sulci effacement (77.5%), cisterns compression (65%), midline shift (65%) and ventricles compression (60%). Also, **Qayyum *et al.*** [(11)]**;** who studied if ultrasound guided measurement of the ONSD accurately predicted elevated ICP as demonstrated by cranial CT features, which were sulcal effacement with significant edema (87%), midline shift greater than 3 mm (29%), collapse of the third ventricle (4%), hydrocephalus (4%) and combination of features (17%).

In the present study, the clinical features (altered mental status, abnormal posturing, unequal dilated and fixed pupils and Cushing's triad) had low specificity (38%), PPV (61.7%), and accuracy (69%) for diagnosis of raised ICP with high significant statistical difference (62% vs 100%) towards group 2. So, these features were not a trustworthy scale for diagnosis of raised ICP. As well, **Mabrouk *et al.*** [(9)] revealed that clinical features

low sensitivity (30%) and specificity (72.5%) for diagnosis of increased ICP, but without significant differences between the study groups (27.5% and 30%). Also, **Tarzamni, *et al.*** [12] and **Amini *et al.*** [13] clarified that physical examination alone is not dependable and often fail to define elevated ICP because of low sensitivity, specificity and diagnostic accuracy.

In the current study, the monocular and binocular mean values of ONSD were much higher in group 2 (6.493 ± 0.586 mm) than group 1 (3.93 ± 0.976 mm). Whereas, the mean values of ONSD in right and left sides in each group were nearly equal. The cutoff value of binocular mean ONSD for diagnosing raised ICP was > 5 mm with sensitivity of 100 %, specificity of 96%, PPV of 100%, NPV of 98.04%, AUC of 0.99 and accuracy of 99%. Similarly, **Altayar *et al.*** [8] stated that the mean value of ONSD measured by US was (6.3 ± 0.6 mm) in group of positive CT criteria for high ICP compared with (5.5 ± 0.7 mm) in negative group with significant difference between 2 groups ($p < 0.001$). ONSD measurement by US and also measured by CT had the same cutoff value > 6.1 mm predicted high ICP determined by invasive measurement with 84.62% sensitivity, 66.67% specificity, 78.6% PPV, 75% NPV and significant AUC of 0.85. Equally, **Mabrouk *et al.*** [9] informed that the mean ONSD was significantly higher ($P <0.001$) in patients with increased ICP (group B) [6.493 ± 0.586 mm] than in patients with normal ICP (group A) [4.047 ± 0.677 mm]. The cutoff value of ONSD for diagnosing increased ICP was >4.95 mm with sensitivity of 100 %, specificity of 95 %, PPV of 95.2%, NPV of 100% and accuracy of 99.6%.

In addition, **Lee *et al.*** [14] conveyed a multicenter study to investigate normal range of ONSD and its optimal threshold for detecting raised ICP confirmed by CT or MRI brain in Korean patients. The ONSD with raised ICP (5.9 mm [5.8–6.2]) was significantly higher than those without raised ICP (5.2 mm [4.8–5.4]) ($P<0.01$) and normal control group (4.9 mm [4.6–5.2]) ($P<0.01$). Between patients without raised ICP and normal control group, the difference of ONSD did not reach statistical significance ($P = 0.31$). The cutoff ONSD >5.5 mm yielded 98.77% sensitivity and 85.19% specificity. Correspondingly, **Aduayi *et al.*** [15] stated that the mean binocular ONSD was obviously higher ($P < 0.01$) in patients with brain injury with cranial CT confirmed features of increased ICP (5.7 ± 0.59 mm) than in patients with brain injury without any cranial CT evidence of increased ICP (4.8 ± 0.39 mm). The controls had a lower mean binocular ONSD (4.5 ± 0.22 mm) than other groups. The cutoff value that best predicts raised ICP was >5.2 mm (sensitivity of 81.2%, specificity of 100% and AUC of 0.9). Similarly, **Shirodkar *et al.*** [16] who evaluated the ONSD as a marker for evaluation and prognostication of ICP and found ONSD cutoffs (4.6 mm for females; 4.8 mm for males) had sensitivity between 84.6 % (females) and 75 % (males) and a specificity of 100 % (both genders) for the detection of MRI signs of elevated ICP. Similarly, **Qayyum *et al.*** [11] informed that the cutoff value of ONSD to predict elevated ICP on cranial CT scan of 5.0 mm yielded a sensitivity of 100%, specificity of 75%, PPV 95.4% and NPV of 100%. Also, **Major *et al.*** [17] who assessed if ultrasound measurement of ONSD can accurately predict the presence of raised ICP in patients in the emergency department reported that the cutoff mean value of ONSD greater than 5.0 mm was 100% specific and 86% sensitive for identification of raised ICP on CT brain.

In the same way, **Wang *et al.*** [18] conducted a study in Chinese. The ONSD of the elevated opening pressure on lumbar puncture (LP) group (4.58±0.46 mm) was significantly higher than that of the normal opening pressure on LP group (3.55±0.38 mm, $p<0.001$). The ONSD cutoff point for the identification of elevated opening pressure on LP was 4.1 mm which yielded a sensitivity of 95% and a specificity of 92%. They concluded that ONSD is an accurate predictor of elevated opening pressure on LP. The cutoff point of this predictor in Chinese was remarkably lower than that found in Caucasian. In a study performed by **Agrawal *et al.*** [7], ONSD demonstrated a modest, statistically significant correlation with ICP. However, a predetermined level of diagnostic accuracy to justify routine clinical use as a screening test was not achieved. The highest expert-measured ONSD; to detect ICP > 22 mm Hg; was greater than 7.2 mm a sensitivity of 82% (48-98%) and specificity of 79% (70-86%) with AUC 0.81 (0.73-0.87) .

In the current study, the binocular mean ONSD was significantly correlated with the severity of TBI, clinical features of raised ICP (unequal dilated, fixed pupil or Cushing's triad), and CT findings of raised ICP (cisterns, ventricular compression or midline shift). Although the outcome was significantly worse ($P <0.01$) in group 2, the ONSD is strong predictor of neurological outcome (GOS) only. The cutoff value of ONSD for prediction of mortality was >6.8 mm with modest sensitivity (46.15%) and accuracy (72%), while for prediction of unfavorable GOS was 6.05% with high sensitivity (80%) and accuracy (87.5%). Similarly, **Mabrouk *et al.*** [9] reported that the mean ONSD was significantly correlated to the class of TBI. There was also a significant correlation between mean ONSD and the presence of ventricles absence/compression on CT brain in patients of group B. Correspondingly, **Canakci *et al.*** [10] found that there was a strong correlation between the ONSD and the survival rate, which was significantly higher ($P<0.001$) in patients with normal ONSD than in patients with increased ONSD (77.4% and 22.6%) respectively. As well, **Gao *et al.*** [19], who evaluated the diagnostic and prognostic value of the ONSD on neurological outcome, stated that ONSD was significantly greater in patients with unfavorable GOS (6.1 ± 0.7 mm) than in patients with favorable GOS (5.5 ± 0.7 mm), ($p = 0.018$). They concluded that ONSD > 5.5 mm predicted poor outcome, with AUC of 0.717, 70% sensitivity, and 69.2% specificity.

The modest sensitivity and diagnostic accuracy of ONSD measurement by ultrasonography for prediction

of mortality in patients with TBI in this study could be explained by the fact that critically ill patients with diminished physiologic reserve are subjected to many complications associated with therapy as hospital acquired infections including ventilator-associated pneumonia, central line-associated bloodstream infection, catheter-associated urinary tract infection, surgical site infection, venous thromboembolism, deep venous thrombosis, and pulmonary embolus. These complications are associated with significantly higher mortality.

Glasgow outcome scale (GOS) has been extensively employed to outcome evaluation of TBI patients taking into consideration their physical, social and cognitive sequelae. Despite some controversies regarding GOS reliability, it is widespread used to evaluate long term outcome of severe brain injured patients [(20)].

CONCLUSION

- The clinical assessment alone is not a reliable indicator of elevated ICP and has low sensitivity, specificity and diagnostic accuracy.
- ONSD measurement via bedside ocular ultrasound is a useful, non-invasive method for early diagnosis of elevated ICP in adult patients with TBI in the emergency department.
- There is strong correlation between ONSD and degree of TBI, clinical features of raised ICP (unequal dilated, fixed pupil or Cushing's triad), and CT findings of raised ICP (cisterns, ventricular compression or midline shift).
- The optimal cutoff point of ONSD for identifying elevated ICP is >5 mm with sensitivity of 100 %, specificity of 96 % and diagnostic accuracy of 99%.
- The optimal cutoff value for prediction of poor neurological outcome is >6.05 mm with sensitivity of 80%, specificity of 100% and diagnostic accuracy of 87.5%.
- The ONSD has a potential prognostic value for a poor neurological outcome and uncertain for mortality.

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