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Original Article

A noninvasive method for the estimation of increased intracranial pressure in patients with severe traumatic brain injury using optic nerve sheath diameter measured on computed tomography head

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ABSTRACT

Background: Measurement of optic nerve sheath diameter (ONSD) using ocular ultrasonography has shown a promise in predicting increased intracranial pressure (ICP). However, this method is dependent on operator technique and equipment availability. We propose an alternative method of measuring ONSD and Marshall score grading by utilizing initial computed tomography (CT) head obtained on admission. We believe that such a technique could help predict patients requiring an invasive ICP monitor on admission.

Methods: Patients were retrospectively selected from the neurosurgery database of a level II trauma center. Control patients originated from a database of nontraumatic brain injury (TBI) patients with a negative CT head and no intracranial pathology. Study subjects included patients aged 18–90 years, who sustained a severe TBI requiring placement of an ICP monitor on admission. All patients had a non-contrast CT head before the placement of an ICP monitor. Patients receiving any intervention for decreasing suspected elevated ICPs and those with any documented orbital fractures before ICP monitor placement were excluded from the study. All measurements were performed by at least of two independent assessors.

Results: A total of 242 patients were reviewed, of which 204 (100 control and 104 intervention) met inclusion criteria for this study. The average age in the control group was 49.1 ± 22.9 years old while the average age of the intervention group was 36.9 ± 15.1 years ($P < 0.0001$). The average Glasgow Coma Scale was 7 in the intervention group. The average ONSD of the control group was 5.73 ± 0.58 mm compared to 6.76 ± 0.83 mm in the intervention group ($P < 0.0001$). Linear regression analysis demonstrated a statistically significant correlation between ONSD and opening ICP ($r = 0.40$, $P < 0.001$) and peak ICP ($r = 0.31$, $P < 0.0001$). An ONSD ≥6.0 mm + Marshall score ≥3 on initial CT head demonstrated a 92.5% sensitivity, 92.6% specificity, and 96.1% positive predictive value for developing an ICP ≥20 mmHg during hospitalization.

Conclusion: Utilizing ONSD in combination with Marshall score grading on initial CT head is a strong predictor of elevated ICP. These criteria can be used in future studies to develop more objective criteria to guide ICP monitor placement.

Keywords: Intracranial pressure, Optic nerve sheath diameter, Traumatic brain injury

INTRODUCTION

Traumatic brain injury (TBI) affects approximately 1.4 million individuals per year in the United States and is a major cause of disability, death, and economic cost to patients, their families, and society as a whole.[19] Current treatment options for the prevention of secondary brain injury center on management of elevated intracranial pressure (ICP) and optimization of cerebral perfusion pressure. The most widely used methods for measuring ICP involve placement of a ventriculostomy or an intraparenchymal monitor. In addition to the risk of procedural complications such as bleeding and infection, these monitors also require specialized training for both physicians and nurses. The BEST-TRIP trial recently called into question the necessity of placing ICP monitors as they found no difference in outcome with the use of ICP monitoring.[6] In light of this study, the most recent Brain Trauma Foundation guidelines for TBI changed the recommendation for ICP monitoring from a specific set of criteria (Glasgow Coma Scale [GCS] 3–8+ abnormal computed tomography [CT] head, age >40 + posturing, or SBP <90 + normal CT head) to a more general recommendation that "ICP monitoring is recommended to reduce in-hospital and 2-week post injury mortality."[5] This change is indicative of the fact that more objective parameters are needed to reliably predict which patients benefit from invasive ICP monitoring. A reliable, noninvasive predictor of increased ICPs would aid in effective triaging of patients to a neurosurgical center. It would also allow health-care providers at non neurosurgical centers to effectively employ therapeutic strategies to reduce suspected increased ICPs and determine who may need early intervention.

Recent studies have examined the efficacy of various noninvasive methods to predict increased ICPs and measurement of the optic nerve sheath diameter (ONSD) using ultrasound or CT has accurately predicted increased ICP or intracranial pathology.[1,2,4,8,10,11,16-18,20,23-26,28,32-34] The optic nerve sheath is anatomically continuous with the dura mater and has a trabeculated subarachnoid space through which cerebrospinal fluid flows. Previous studies have shown that the fibrillary arrangement and density of the arachnoid trabeculations are responsible for the distensibility of the nerve sheath – allowing it to expand should ICP increase. ONSD has been validated in several studies as an independent predictor of morbidity and mortality in TBI.[14,21] A limitation to this method is that it is dependent on operator technique, equipment availability, and variable anatomy.[3,8,9,12,23,29,31,36,37] CT measurement of ONSD has been studied and correlated with ICP; however, no studies have demonstrated an ability to predict developing elevated ICP. Marshall grading score is a CT score validated in the literature that classifies TBI according to the radiographic severity of injury. This has shown good prognostic value in predicting increased ICP in severe TBI patients. However, no studies in the literature that establish a quantitative relationship between Marshall grading system and other noninvasive methods to predict elevated ICPs. The purpose of our study is to establish a method for measuring ONSD by utilizing the initial CT head and demonstrate that such a technique, in correlation with Marshall grading, will help predict patients requiring an invasive ICP monitor on admission.

METHODS

This is a retrospective review of a prospectively collected database from two level II trauma centers. Study subjects included patients aged 18–90 years old who sustained a severe TBI (GCS ≤8) that had an ICP monitor placed on admission. All patients had a non-contrast CT head before placement of an ICP monitor. Patients receiving a craniotomy or craniectomy for decreasing suspected elevated ICPs before ICP monitor placement were excluded. Furthermore, patients with any documented orbitofacial trauma or concerns for cerebrospinal fluid leak were excluded from the study. The opening pressure after placement of the ICP monitor and peak ICP during hospitalization was recorded (mmHg). The same CT head was used to determine the Marshall score. We established a control group that consisted of 100 patients with negative CT head. McKesson Radiology PACS and Sectra PACS were used as the software for measuring ONSDs. The ONSD was measured by a team comprising of senior neurosurgery residents, staff neurosurgeon, and neuroradiologist at our respective institutions. The thickness of the CT slices was 5 mm in all subjects.

ONSD measurement protocol

Measurements of ONSD were obtained by adhering to a strict protocol established by our team to minimize interobserver variability. The mediastinum window was used to obtain all measurements. The ONSD was measured 3 mm behind the posterior aspect of the globe on axial sequences [Figure 1]. Bilateral ONSD was measured in all patients. The average of ONSD was also used in our statistical analysis to help minimize the effects of the laterality of any lesions.

Data analysis

All data points were entered into our study database. The average ONSD of the left, right, and both eyes was calculated, and a linear regression analysis was conducted to determine the relationship between ONSD and ICP. Sensitivity, specificity, and positive predictive value calculations were also conducted. Fisher's exact test was used to determine significance, which was defined as $P < 0.05$.

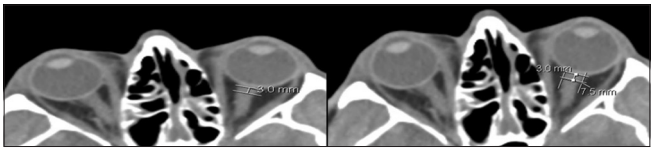

Figure 1: Computed tomography imaging illustrating the appropriate axial cut necessary to accurately measure the optic nerve sheath diameter at a point 3.0 mm posterior to the globe.

RESULTS

A total of 242 patients from 2012 to 2018 were identified from our database, and 204 patients (104 intervention, 100 control) met the inclusion criteria for this study. The average age in the intervention group was 37.1 years old and median initial GCS was 6.6. All ICP monitoring was in the form of external ventricular drain (EVD) placement. The total number of males overall (58 control and 83 intervention) was statistically significant ($P = 0.0008$).

Control group

Our control group consisted of 100 patients (58 males and 42 females) with no evidence any intracranial abnormality or severe head injury. Mean ONSD in the control group was 5.73 ± 0.58 mm. Mean ONSD in the male population was 5.82 ± 0.53 mm and 5.60 ± 0.63 mm in the female population. The ONSD range was 4.25–7.15 mm [Table 1]. The average age of the control group was 49.1 ± 22.9 years old, and all patients were GCS 15 with no evidence of any pathology.

Intervention group

The average ONSD of both the eyes was 6.72 ± 0.79 mm. The average ONSD of the left eye was 6.76 ± 0.83 mm and the right eye was 6.63 ± 0.79 mm. The average age in the intervention group was 36.9 ± 15.1 years [Table 2]. The difference in average ONSD from the control group was statistically significant ($P < 0.0001$). The average opening pressure at the time of ICP monitor placement was 16.6 ± 10 mmHg. Correlation analysis showed a trend in increasing opening ICP with increasing ONSD, particularly when ONSD was >6.0 mm ($P < 0.0001$, $r = 0.40$) [Figure 2].

Further analysis revealed differences in the sensitivity and specificity between the laterality and mean ONSD measurements [Figure 3]. The left ONSD in our population had a sensitivity of 92.2% and a specificity of 33.3% with a positive predictive value of 79.7% ($P = 0.0002$). The right ONSD had a sensitivity of 81.8% and a specificity of 25.9% with a positive predictive value of 75.9% ($P = 0.41$). The mean ONSD value in our population had a sensitivity of 87.2% and specificity of 33.3% with a positive predictive value of 78.8% ($P = 0.04$). A Marshall score ≥3 had a sensitivity of 66.2%, specificity of 81.4%, and positive predictive value of 91% ($P = 0.0001$). When the ONSD cutoff of 6.0 mm was combined with an admission of Marshall score ≥3, it yielded a sensitivity of 92.5%, specificity of 92.6%, and positive predictive value of 96.1% that a patient would have peak ICP ≥20 mmHg during the hospital course ($P = 0.001$).

Table 1: The normative measurements in our study from a sample of normal individuals without any trauma or pathology seen on CT.

Measurement	Male (n=58)	Female (n=42)	Total (n=100)
Mean±SD	5.82±0.53	5.60±0.63	5.73±0.58
Range	4.8–7.15	4.25–7.15	4.25–7.15
Average age	45.2	54.48	49.1

CT: Computed tomography, SD: Standard deviation

Table 2: Measurements of the intervention group in those whom an intracranial pressure monitor was placed.

Measurement	Male (n=83)	Female (n=21)	Total (n=104)
Mean±SD	6.76±0.79	6.45±0.62	6.72±0.79
Range	4.8–8.55	5.6–8.0	4.8–8.55
Average age	36.5	38.2	37.1

SD: Standard deviation

DISCUSSION

Measurement of ONSD on CT is an alternative method of measuring ONSD that has been previously validated and was used in this study.[35] Its clinical application is similar; however, CT measurement has a tendency to overestimate ONSD by 10% in comparison to ultrasonography.[7] Different techniques have been employed in CT measurement of ONSD with authors measuring 3 mm behind the globe and others measuring up to 10 mm behind the globe.[3] This accounts for the great heterogeneity in normal

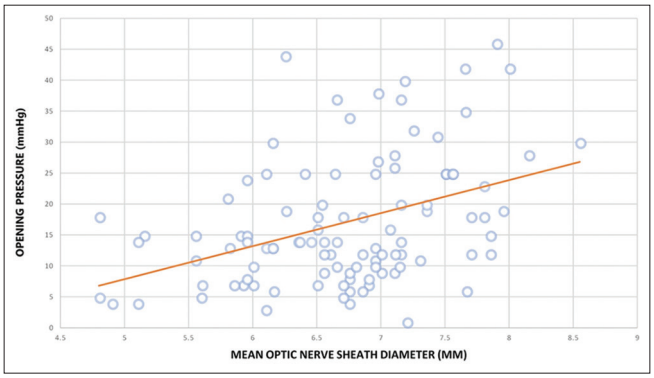

Figure 2: The correlation of increasing optic nerve sheath diameter with increasing opening pressure at the time of intracranial pressure monitor placement (r= 0.40, $P < 0.001$).

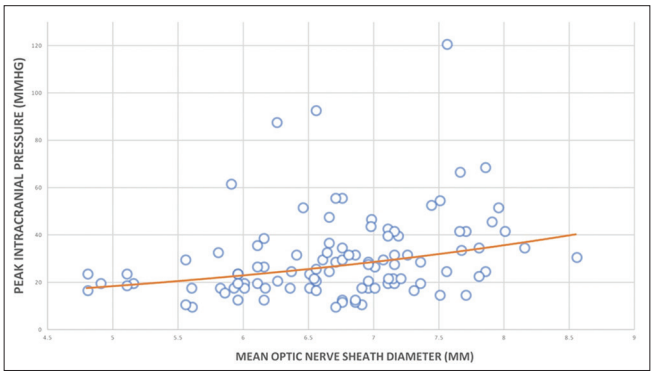

Figure 3: Peak intracranial pressure measurements and their correlation of the left optic nerve sheath diameter in all patients studied (r = 0.31, $P < 0.0001$).

cutoff values. The trabeculations in the anterior segment of the optic nerve sheath are sparse compared to the posterior segment, making it more distensible than the posterior segment.[12,13] Prolonged distension of the optic nerve sheath results in papilledema. While a reliable indicator of elevated ICP, it can take hours, even days to develop, and is challenging to detect without a dilated funduscopic examination.[22] In a review by Bekerman *et al.*, papilledema was detected in only 52% of patients with documented intracranial hypertension.[3] In contrast, evaluation of the optic nerve sheath utilizing ultrasonography detects increased ICP within seconds, making it more useful in an acute setting.[13,30] Changes in ONSD can be observed instantaneously with any change in ICP. This phenomenon was described by Maissan *et al.* in a study of 18 TBI patients with ICP monitors that demonstrated simultaneous changes between ICP and ONSD.[23]

We were able to show that an ONSD of 6.0 mm and Marshall score ≥3 were both highly sensitive markers of elevated ICP and, when combined, are reliable indicators of whether an ICP monitor should be placed. The ONSD of the left eye had a higher sensitivity for detecting elevated ICP. This was initially attributed to the effects of midline shift and laterality of lesions; however, we did not observe a pattern to support this. Our specificity of 92.5% and positive predictive value of 96.1% are among the highest in the literature utilizing CT-measured ONSD in TBI. Luyt *et al.* demonstrated 100% specificity with a cutoff of 5.0mm; however, their study was performed in non-traumatic patients.[22] Das *et al.* demonstrated a correlation between ONSD and Rotterdam scoring to indicate elevated ICP; however, their study did not include any invasive ICP monitoring to better quantify this correlation.[7] Our data demonstrate a statistically significant correlation between opening pressure on ICP monitor placement, peak ICP during hospitalization, and ONSD.

Literature review

Several studies have found a correlation between ONSD on ultrasound and ICP measured through traditional monitoring. Robba *et al.* showed that ONSD measured on ultrasound had the strongest correlation in predicting increased ICPs in patients with invasive ICP monitoring.[31] In another prospective observational study, Kimberly *et al.* showed that an ONSD >5.0 mm had a sensitivity and specificity of 88% and 93% in detecting ICP > 20 cm H_2O in patients with an ICP monitor.[18] Raffiz *et al.* showed that the ONSD cutoff of 5.2 mm had a 95% sensitivity and 80% specificity in predicting increased ICPs.[29] They also saw that these values were higher in patients who had acute increases in ICPs due to trauma compared to non-traumatic reasons. A study by Irazuzta *et al.* found that an ONSD >4.5 mm had 100% sensitivity in predicting increased ICPs.[15] In a 2011 meta-analysis, six studies looking at the results of 231 patients were reviewed. It showed a pooled sensitivity of 90% when using ONSD to detect increased ICP. However, this analysis is underpowered now that several more studies have been published as shown in Table 3.[8]

Another method of estimating ICP uses the ratio of the ONSD to the transverse diameter of the eyeball (eyeball transverse diameter), as described by Vaiman and Bekerman, who have conducted the largest studies to date analyzing ONSD on CT. The advantage of this technique is that it reduces variation that occurs from involuntary eye movements during CT scan.[3,36,37] In their review of 1766 adult patients, they assessed ONSD in patients with a variety of pathologies with intracranial hypo- or hyper-tension. They found that, at ICPs below 13 mmHg and above 30 mmHg, there is no longer a linear correlation between ONSD and ICP. This was attributed to the already minimal CSF content within the optic nerve under normal conditions, and in low-pressure states, there can be no discernible changes due to the lack of CSF within the sheath. At ICPs >30 mmHg, it is likely that the sheath has reached maximum distensibility and there is no ability for the diameter of the optic nerve sheath to increase.[3]

While these studies prove that this is a reliable noninvasive technique, generalizing such a method for measuring ONSD is difficult due to differences in operator experience, technique, and the modality used. This is evidenced by the great heterogeneity in the cutoff values as shown in Table 4. Finding a normative value of ONSD in patients with negative CT head is important in establishing a quantitative relationship between increase ICP and its effect on optic nerve sheath distention. Ozgen and Ariyurek evaluated the orbital structures of 100 healthy subjects and found that the mean optic nerve sheath complex was 4.4 mm with an estimated normal range of 3.2–5.6 mm.[27] While this provides useful information, their standard measurements do not necessarily provide a clinical application because their point of measurement was more posterior than the commonly used

Table 3: Sensitivity and specificity analysis of optic nerve sheath diameter and Marshall score demonstrating the increasing sensitivity, specificity, and positive predictive value when combining Marshall score and optic nerve sheath diameter (P=0.001).

Measurement	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
ONSD ≥6.0 mm			
Mean	87.2	33.3	78.8
Left	92.2	33.3	79.7
Right	81.8	25.9	75.9
Marshall score ≥3	66.2	81.4	91.0
ONSD ≥6.0 mm+Marshall score ≥3	92.5	92.6	96.1

ONSD: Optic nerve sheath diameter

Table 4: Chart comprising studies that have evaluated optic nerve sheath diameter using various modalities, their respective cutoff parameters, and their sensitivities and specificities.

Study	*n*	Modality	ONSD cutoff (mm)	Sensitivity/specificity (%)
Lee *et al.*[20]	64	CT	5.3	88/79
Robba *et al.*[31]	64	US	5.0	N/A (AUC 0.91)
Das *et al.*[7]	150	CT	6.0	97/42
Jeon *et al.*[16]	62	US	5.6	93.75/86.67
Raffiz *et al.*[29]	41	US	5.2	95.8/80.4
Bekerman *et al.*[3]	1766	CT	5.5*	90/86; 98/77 (intracranial hypotension)
Vaiman *et al.*[37]	78	CT	5.5	91/83
Irazuzta *et al.*[15]	16	US	4.5	100/100
Luyt *et al.*[22]	67	CT	4.8; 5.0	92.9/97.6; 85.7/100
Mehrpour *et al.*[25]	32	US	R-5.95 L-5.86	100/83
Sekhon *et al.*[33]	57	CT	6.0	97/42
Sahoo and Agrawal[32]	20	US	6.3	100/72.7
Amini *et al.*[1]	50	US	5.5	100/100
Qayyum and Ramlakhan[28]	24	US	5.0	100/75
Major *et al.*[24]	26	US	5.0	86/100
Moretti and Pizzi[26]	53	US	5.2	94/76
Goel *et al.*[11]	100	US	5.0	98.6/92.8
Geeraerts *et al.*[10]	38	MRI	5.82; 5.3	90/92; 100/100
Soldatos *et al.*[34]	50	US	5.7	65/74
Beare *et al.*[2]	14	US	4.2	100/86
Tayal *et al.*[35]	59	US	5.0	100/63
Geeraerts *et al.*[9]	31	US	5.7	100/68
Karakitsos *et al.*[17]	54	US	5.9	65/74
Blaivas *et al.*[4]	35	US	5.0	100/95

ONSD: Optic nerve sheath diameter

measurements in the literature. Using our control group of 100 patients, which is among the largest control groups analyzing ONSD on CT, we were able to demonstrate that the normal ONSD range varies from 4.25 to 7.15 mm with a mean of 5.73 ± 0.58 mm that is consistent across both male and female subjects. In our intervention group, there were 4 times as many males in our intervention group ($P < 0.0001$), which is not unexpected given that males are twice as likely to suffer a TBI.[19] The age difference between the control (49.1 ± 22.9) and intervention (36.9 ± 15.1) groups was also statistically significant ($P < 0.0001$). We attribute this to the fact that ages 0–19 years old are more likely to suffer a TBI than any other age group.[19]

Limitations

The retrospective nature of our study is an inherent limitation due to selection bias. Another limitation of our study and utilizing CT head for ONSD measurement is the heterogeneity in the measurements of the ONSD due to the gantry differences between each scan. Patients' head positioning within the scanner, time from injury to CT scan, and presenting GCS also skew these measurements. Future studies utilizing this method should include appropriate cuts through the optic nerves so that the most accurate measurements of the ONSD can be obtained. An additional limitation is the variation in EVD placement as well as differences in measurement of the opening pressure as some measured opening pressure based on centimeters of water (cmH_2O) above the external auditory canal while others utilized millimeters of mercury (mmHg) as measured by an electronic transducer. In addition, distention of the optic nerve sheath in response to changing ICP is dependent on the sheath's elasticity. Individual variability in the sheath's elastic properties makes establishing a quantitative relationship between ONSD and ICP difficult. The ICP values used in our study were the first recorded ICP numbers. Even though institutional protocol for placing ICP monitors warrants measurement of ICPs before any CSF drainage, it would be hard to reliably guarantee such practice in a retrospective study.

CONCLUSION

Our study's main objective was to use ONSD on initial CT head to predict who would benefit from invasive ICP monitoring. We found that an ONSD >6.0 mm on CT in the setting of trauma strongly correlated with increased ICP and, when combined with Marshall scoring on admission, is a very sensitive and specific predictor for developing critical ICP (≥20 mmHg). This is the only large retrospective study to establish a large control group using CT measurement of ONSD. This cohort of individuals can be used as a control group in future studies. Although ONSD measured

on ultrasound has been validated as a reliable indicator of rising ICP, operator experience and variability of measurements limit its generalizability. Further studies are needed to better stratify ONSD values in combination with individual parameters, which may include the utilization of both dynamic ONSD monitoring (US) and precise ONSD measurements (CT). This combination of dynamic, objective, and validated criteria will be an effective tool that changes the way we determine which patients need invasive ICP monitoring.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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