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A prospective study of optic nerve ultrasound for the detection of elevated intracranial pressure in severe traumatic brain injury (ONUS-TBI)

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Abstract

Objective: Intracranial pressure (ICP) monitoring plays a critical role in the management of severe traumatic brain injury (TBI). Our objective was to evaluate the accuracy of Optic Nerve Sheath Diameter (ONSD) as a non-invasive screening test for the detection of elevated ICP and prediction of ICP treatment intensity.

Design: Prospective, blinded study of diagnostic accuracy.

Settings: Neurotrauma intensive care unit.

Participants: Consecutive patients with severe TBI.

Interventions: Optic nerve ultrasound (ONUS) was performed daily and ONSD measured at the point-of-care (POC) as well as remotely by an expert blinded to all patient details. Optic disc elevation (ODE) was also measured. The index test was the highest remote-expert ONSD for the admission. The reference standard was the concurrent invasive ICP, with test-positivity set at

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Location: This study was performed at the All India Institute of Medical Sciences (AIIMS), New Delhi, India AND the University of Michigan, Ann Arbor, United States

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ICP>22mmHg. A priori the minimally acceptable sensitivity threshold was 90% with corresponding specificity 60%. We also evaluated the ability of ONSD to predict a Therapeutic Intensity Level (TIL)>10.

Results: 120 patients were enrolled. The intra-class coefficient (ICC) between POC and expert ONSD after enrollment of 50 subjects was poor at 0.16 (–0.08–0.41) but improved to 0.87 (0.81–0.92) for the remaining subjects after remedial training. The Area Under the Curve (AUC) of the Receiver Operating Curve (ROC) curve of the highest expert-measured ONSD to detect ICP>22mmHg was 0.81, (0.73–0.87); AUC for prediction of TIL>10 was 0.51 (0.42–0.60). ONSD>0.72 demonstrated sensitivity 82% (48–98%) and specificity 79% (70–86%) for ICP>22mmHg. The AUC of highest measured ODE to detect ICP>22mmHg was 0.84 (0.76–0.90). ODE>0.04cm attained sensitivity 90% (56–100%) and specificity 71% (61–79%).

Conclusion: While ONSD demonstrated a modest, statistically-significant correlation with ICP, a predetermined level of diagnostic accuracy to justify routine clinical use as a screening test was not achieved. Measurement of ODE appears promising for the detection of elevated ICP, however, verification from larger studies is necessary.

Keywords

Optic nerve; Optic disk; Intracranial Hypertension; Ultrasonography; Intracranial Pressure; Traumatic Brain Injury

INTRODUCTION

Monitoring and management of Intracranial Pressure (ICP) is integral to the management of Severe TBI, defined by a Glasgow Coma Scale (GCS) ≤8.(1–3) The Brain Trauma Foundation (BTF) recommends treatment of ICP >22mmHg.(3) While invasive ICP monitoring is the gold standard, this carries the risk of bleeding and infection, generally requires on-site neurosurgical expertise and is associated with significant cost. An unmet need exists for a noninvasive tool to detect elevated ICP.

Optic nerve ultrasound (ONUS) is a non-invasive tool to assess ICP in widespread clinical use.(4–7) The optic nerve sheath (ONS) is a continuation of the dura and contains the subarachnoid space. An increase in ICP is transmitted through the subarachnoid space and results in distension of the retrobulbar ONS.(8, 9) The Optic Nerve Sheath Diameter (ONSD) can be measured posterior to the globe with ultrasound, and a threshold ONSD used to identify the presence of elevated ICP.(10–19) The optimal ONSD threshold has varied greatly between studies, but has ranged between 0.50–0.60cm in clinical practice.(10–14) Limitations of prior studies include incomplete blinding, small sample size, and operators with variable expertise. Most studies have focused on the ability of ONUS to detect point-elevations in ICP, which may occur in the context of transient provocation. Identification of TBI patients requiring aggressive therapeutic measures for control of ICP may facilitate triage and transfer decisions in the emergency department and resource-constrained environments.

Our primary objective was to identify the accuracy of ONSD for the detection of elevated ICP in severe TBI and to identify the optimal ONSD threshold. Additional aims were to

study the ability of ONSD to predict Therapeutic Intensity Level (TIL) for control of elevated ICP,(20) and poor outcome at discharge.

METHODS

This was a prospective blinded study of diagnostic accuracy in consecutive patients with severe TBI funded by the National Institute of Health (R03-EB01935202). Institutional review board approval was obtained. The setting was a 20-bed neurotrauma intensive care unit (ICU). Inclusion criteria were: age >18 years, severe TBI, first ONSD measurement feasible within 48 hours of injury, and presence of an invasive ICP monitor. Exclusion criteria were: patient unlikely to survive >48 hours from enrollment, injury to globe of the eye or ONS on either side, pre-existing ocular disease other than errors of refraction and Therapeutic Intensity Level (TIL) summary score >10 attained or expected prior to first ONSD measurement.(20) All TBI admissions to the neurotrauma ICU between January 1, 2016 and July 1, 2018 were screened for eligibility. Legally authorized representatives were approached for informed consent.

The reference standard was ICP measured by a Codman Microsensor™ (Integra Lifesciences, Plainsboro, New Jersey, United States of America) intraparenchymal probe. While concomitant use of external ventricular drains was allowed, intraparenchymal probes served as the reference standard for availability of continuous measurements. Criteria for invasive ICP monitoring were based on BTF guidelines.(21) The intraparenchymal monitor was typically removed when the ICP was <20mmHg for at least 24 hours, but could be left in place longer at the discretion of the clinical team.

The index test was sonographic measurement of ONSD, performed at enrollment and at least once daily until one of the following endpoints was reached- removal of the ICP monitor, TIL>10, a maximum of 7 days or death. All measurements were performed using a Sonosite™ L25 linear 13–6 MHz array transducer, ophthalmic preset, and a Sonosite™ M-Turbo (SonoSite Inc., Bothell, WA, USA) ultrasound machine. Four investigators performed ONUS studies at the point-of-care (POC), none had prior experience with ONUS. ONSD measurements were then repeated by expert investigators blinded to the POC-investigator's measurement, invasive ICP and all clinical details of the patient. These blinded expert-measurements served as the index measurement in the analyses of diagnostic accuracy, while the POC measurements were used to assess the reliability of measurements performed by inexperienced personnel. The POC investigators were trained by the two expert investigators, each with >5 years' clinical and research experience with ONUS. Details of initial and remedial training are in supplemental table 1. The POC investigators were blinded only to invasive ICP at the time of the study, achieved by covering or turning the monitor away, while the bedside nurse recorded the highest measured ICP during the study. These investigators were not blinded to medical records or clinical details. The clinical team was blinded to ONSD measurements, since the reference standard measure (invasive ICP) was available for clinical management. The technique of ONSD measurement has been previously described.(14) Images were acquired in the axial (transverse) plane. The acquired study was considered to be of adequate quality only if all of the following were delineated (FIGURE 1)- globe, retina, ONS with clearly demarcated margins on both sides, and the

optic nerve within the ONS. A ten-second video-clip was recorded from each eye and POC-ONSD measurement performed from a still-image obtained by scrolling through the acquired sequence of images. ONUS videos were uploaded in Digital Imaging and COmmunications in Medicine (DICOM) format to the Research Electronic Data Capture (REDCap) system. These anonymized videos were then transferred to a separate online folder, where they were accessed by one of the expert investigators. The expert investigator scrolled through the video and measured ONSD from the optimal still-image. When the uploaded study was judged to be of insufficient quality, ONSD measurement was not performed. ONSD measurement technique was the same for POC and blinded-expert measurements. A caliper was used to identify a point 3mm posterior to the globe, and the ONSD measured at that point in a plane perpendicular to the long-axis of the ONS. In addition, the expert investigator measured the optic disc elevation (ODE) above the retina using a zoomed-in view (FIGURE 1), this measurement was not performed by POC investigators. Interim quality assessment was performed of image acquisition and POC-ONSD measurement following enrollment of the first 50 subjects. Remedial instruction in image acquisition and measurement technique was provided to POC investigators if poor agreement was found between POC and expert ONSD at interim analysis (supplemental table 1).

The Therapeutic Intensity Level (TIL) is used to quantify treatment directed toward control of ICP.(20, 22) A TIL summary score for the admission was calculated daily and at the time of ICU discharge. A TIL summary score >10 identifies patients requiring the highest stratum of treatment for refractory ICP elevation. The Glasgow outcome scale (GOS) score was estimated at the time of discharge.(23) Clinical management of severe TBI was consistent with recommendations of the BTF.(3)

Statistical analysis

Descriptive statistics were calculated using proportions for categorical variables and median with interquartile range (IQR) for continuous variables. Associations between variables and outcomes of interest were tested using the chi-square or Fisher Exact test for categorical variables and the Mann-Whitney test for continuous variables. The threshold for statistical significance was $p<0.05$. Logistic regression was performed to identify independent baseline predictors of occurrence of sustained ICP elevation at any subsequent time, defined as ICP>22mmHg for >10 minutes while at rest. An intra-class correlation (ICC) was computed with a 95% Confidence Interval (95%CI) using a random-effect model to assess agreement between highest measured POC-ONSD for the admission and the corresponding blinded-expert measurement. If the ICC was <0.80 at the time of interim analysis, remedial instruction was provided to POC investigators. The Spearman rank correlation (ρ) was calculated between highest expert-measured ONSD for the admission and concurrent ICP.

The primary index diagnostic assessment was the highest expert-measured ONSD during the admission for each subject. The corresponding reference standard was the concurrently recorded invasive ICP. A Receiver Operating Characteristic (ROC) curve was constructed to evaluate the ability of highest expert-measured ONSD measurement to detect “high” ICP (gold standard with test-positivity set at >25mmHg) and the Area Under the Curve (AUC)

calculated. Since the 2016 BTF guidelines revised the recommended ICP treatment threshold to 22mmHg, we performed additional analysis with reference-standard test-positivity set at ICP>22mmHg. *A priori*, we assumed that ONUS was most likely to be utilized as a screening test and that the detrimental effects of missing ICP elevation to be more dire than misclassification of patients with lower ICP. Therefore, the *optimal* sensitivity was set at ≥98% with corresponding specificity ≥80%. If an ONSD threshold with sensitivity ≥98% and corresponding specificity ≥80% could not be identified, we set the *minimum acceptable* ONSD threshold at 90%, with *minimum* corresponding specificity of 60%. This analysis was repeated to evaluate the accuracy of ODE. ROC curves were also constructed to evaluate the ability of highest measured ONSD to predict TIL summary score >10 for the admission, and poor outcome at discharge (defined as a GOS<3).

We examined the ability of serial ONSD measurements in individual patients to identify elevated ICP. A generalized linear mixed model was used to model ICP as a function of ONSD. Normal and binary distribution was assumed for the continuous and binary ICP outcome, respectively. A random effect was included in the model to consider the correlation between multiple measurements per subject. ROC analysis was performed using the predicted probabilities derived from the model with the binary ICP outcome.

Statistical analyses were performed using MedCalc for Windows, version 19.1.3 (MedCalc Software, Ostend, Belgium) except for the analysis of serial measurements which was performed using PROC GLIMMIX in SAS for Windows version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

A total of 858 patients were screened and 120 enrolled. The participant flow diagram is shown in FIGURE 2.

The distribution of baseline variables, discharge variables and outcomes is in TABLE 1. A total of 292 ONUS studies were performed on 120 subjects, with a median of 2 (IQR 2–3) days of measurement per subject. The frequency of ICP elevations is shown in supplemental table 2. A total of 15/292 (5%) videos were rejected for unacceptable quality by the remote expert. Every subject had at least one ONUS study of acceptable quality.

At interim analysis following enrollment of 50 subjects, the ICC between POC and expert ONSD measurement was poor (0.16, 95%CI –0.08 to 0.41) and 10/110 studies (9%) were of insufficient quality to permit ONSD measurement. Remedial instruction was therefore performed with POC investigators. Subsequent interim QA demonstrated good agreement, with ICC 0.87 (0.81–0.92) for the remaining 70 cases with only 5/182 (3%) studies of unacceptable quality for ONSD measurement. The ICC for all 120 subjects was 0.43 (0.21–0.60).

The Spearman rank-correlation between highest expert-measured ONSD and concurrent invasive ICP was 0.36 (0.20–0.51, p<0.0001). Scatter-diagrams are presented in Supplemental Figures 1 and 2. The ROC curves of ONSD and ODE for detection of elevated ICP are shown in FIGURE 3, detailed results of ROC analysis are in supplemental table 3.

The AUC of ONSD for ICP>25mmHg was 0.76 (0.67–0.83), p(AUC=0.5)=0.0395. The optimal threshold was >0.72cm, with sensitivity 83% (36–100%) and specificity 76% (67–84%). The AUC of ONSD for ICP>22mmHg was 0.81 (0.73–0.87), p(AUC=0.5)<0.0001. The optimal threshold was >0.72cm, with sensitivity 82% (48–98%) and specificity 79% (70–86%). The AUC of ODE for ICP>22mmHg was 0.84 (0.76–0.90), p(AUC=0.5)<0.0001. Optimal ODE threshold was >0.04cm, with sensitivity 90% (56–100%) and specificity 71% (61–79%).

No ONSD threshold could be identified with sensitivity ≥98% and specificity ≥80%, nor with sensitivity ≥90% and specificity ≥60%. The previously reported ONSD thresholds of 0.50cm,(12, 14) and 0.57cm(10, 18) both achieved sensitivity 100% (72%–100%) and specificity of <15% for ICP thresholds of 20mmHg, 22mmHg and 25mmHg.

In the analysis of serial measurements, we found that ONSD was associated with continuous ICP measurements (p=0.0002) and also predictive of ICP dichotomized at <=22mmHg vs >22mmHg. The odds ratio was 3.72 (1.68–8.24; p=0.0014) for every 0.1 unit increase in ONSD, with AUC 0.88. Time trends in ICP, TIL, ONSD and ODE are presented in supplemental figures 3 to 7.

The AUC of ONSD for prediction of TIL>10 was 0.51 (0.42–0.60, p=0.89), and for prediction of discharge GOS <3 was 0.55 (0.46–0.64, p=0.57).

DISCUSSION

In our study, expert-measured ONSD achieved AUC >0.8 for the detection of concurrent ICP>22mmHg in analyses of both single and serial measurements. These findings, along with those of multiple prior studies, confirm a biological association between ONSD and ICP. The presence of a biological association, however, does not automatically translate to acceptable diagnostic accuracy in a specified clinical role. Since ONSD is most likely to be used as a non-invasive screening test to identify patients requiring invasive monitoring, transfer to a referral center or empiric initiation of therapy, high sensitivity is paramount. A test with excessively low specificity, however, is unlikely to out-perform routine clinical assessments or meaningfully decrease the need for invasive testing. For example, the BEST-TRIP trial demonstrated that severe TBI patients could be monitored and managed with frequent clinical and CT evaluation, in a relatively resource-constrained environment.(24) We could not identify an ONSD threshold that met our predetermined minimum criteria for acceptable accuracy- the optimal threshold achieved only a sensitivity of 80% (in conjunction with minimal specificity 60%). Using this threshold, approximately one in five patients with true ICP elevation would be misclassified, which is likely unacceptable given the grave consequences of untreated ICP elevation. In addition, over two-thirds of individuals diagnosed with elevated ICP using this ONSD threshold will in reality not have intracranial hypertension (supplemental table 3), and may be exposed to the risks of empiric therapy. Previously proposed ONSD cutoffs (0.50cm and 0.57cm)(10, 12, 14, 18) performed poorly in our study, and the strength of correlation (ρ=0.36) was lower than previously reported.(14) ONSD performed poorly for the identification of patients requiring a high therapeutic intensity for treatment of ICP. Also of concern was the poor initial inter-rater

agreement among inexperienced clinicians compared to experts, since clinicians with access to point-of-care ultrasound but limited training may represent a significant proportion of individuals performing this study in practice. This decay in skills has recently been demonstrated with critical care echo and lung ultrasound- in one study, retraining at 8 weeks was necessary to preserve motor and cognitive skills.(25)

In our study, optic disc elevation threshold of >4mm achieved sensitivity 90% and specificity 71% for detection of concurrent ICP>22mmHg. This measure, when performed with ultrasound, has been studied to a lesser extent than ONSD,(26) and requires further validation before use in clinical practice is considered.

Our study has several strengths. It is the largest prospective study comparing ONSD to the gold-standard of simultaneous invasive ICP monitoring. It is the only study to evaluate the ability of ONSD to identify patients requiring high therapeutic intensity for the management of refractory ICP, which may be particularly significant for triage purposes. Both single and serial measurements were used in the analysis. Importantly, we assessed the ability of inexperienced sonographers to accurately measure ONSD. We also attempted to address some of the limitations of prior studies. The population studied was homogenous (severe TBI). Most importantly, blinding, which the Standards for Reporting Diagnostic Accuracy (STARD) identifies as a critical element of high-quality diagnostic studies,(27) was complete and rigorous. While some prior studies did not blind sonographers to the invasive ICP, almost all have failed to blind the individual performing the index evaluation to the clinical details of the patient, as well as the ICP before and after the ONUS study.(14, 16) Incomplete blinding of the individual measuring ONSD, that permits any knowledge of the patient's clinical condition, might result in biased identification of the margins of the ONS (FIGURE 3) and an overestimation of accuracy.

Some smaller studies have found ONUS to be inaccurate in TBI and acute liver failure.(15, 19) Several other studies, including a study by one of the authors,(14) have demonstrated high accuracy of ONSD for the detection of concurrent ICP elevation.(10, 12–14, 17, 18) The wide variation in cutoff values across these studies has always been a reason for concern and limited clinical utility of this tool. It is possible that a single universal ONSD cutoff may not accurately detect ICP elevation in all patients. A recent study suggested that the degree of ONS distension with elevation in ICP may vary by individual.(28) Hysteresis- a delay in ONS responsiveness to changes in ICP- may compromise accuracy. A study using a cadaveric model suggests that the reversibility of ONS distension may be delayed and incomplete following periods of intracranial hypertension.(9) Clinical data suggests that the accuracy of ONSD may vary based on the degree of ICP fluctuation at the time of measurement.(29) It is also possible that dichotomization of ICP as "high" vs "low" at a single number (20/22mmHg) is suboptimal and that a "grey zone" exists between clearly normal ICP and elevated ICP that adversely impacts oxygen delivery and neuronal function.

Our study has several limitations. A larger sample size may have narrowed the confidence intervals in the estimates of accuracy- there were only 11 (9%) ICP elevations (>22mmHg) in the primary analysis. All patients had bilateral reactive pupils, therefore patients with the most severe injury were likely excluded. However 18% of subjects presented with GCS≤5,

suggesting a significant proportion were severely injured. The median duration of ICP monitoring was 2 days, which may reflect the aggressive use of decompressive craniectomy (41% of patients with ICP elevation). In general, investigators could only measure ONSD once daily, and we were unable to study the response of ONSD to treatment. The median ONSD in our study was higher than in some prior studies, but was consistent with the ONSD of 0.67–0.68cm described in severe TBI patients with elevated ICP in which ONSD was measured using CT,(30, 31) which may be less prone to operator error. We did not study diagnostic accuracy of the globe-to-ONSD ratio, which has demonstrated greater accuracy than ONSD alone in preliminary studies,(32, 33) but plan to do so with our existing dataset. Similarly, the use of multivariate clinical prediction models for ICP elevation deserves further study.

In conclusion, while ONSD demonstrated a modest, statistically-significant correlation with ICP, a predetermined level of diagnostic accuracy to justify routine use in clinical practice as a noninvasive screening tool was not achieved. Measurement of optic disc elevation may be a promising technique to detect elevated ICP, however, verification from larger studies is necessary.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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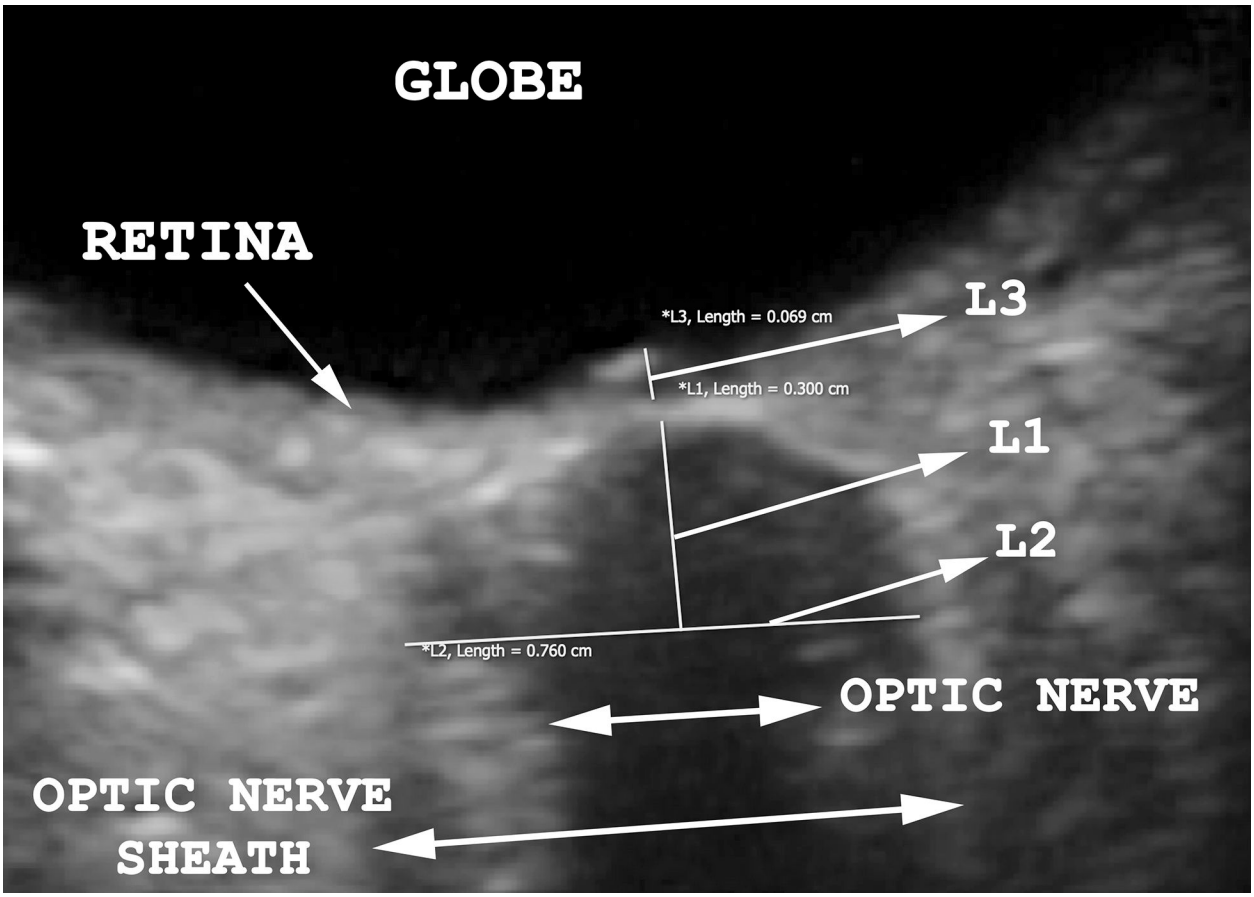

FIGURE 1:

Measurement of optic nerve sheath diameter (ONSD) and optic disc elevation (ODE). An axial (transverse) view of the globe reveals the globe anteriorly, with the retina and retrobulbar region with the optic nerve sheath (ONS) visible posteriorly. The optic nerve is visible within the optic nerve sheath. The caliper L1 marks out a point 3mm posterior to the posterior scleral border. The caliper L2 measures the ONSD at this point, in a plane perpendicular to the long axis of the optic nerve. The caliper L3 measure the maximum height of the optic disc above the retina.

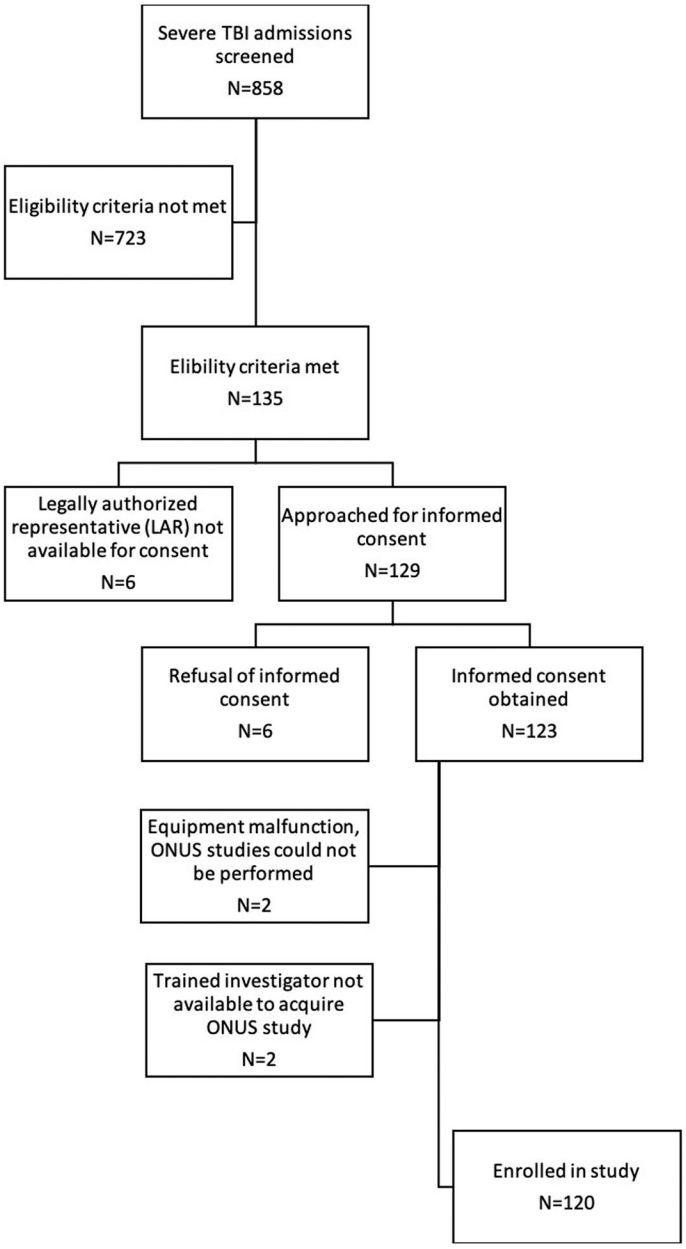

FIGURE 2:
Flowchart of subject enrollment.

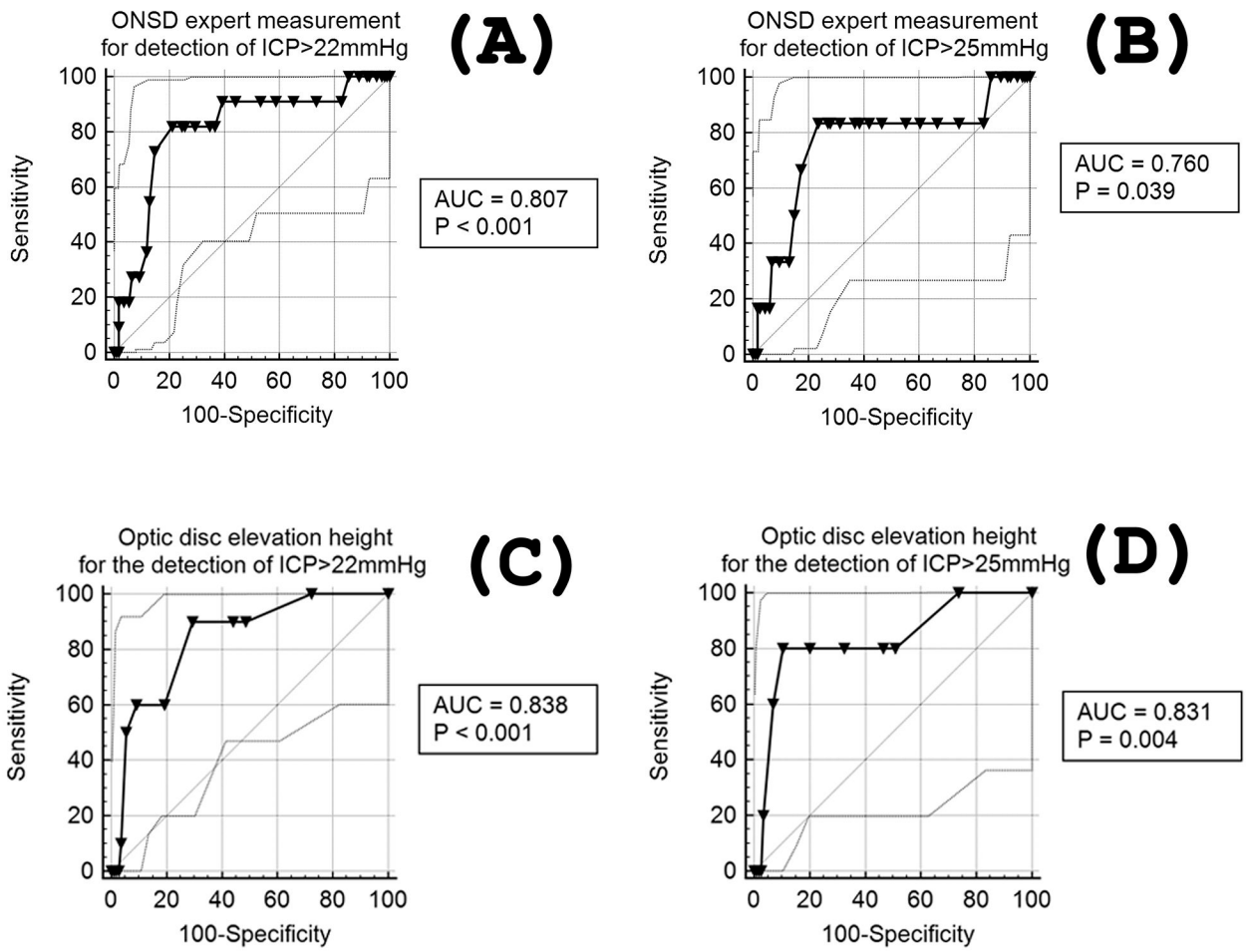

FIGURE 3:

Receiver Operating Characteristic (ROC) curves of: (A) Optic nerve sheath diameter (ONSD) for the detection of ICP>22mmHg, (B) ONSD for the detection of ICP>25mmHg, (C) Optic disc elevation (ODE) for the detection of ICP>22mmHg and (D) ODE for the detection of ICP>25mmHg.

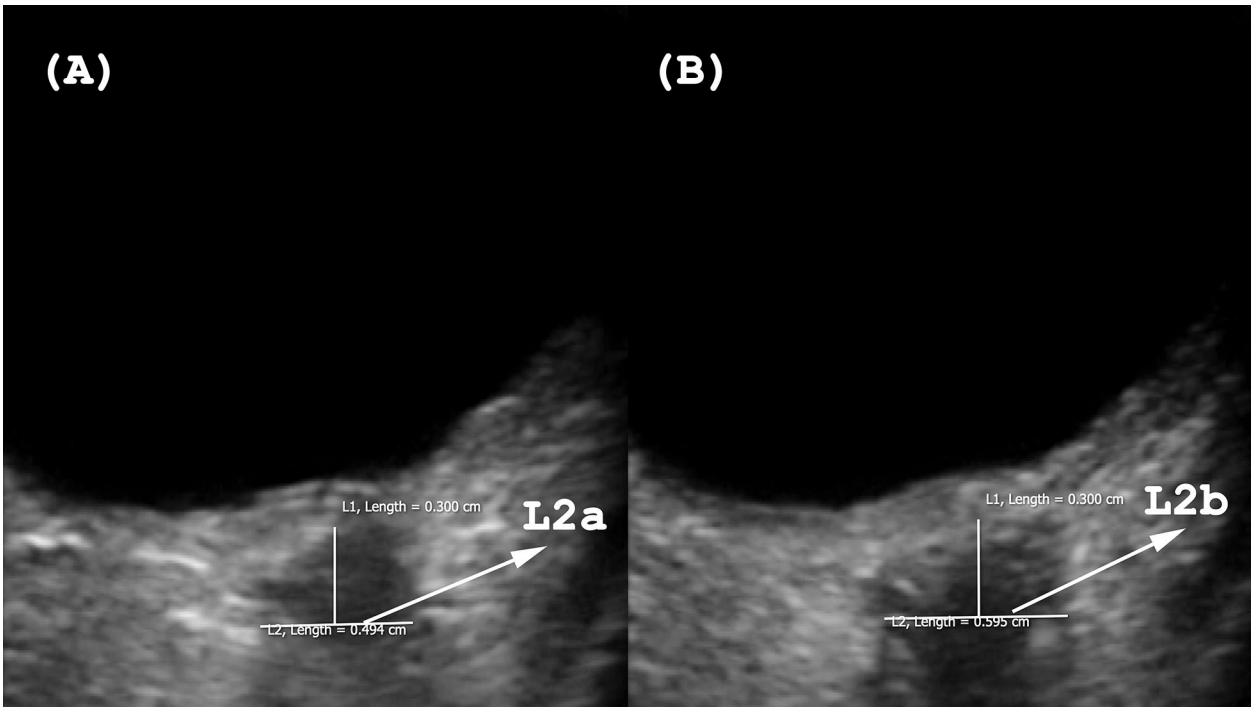

FIGURE 4:

ONSD measurement error. In Figure (A), the caliper L2 measures the ONSD at 0.49cm. However, the image is of insufficient quality because the boundaries of the optic nerve are not clearly delineated within the optic nerve sheath. In Figure (B), a minor alteration in transducer position in the same patient provides an image of acceptable quality, with the more hypoechoic optic nerve now clearly delineated within the sheath. Caliper L2 now measures the ONSD at 0.60cm.

Table 1:

Baseline variables and outcomes in the study population, and in patients who did and did not demonstrate sustained intracranial hypertension during their admission, defined as an ICP>22mmHg for >10 minutes while at rest.

VARIABLE	ALL SUBJECTS N=120	NO ICP ELEVATION DURING ADMISSION N=93	ICP ELEVATION DURING ADMISSION (Sustained >22mmHg) N=27	P value (bivariate)
Baseline variables				
Age in years, median (IQR)	31 (25–43)	34 (25–45)	25 (21–32)	0.003
Gender= Male, N (%)	102 (85%)	81 (87%)	21 (78%)	0.23
GCS, median (IQR)	7 (6–7)	7 (6–7)	7 (6–7)	0.42
Pupillary reactivity, N (%)				-
Both reactive	120 (100%)	93 (100%)	27 (100%)	
One reactive	0 (0%)	0 (0%)	0 (0%)	
Neither reactive	0 (0%)	0 (0%)	0 (0%)	
Mechanism of injury, N (%)				0.28
Motor vehicle collision	93 (78%)	71 (76%)	22 (81%)	
Fall	19 (16%)	14 (15%)	5 (19%)	
Other	8 (7%)	8 (9%)	0 (0%)	
Admission Systolic Blood Pressure in mmHg, median (IQR)	120 (110–130)	120 (110–131)	118 (109–126)	0.09 *
Admission pO2 in mmHg, median (IQR)	149 (101–201)	151 (101–201)	146 (100–201)	0.84
CT Marshall Grade, N (%)				0.0003 *
I	3 (3%)	2 (2%)	1 (4%)	
II	14 (12%)	12 (13%)	2 (7%)	
III	24 (20%)	19 (20%)	5 (19%)	
IV	5 (4%)	3 (3%)	2 (7%)	
Nonevacuated hematoma	64 (53%)	55 (59%)	9 (33%)	
Evacuated mass lesion	10 (8%)	2 (2%)	8 (30%)	
ONSD, first recorded, in cm, median (IQR)	0.65 (0.61–0.71)	0.64 (0.60–0.68)	0.69 (0.61–0.75)	0.02 *
Optic disc elevation, first recorded, in mm (IQR)	2 (1–5)	2 (1–4)	4 (2–7)	0.001
Discharge variables and outcomes				
No. of days ONSD was measured, median (IQR)	2 (2–3)	2 (2–3)	2 (1–3)	0.74
ONSD, highest recorded, in cm, median (IQR)	0.66 (0.63–0.73)	0.66 (0.62–0.71)	0.73 (0.64–0.76)	0.005
Optic disc elevation, highest recorded, in mm (IQR)	3 (1–5)	2 (1–5)	5 (4–7)	0.004
ICP, highest recorded, in mmHg, median (IQR)	20 (16–22)	17 (15–20)	28 (26–32)	<0.0001

VARIABLE	ALL SUBJECTS N=120	NO ICP ELEVATION DURING ADMISSION N=93	ICP ELEVATION DURING ADMISSION (Sustained >22mmHg) N=27	P value (bivariate)
Therapeutic Intensity Level, Summary Score, median (IQR)	6 (5–8)	6 (5–7)	6 (5–11)	0.04
Decompressive craniectomy performed, N (%)	21 (18%)	10 (11%)	11 (41%)	0.0002
Tracheostomy performed, N (%)	62 (52%)	43 (46%)	19 (70%)	0.028
Death, N (%)				
All causes	14 (12%)	6 (6%)	8 (30%)	0.001
Neurological	4 (3%)	2 (2%)	2 (7%)	0.74
Glasgow Outcome Score at discharge, N (%)-				0.01
Death	14 (12%)	6 (6%)	8 (30%)	
Persistent vegetative state	1 (1%)	1 (1%)	0 (0%)	
Severe disability	76 (63%)	60 (65%)	16 (59%)	
Moderate disability	14 (12%)	12 (13%)	2 (7%)	
Good recovery	15 (13%)	14 (15%)	1 (4%)	

*- Baseline variables that achieved statistical significance in multivariate analysis for prediction of sustained intracranial hypertension, these were admission systolic blood pressure (OR 0.92 [0.87–0.98]), Marshall CT grade V (evacuated mass lesion, OR 94 [6–1365]) and first measured ONSD (OR 36×10^3 [16 – 84×10^6]).