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Report: "A study of bedside ultrasonography of optic nerve sheath diameter for detection of...

"A study of bedside ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure in nontraumatic neurocritically ill patients in a tertiary hospital."

by SAHIL KATARIA

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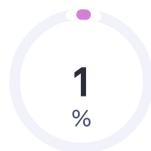| 16,388	2,535	131	10 min 8 sec	19 min 30 sec
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"A study of bedside ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure in nontraumatic neurocritically ill patients in a tertiary hospital."

INTRODUCTION

Raised intracranial pressure (ICP) is a dreaded complication in the intensive care unit (ICU) which may occur either as a result of a primary neurological disorder or as a secondary complication in patients admitted due to other causes. A delay in detecting raised ICP can lead to poor clinical outcomes and increased mortality. The latest Brain Trauma Foundation (BTF) guidelines now recommend a cut off 22 mmHg to initiate ICP-lowering therapies.[1] Gold standard for measuring raised ICP is the intraventricular catheter. However, it is not widely available, requires expertise in insertion and maintenance and may be associated with many risks like infection, the collapse of ventricles and haemorrhage.[2] Hence, non-invasive methods like computed tomography (CT) scan or magnetic resonance imaging (MRI) are increasingly used to diagnose raised ICP. However, they are associated with transport risk and radiation exposure, in the case of CT scans, leading to logistical issues and limited repeatability.

Determination of optic nerve sheath diameter by ultrasonography (US-ONSD) is a simple bedside test with a rapid learning curve, low intra and interobserver variation and good repeatability[3,4]. Studies have shown good accuracy even when performed by non-radiologists.[5] In modern ICUs, bedside

ultrasonography is integrated into routine clinical examination and is readily available. ONSD is frequently used across neuro-surgical ICUs as a tool for ICP monitoring and is particularly useful in patients with invasive ICP monitoring criteria that are not met or are contraindicated. However, the spectrum of disease and comorbidities of patients admitted to neuro-medical ICUs are distinct from neurosurgical ICUs. There need to be more practical bedside screening tools to detect raised ICP in neuro-medical ICUs timely; hence, we aimed to validate ONSD in neuro-medical ICU patients.

METHODS

We conducted this study to determine the diagnostic accuracy of ONSD in adult non-traumatic neuro-critically ill patients after approval from the institutional ethics committee (TS/MSSH/MHIL/SKT/MHEC/CC/20-16). Our inclusion criteria were patients older than 18 years admitted to the neuro-medical ICU with signs and symptoms suggestive of raised ICP. Our exclusion criteria were previously known history of neurological conditions like chronic hydrocephalus, in situ ventriculoperitoneal shunt, known ocular mass, ocular trauma, conjunctival oedema, orbital oedema, cavernous sinus pathology or arachnoid cysts, and patients having optic nerve disease. Additionally, patients in whom CT/MRI could not be performed within 24 hours of US-ONSD were excluded from the analysis.

For the prospective study, the sample size required was calculated according to the following formula:

$$Z\alpha2 * SN * (1 - SN)$$

$$n = d2 * P$$

Where,

n = required sample size

Z = SNV at α = 5% = 1.96

S.N.SN = Anticipated Sensitivity

d = Absolute precision desired on either side

P = Expected prevalence in the population or based on the previous/pilot studies.

For this study, a 95% confidence level with an appropriate effect size and a statistical power of 80% was taken. In a previous study by Salahuddin et al., the expected prevalence of non-traumatic raised ICP in a medical ICU was 30.4%.6 The pooled sensitivity of ONSD to determine raised ICP was 90%, as determined by a systematic review and metanalysis by Dubourg et al.3 Keeping these values for the calculation of the sample size, our required sample size was 114.

We serially enrolled patients who fulfilled the inclusion criteria. After written informed consent was obtained, ocular USG was done by critical care specialists trained in critical care ultrasonography, using a 7-15 MHz ultrasound probe in B mode to determine the ONSD 3 mm distal to the optic disc in both eyes. A fibrous trabecular network connects the optic nerve and its sheath. Studies have shown a greater degree of mesh 6 to 12 mm behind the globe, whereas there is a lesser degree of mesh 3 mm behind the globe. Therefore, 3 mm behind the globe expands to a greater degree than 6 to 12 mm behind the globe, with the maximum expansion dependent on the individual's trabecular density.7 Hansen et al. first validated ONSD and standardized the method to document it by B mode ultrasonography by measuring it 3 mm behind the globe.8 Two readings were taken for each eye, and a mean value was calculated to represent the final ONSD. ONSD more than 5.7 mm was taken as a threshold for determining raised ICP.3 CT/MRI scans of the brain were done within 24 hours of US-ONSD, and the images were reviewed for signs of raised

ICP. Raised ICP or non-traumatic radiographic cerebral oedema [NTRCE] was defined on imaging as significant brain oedema, midline shift, compression of basal cisterns or ventricles, effacement of sulci, insufficient grey/white differentiation and transalpine herniation. Clinical history, general and systemic examination findings, SOFA and APACHE 2 scores and patient outcomes were recorded.

Statistical analysis

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using the SPSS-PC-25 version. Quantitative data were expressed in mean ± standard deviation (SD) or median with interquartile range (IQR), and depending upon normality distribution, the difference between two comparable groups was tested by student's t-test (unpaired) or Mann Whitney' U' test. Qualitative data were expressed in percentages, and statistical differences between the proportions were tested by the chi-square or Fisher's exact test, as appropriate. For all statistical tests, a p-value less than 0.05 was taken as valid evidence for the statistical significance of the data.

The performance of the diagnostic tests was estimated using 2x2 contingency tables to calculate sensitivity, specificity, overall diagnostic accuracy, positive and negative predictive value, likelihood ratios (LRs) and 95% confidence intervals (CI). Post-test probability was determined using Bayes's nomogram. Discrimination was tested using the receiver operating characteristic (ROC) curves. The best cut-off value for ONSD was calculated by using Youden's index.

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RESULTS

114 patients with signs and symptoms suggestive of raised ICP were included in the analysis. Out of these, raised ONSD (> 5.7 mm) was found in 45 (39.5%) patients. The mean age of patients in our study cohort was 64.05 (±16.80) years, with a predominantly male population (59.3%). Table 1 shows that the patient comorbidities, clinical symptoms and signs, except Glasgow Coma Scale (GCS), on admission were comparable across both groups. Lower GCS was significantly associated with raised ICP (p=0.009). Raised ICP on imaging was seen in 49 patients (43%). The most common feature of raised ICP patients on imaging was diffuse cerebral oedema (38.1%) followed by effacement of sulci (32.7%), insufficient grey/white differentiation (30.1%), compression of ventricles (21.2%), midline shift (20.4%) and transfalcine herniation (1.8%). There was a statistically significant correlation between raised ONSD and increased ICP features on CT/MRI scans (p<0.001). As shown in table 2, the sensitivity, specificity, and positive and negative predictive values at this cut-off were 77.55%, 89.06%, 84.44% and 83.82%, respectively. The AUROC was 0.844. The best cut-off value for ONSD calculated using Youden's index was 5.75mm.

The commonest diagnosis was septic/metabolic encephalopathies (27.4%). Other diagnoses were acute intracranial bleeding (21.2%), acute ischaemic stroke (20.4%), meningoencephalitis (13.3%), super refractory status epilepticus (4.4%), newly diagnosed space-occupying lesion (1.8%), cerebral venous sinus thrombosis (CVST) (1.7%) and hypoxic-ischaemic encephalopathy

(1.7%). Of the 31 patients presenting with septic/metabolic encephalopathy, 26 (83.9%) had a normal ONSD.

Patient outcomes, including ICU length of stay (LOS) and ICU mortality, were comparable across both groups, as shown in table 3. Raised ONSD had a statistically higher requirement of surgical intervention (p=0.006). The surgical procedures were decompressive craniotomy in 6 patients, ventriculoperitoneal shunt (VP shunt) in 3 patients and extra-ventricular drain (EVD) insertion in 2 patients. One patient underwent EVD followed by a VP shunt with Omaya reservoir.

DISCUSSION

Invasive ICP monitoring is not widely available across the ICUs, especially in resource-limited settings. An internet-based survey of critical care physicians in India in 2013 showed that only 36.42% had access to exclusive neurocritical care units, and 63.4% of consultants did not monitor ICP. Amongst the physician who monitored for raised ICP, 60.32% used CT / MRI scans, 28.57% intraventricular catheter with external transducer, and 11.11% used Codman microsensor.[9] This shows the extent of the deficit in terms of advanced neuro-monitoring facilities across ICUs in resource-limited settings. US-ONSD provides a lucrative alternative to the available methods for ICP monitoring. We conducted a prospective study with the primary objective of validating ONSD by bedside ultrasound compared to features of raised ICP on the CT/MRI brain. Our study found a significant association between raised ONSD (> 5.7 mm) and findings of raised ICP on imaging. The sensitivity and specificity, at this cut-off, were 77.55% and 89.06%, with an AUROC were 0.844. The positive and negative predictive values were 84.44% and 83.82%, respectively. The best cut-off value for ONSD determined by Youden's index was 5.75 mm.

Physical findings of raised ICP are nonspecific and lack accuracy in diagnosing raised ICP. Diagnosis of raised ICP is essential as it may be associated with poor clinical outcomes. Early intervention using osmotherapy with hypertonic saline or mannitol has been shown to be effective in lowering ICP.10-12 GCS is commonly used for monitoring neuro-critically ill patients. Poor motor performance has been associated with raised ICP and poor prognosis.13 In our study, the most common symptom in patients with suspected raised ICP was altered mental status, and poor GCS score was significantly associated with raised ONSD. This was in accordance with a study of patients with traumatic brain injury (TBI) where raised ONSD was compared to 3 groups of GCS 3-5, 6-8, >8 and a statistical significance was found between poor GCS and raised ONSD.14 In patients whose GCS cannot be assessed due to ongoing sedatives or paralytic agents, raised ONSD can be used as an indicator for raised ICP warranting further evaluation. However, further studies are required to establish any linear relationship between deteriorating GCS and increasing ONSD.

Out of our entire study population, 49 patients (42.98%) showed the presence of NTRCE. In a study in general medical ICU by Salahuddin et al., NTRCE was found to be 30.4 %.9 Higher prevalence of NTRCE in our study can be explained by the fact that it was done in neuro-medical ICU patients with suspected raised ICP, as opposed to the study mentioned above, which was done in a general medical ICU.

For over 10 years, the upper limit of normal for US-ONSD was considered to be 4.5 to 5.0 mm. However, recent studies have shown a higher threshold. Geeraerts et al. reported that an ONSD cut-off of 5.7 to 5.8 mm could exclude

raised ICP with sensitivity and a negative predictive value of >90%. If the ONSD was < 5.7 mm, the probability of ICP above 20 mmHg was less than 5%.15 Another study on 100 stroke patients with mass effect compared US-ONSD with signs suggestive of raised ICP on a brain CT scan and showed that an ONSD cut-off of > 5.7 mm positively correlated with CT scan findings.14 In the present study, we found the best cut-off for ONSD using Youden's index as 5.75 mm, per the recent data.16

Our study found a statistically significant association between raised ONSD (> 5.7 mm) and raised ICP on CT/MRI brain. Raised US-ONSD was a good screening tool for raised ICP with a sensitivity and specificity of 77.55% and 89.06%, respectively, and AUROC was 0.844. However, the terms sensitivity and specificity do not account for disease prevalence and are more applicable at a population level. L.R.sLRs depend on disease prevalence and can be used to quantify the probability of disease in an individual patient. In our study, the positive and negative L.R.LR was 7.09 and 0.25. The disease prevalence (raised ICP) in our study was 43%. Using Baye's nomogram suggests that if ONSD is more than 5.7 mm, there is an 84% probability of a patient having raised ICP. On the other hand, if ONSD is less than 5.7 mm, the probability of raised ICP is only 16% (CI:10-24%). Hence, in neuro-medical ICUs where raised ICP has a high prevalence, ONSD is a good screening test to detect raised ICP but may need to be more accurate to rule out raised ICP. When the same LRs are applied to a low prevalence population, like in a study by Tayal et al. where raised ICP was found to be prevalent in only 14% of patients presenting to the emergency department with a suspected acute head injury requiring CT, the positive post-test possibility was 54%, and negative post-test probability was less than

4%.17 Therefore, in a population with a low prevalence of raised ICP, the optic nerve sheath diameter may be good for ruling out the diagnosis of raised ICP.

Most studies on ICP monitoring and US-ONSD have been conducted in neurosurgical ICU, where trauma and strokes form the bulk of the disease. Primary pathology of neurocritical illness is different in medical ICUs.3,4 A previous study of ONSD in a medical ICU found that the common causes of coma were septic or metabolic encephalopathy (25.4%) followed by new intracranial vascular event (17.6%), anoxic brain injury (4.9%), hepatic encephalopathy (21.5%), intracranial malignancy (8.8%) and others (intracranial infection, reversible posterior leukoencephalopathy syndrome (RPLS), subclinical seizures) in 21.5%.9 Similarly, our study also found septic/ metabolic encephalopathy to be the commonest cause, with the majority (83.9%) of these patients having a normal ONSD. As septic/metabolic encephalopathy forms a large cohort of patients with altered sensorium in a medical ICU, it would be worthwhile to conduct an adequately powered study to validate ONSD in these patients. This gives an insight into the spectrum of diseases causing signs and symptoms of raised ICP in a neuromedical ICU.

There was no statistically significant difference between raised ONSD and SOFA scores and APACHE II scores. The severity of the disease seems to have no impact on ONSD. The hospital LOS, ICU LOS, and ICU mortality did not show any statistical correlation with ONSD. Hence, ONSD may not be a good test for prognostication in a neuro-medical ICU. However, patients with raised ONSD had a statistically higher rate of surgeries in our study and raised ONSD may indicate a greater likelihood for surgical intervention.

There are several strengths in our study. We included a reasonably large number of patients. This was a prospective study with a well-defined study protocol. The study was done in a single centre, so the ICU admission protocol and management strategies were uniform and standardized. We used CT/MRI brain as the gold standard for comparison with US-ONSD. We acknowledge the inferiority of CT/MRI to invasive gold standard measures of raised ICP. However, as invasive ICP monitoring is not readily available, CT/MRI shows a more real-life situation and may have better external validity, especially in resource-poor settings. Limitations were that all data were obtained from a single centre database, which may result in concerns regarding the generalization of the conclusions. We did not perform serial ONSD measurements or ONSD pre and post-treatment or procedures undertaken for raised ICP. Hence, the effect of therapeutic strategies on delta ONSD is not available.

CONCLUSIONS

Given the good sensitivity, positive LR and AUROC, ONSD can be used as a screening test to detect raised ICP in a medical ICU and future potential as a threshold trigger to escalate the management of raised ICP. This can help decrease the time gap between the episode of raised ICP and the initiation of treatment.

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1.	*patients older than 18 years admitted to the*	Comparison of the Mortality in Emergency Department Sepsis Score, Modified Early Warning Score, Rapid Emergency Medicine Score and Rapid Acute Physiology Score for predicting the outcomes of adult splenic abscess patients in the emergency department	Originality
2.	*mean ± standard deviation (SD) or median with interquartile range (IQR), and*	Clinical presentation of perineal endometriosis and prognostic nomogram ... https://bmcwomenshealth.biomedcentral.com/articles/10.1186/s12905-022-02068-3	Originality
3.	*The mean age of patients in our study*	Microbiological profile and risk factors for in-hospital mortality of infective endocarditis in tertiary care hospitals of south Vietnam	Originality
4.	*mannitol has been shown to be effective in*	The Effect of Mannitol on Intracranial Pressure and Cerebral Blood Flow https://link.springer.com/chapter/10.1007/978-3-642-65486-2_30	Originality