

Correlation of Optic Nerve Sheath Diameter with Direct Measurement of Intracranial Pressure

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Abstract

Background: Measurements of the optic nerve sheath diameter (ONSD) using bedside ultrasound (US) have been shown to correlate with clinical and radiologic signs and symptoms of increased intracranial pressure (ICP).

Objectives: Previous literature has identified 5 mm as the ONSD measurement above which patients exhibit either clinical or radiologic signs of elevated ICP. The goals of this study were to evaluate the association between ONSD and ICP and to validate the commonly used ONSD threshold of 5 mm using direct measurements of ICP as measured by ventriculostomy.

Methods: A prospective blinded observational study was performed using a convenience sample of adult patients in both the emergency department (ED) and the neurologic intensive care unit (ICU) who had invasive intracranial monitors placed as part of their clinical care. Ocular USs were performed with a 10–5 MHz linear probe. Emergency physicians (EPs) with previous ocular US experience performed ONSD measurements while blinded to the contemporaneous ICP reading obtained directly from invasive monitoring. The association between ONSD and ICP was assessed with the Spearman rank correlation coefficient, and a receiver operator characteristic (ROC) curve was created to determine the optimal ONSD cutoff to detect ICP > 20 cm H₂O.

Results: Thirty-eight ocular USs were performed on 15 individual patients. Spearman rank correlation coefficient of ONSD and ICP was 0.59 ($p < 0.0005$) demonstrating a significant positive correlation. An ROC curve was created to assess the ability of ONSD to distinguish an abnormal ICP greater than 20 cm H₂O. The area under the ROC curve was 0.93 (95% confidence interval [CI] = 0.84 to 0.99). Based on inspection of the ROC curve, ONSD > 5 mm performed well to detect ICP > 20 cm H₂O with a sensitivity of 88% (95% CI = 47% to 99%) and specificity of 93% (95% CI = 78% to 99%).

Conclusions: Using an ROC curve the authors systematically confirmed the commonly used threshold of ONSD > 5 mm to detect ICP > 20 cm H₂O. This study directly correlates ventriculostomy measurements of ICP with US ONSD measurements and provides further support for the use of ONSD measurements as a noninvasive test for elevated ICP.

ACADEMIC EMERGENCY MEDICINE 2008; 15:201–204 © 2008 by the Society for Academic Emergency Medicine

Keywords: ultrasound, intracranial pressure, optic nerve sheath diameter

The diagnosis of elevated intracranial pressure (ICP) is both challenging and critical, because prompt recognition and treatment are essential to prevent possible brain damage or death. Bedside ocular ultrasound (US) is emerging as a noninvasive technique

to detect elevated ICP. Increased ICP is transmitted to the subarachnoid space surrounding the optic nerve, causing optic nerve sheath expansion.¹ Measurement of the optic nerve sheath diameter (ONSD) has been studied in postmortem specimens,² intrathecal infusion models,³ children with ventriculoperitoneal shunts,⁴ and emergency department (ED) patients with head injuries.^{5,6} In the clinical studies performed to date, ONSD has been correlated with clinical symptoms or computed tomography (CT) abnormalities, both surrogate indicators of elevated ICP.

Intracranial pressure can be definitively measured and monitored through placement of invasive monitoring devices such as an extraventricular drain (EVD).^{7,8}

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Received July 30, 2007; revisions received September 10 and September 27, 2007; accepted September 30, 2007.

Presented at the Annual Meeting of the Society for Academic Emergency Medicine, May 16–19, 2007, Chicago, IL.

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To the best of our knowledge, no studies thus far have examined the correlation between ONSD and direct ICP measurements from EVD. The goals of the study were to evaluate the correlation between ONSD and direct ICP measurements, to test the sensitivity and specificity of ONSD measurements to detect elevated ICP (> 20 cm H₂O) and to evaluate the validity of the previously published consensus ONSD measurement of 5 mm as being the upper limit of normal.

METHODS

Study Design

We performed a prospective, blinded, observational study of adult ED and neurologic intensive care unit (ICU) patients with invasive intracranial monitoring placed as part of their clinical care. Surrogate written consent was obtained from patients' family members or health care proxies, and the study was approved by the institutional review board of the participating hospital.

Study Setting and Population

This research was conducted at a large, urban, academic ED and Level 1 trauma center with an annual ED patient volume of approximately 75,000 patients. Patients were enrolled between May 1, 2006, and December 20, 2006. Exclusion criteria included patients less than 18 years of age or patients with significant ocular trauma.

Study Protocol

Patients were enrolled as a convenience sample based on availability of study physicians. Measurements were obtained when possible on Days 1, 2, and 3 during intracranial monitoring. Two emergency physicians (EPs), each with at least 3 years' experience in emergency US scanning and with at least 60 prior ocular US scans examining the ONSD, performed the scans. Based on prior research with normal subjects, the two EPs have shown acceptable interrater reliability for ONSD US.⁹

US Measurements Ocular USs were performed on a Sonosite Micromaxx (SonoSite Inc., Bothell, WA) machine with a 10–5 MHz linear probe using a standard technique described in the literature.¹ Briefly, subjects were examined in the supine position. Conductive US gel was placed over a closed eyelid. A linear probe was used to obtain axial cross-sectional images of the optic nerve, and the ONSD was measured 3 mm posterior to the orbit. For each subject, the sonographer performed three measurements on each eye. The resulting six measurements were then averaged to yield a mean ONSD, to minimize intraoperator variability.

ICP measurement Contemporaneous to the US measurements of ONSD, the patient's nurse clamped the EVD and the ICP was recorded electronically each minute during the US measurements. The ICP measurements were averaged to yield a mean ICP for each subject during the approximately 5 minutes required to perform US measurements for both eyes. Four US measurements were taken simultaneously to the EVD placement, and the opening pressure was used as the

ICP. Ultrasonographers were blinded to the contemporaneously-obtained ICP measurements.

Data Analysis

Data logs were kept and transferred to an SPSS database (Version 14, SPSS, Chicago, IL). A scatterplot was produced to examine the data, and the ONSD and ICP distributions were tested for normality. The Spearman rank correlation coefficient with a two-tailed p-value was used to assess for an association between the two measurements. Two-tailed Student's t-test was used to compare the 38 ONSDs in patients with ICP greater or less than 20 cm H₂O. To account for repeated measurements or clustering of the 38 measurements within 15 patients, the t-test was repeated after averaging the ONSD and ICP values for each patient. No weighting was used to account for the number of measurements per patient. A receiver operator characteristic (ROC) curve was constructed to determine the optimal ONSD cutoff to detect ICP > 20 cm H₂O. Descriptive statistics, Kolmogorov-Smirnov (K-S) tests for normality, Spearman rank correlation, Student's t-test, and ROC curve construction were performed using SPSS. Ninety-five percent confidence intervals (CIs) for sensitivity and specificity were computed using exact statistics with Statxact (Statxact 3, Cytel Software, Cambridge, MA).

RESULTS

Thirty-eight ocular USs were performed on 15 individual patients, 10 male and 5 female, with an average age of 60 years (range 27–83 years). Four patients had traumatic injuries, and 11 had spontaneous intracerebral hemorrhages. One ultrasonographer performed 26 scans, the other performed 12 scans. Of the 15 patients, 1 patient had one scan, 6 patients had two scans, 7 patients had three scans, and 1 patient had four scans. All patients were intubated and had invasive ICP monitoring placed as part of their clinical care. No patients were known to have ocular disease that might affect the US measurements. Additionally, 10 of the patients had magnetic resonance imaging scans during their hospitalization, and none had evidence of optic nerve pathology.

We first assessed the relationship between ONSD and ICP. Based on the biologic characteristics of a nerve sheath, we did not expect a purely linear expansion of the ONSD. Prior studies suggested that with increasing ICPs there might be a maximum nerve sheath diameter that would create an asymptotic relationship.³ A scatterplot of ICP as a function of ONSD demonstrates this relationship with the maximum ONSD in this population of 6.2 mm (Figure 1). Furthermore, using the K-S test for normality, the ONSD values had a p-value of 0.20, consistent with a normal distribution, but the ICP values had a p-value of < 0.0005, not consistent with normality. Thus, the nonparametric Spearman rank correlation coefficient was used to assess the relationship between the two variables, and it was found to be 0.59 (p < 0.0005).

The ONSD measurements in patients with ICP less than or greater than 20 cm H₂O were compared. For the eight patient measurements with ICP > 20 cm H₂O,

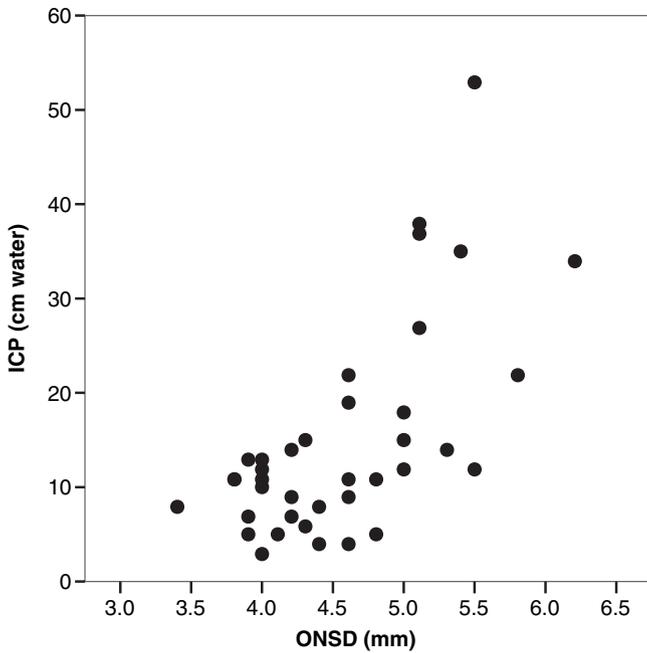


Figure 1. Scattergram of ICP versus ONSD. ICP = intracranial pressure; ONSD = optic nerve sheath diameter.

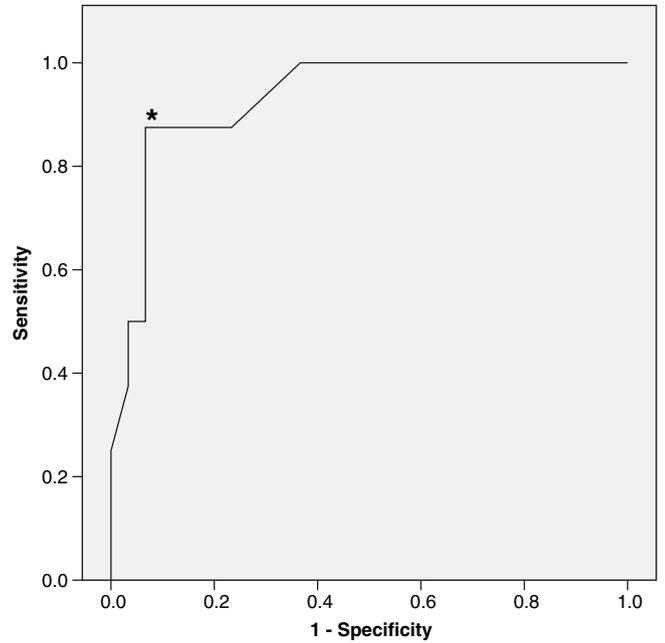


Figure 3. ROC curve for ONSD as a test for ICP > 20 cm water. *The threshold of ONSD = 5 mm. ROC = receiver operator characteristic; ONSD = optic nerve sheath diameter; ICP = intracranial pressure.

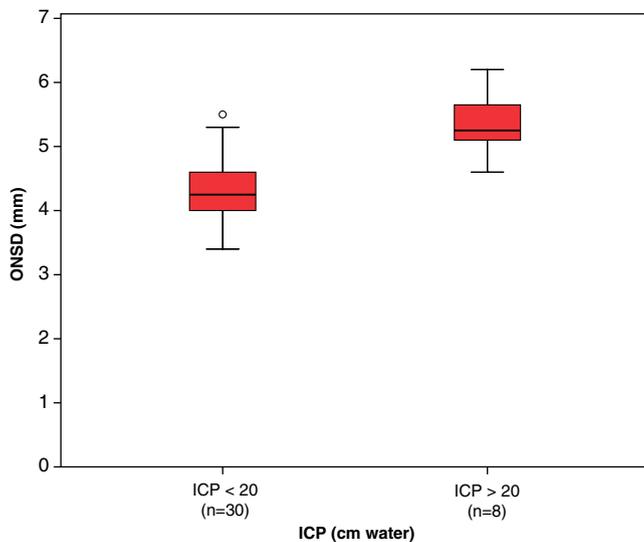


Figure 2. Boxplot of ONSD for patients with ICP greater or less than 20 cm H₂O. The central line is the median, the box represents the interquartile range, the whiskers extend to the largest and smallest values within 1.5 box lengths, and the circle represents an outlier. ONSD = optic nerve sheath diameter; ICP = intracranial pressure.

the mean ONSD was 5.4 ± 0.49 mm, and for those 30 patient measurements with ICP < 20 cm H₂O, the mean ONSD was 4.4 ± 0.49 mm (Figure 2). K-S testing suggested both distributions were consistent with normality. Student's t-test comparison of the means demonstrated a mean difference of 1.0 (95% CI = 0.6 to 1.4). The t-test was repeated using the average values for each patient and the 15 patients as the units of analysis. The mean difference in ONSD was found to be 1.2 (95% CI = 0.5 to 1.8).

Because we were able to use actual ICP as the criterion standard, we created an ROC curve (graph of sensitivity vs. 1 - specificity) to establish the optimal cutoff to optimize ONSD sensitivity and specificity (Figure 3). The ROC curve demonstrated an area under the curve of 0.93 (95% CI = 0.84 to 0.99). The commonly used cutoff of ONSD > 5.0 mm yielded the most favorable balance of test characteristics, with a resulting sensitivity of 88% (95% CI = 47% to 99%) and specificity of 93% (95% CI = 78% to 99%). Using an ONSD of 4.5 mm gives a sensitivity of 100%, but a specificity of only 63% in this sample.

DISCUSSION

This study sought to correlate US measurements of ONSD performed at the bedside with direct invasive measurement of ICP. Our findings, using ventriculostomy as the criterion standard, confirm prior literature findings for this emerging ICP evaluation technique.

Two recent studies compared US measurements of ONSD with head CT findings of increased ICP in the ED. Blaivas et al.⁵ evaluated 35 patients suspected of having increased ICP from either head trauma or intracranial hemorrhage and reported sensitivity of 100% with specificity of 95% (no CI reported) for an upper limit cut-off value of 5 mm for normal ONSD.⁵ Similarly, Tayal et al.⁶ evaluated 59 ED patients with suspected increased ICP and reported ONSD to have sensitivity of 100% (95% CI = 68% to 100%) and specificity of 63% (95% CI = 50% to 76%).⁶ However, head CT does not provide direct measurement of ICP, and the surrogate findings on head CT are not always predictive of ICP.^{7,10}

Our US study is the first, to our knowledge, to use invasive intracranial monitoring as a reference standard.

Additionally, we were able to create an ROC curve with our data, which permits the threshold value to be altered to optimize either sensitivity or specificity. Thus in this study, an ONSD of > 5 mm yields an attractive combination of sensitivity (88%) and specificity (93%) to detect ICP > 20 cm H₂O. An ONSD of > 4.5 mm would detect elevated ICP with 100% sensitivity in this sample, but at the cost of decreased specificity (63%).

A noninvasive, rapid, bedside method of determining elevated ICP, or ruling out elevated ICP, would be useful in a variety of clinical settings. This technique could be useful while waiting for CT or to monitor changing clinical exams both in the ED and in the ICU. It would also be useful in more remote or international locations, disaster scenes, long transports, or other situations where radiologic imaging is unavailable, but clinical management would change based on a diagnosis of elevated ICP.

LIMITATIONS

The study is limited by its small size and the results should be validated in larger trials. This was also a convenience sample based on investigator availability. The observations were performed by two investigators with experience in ocular US, which may limit generalizability to other observers. While we used the standard technique, there may be other ways to measure ONSD more accurately, which is an area of ongoing research. Repeated measurements of the same patients were made over the course of a few days while the ICP fluctuated. These data points may not have been truly independent, and this could decrease the variance in the ONSD measurements. However, the difference in ONSD between patients with and without elevated ICP remained significant, even when collapsing the data to 15 patient data points.

CONCLUSIONS

A noninvasive bedside test to detect increased ICP could have wide ranging applications for this potentially devastating clinical process. In this pilot study, we confirmed the commonly used threshold of ONSD > 5 mm to detect increased ICP and again demonstrated the significant positive correlation between ONSD measurements by US and ICP. Bedside ocular US measurement of the ONSD has the potential to be a

useful clinical and research test for elevated ICP if the technique can be validated in larger trials.

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