

Reliability of Optic Nerve Ultrasound for the Evaluation of Patients with Spontaneous Intracranial Hemorrhage

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Abstract

Introduction The aim of our study is to confirm the reliability of optic nerve ultrasound as a method to detect intracranial hypertension in patients with spontaneous intracranial hemorrhage, to assess the reproducibility of the measurement of the optic nerve sheath diameter (ONSD), and to verify that ONSD changes concurrently with intracranial pressure (ICP) variations.

Methods Sixty-three adult patients with subarachnoid hemorrhage ($n = 34$) or primary intracerebral hemorrhage ($n = 29$) requiring sedation and invasive ICP monitoring were enrolled in a 10-bed multivalent ICU. ONSD was measured 3 mm behind the globe through a 7.5-MHz ultrasound probe. Mean binocular ONSD was used for statistical analysis. ICP values were registered simultaneously to ultrasonography. Twenty-eight ONSDs were measured consecutively by two different observers, and interobserver differences were calculated. Twelve coupled measurements were taken before and within 1 min after cerebrospinal fluid (CSF) drainage to control elevated ICP.

Results Ninety-four ONSD measurements were analyzed. 5.2 mm proved to be the optimal ONSD cut-off point to predict raised ICP (>20 mmHg) with 93.1% sensitivity (95% CI: 77.2–99%) and 73.85% specificity (95% CI: 61.5–84%). ONSD–ICP correlation coefficient was 0.7042 (95% CI for $r = 0.5850$ – 0.7936). The median interobserver ONSD difference was 0.25 mm. CSF drainage to control elevated ICP caused a rapid and significant

reduction of ONSD (from 5.89 ± 0.61 to 5 ± 0.33 mm, $P < 0.01$).

Conclusion Our investigation confirms the reliability of optic nerve ultrasound as a non-invasive method to detect elevated ICP in intracranial hemorrhage patients. ONSD measurements proved to have a good reproducibility. ONSD changes almost concurrently with CSF pressure variations.

Keywords Optic nerve sheath diameter · Ultrasound · Intracranial hemorrhage · Intracranial pressure

Introduction

Intracranial hypertension is a common complication of spontaneous intracranial hemorrhage. Its early recognition in comatose patients is urgently needed for diagnosis and therapeutic reasons.

The optic nerve is ontogenetically a part of the central nervous system, and it is surrounded by subarachnoid cerebrospinal fluid (CSF) and dura mater (optic nerve sheath, ONS). ONS diameter (ONSD) changes following CSF pressure variations [1, 2].

Bedside ultrasonographic measurement of ONSD has been proposed as a reliable means to detect raised intracranial pressure (ICP), both in experimental [3] and in clinical settings, with a good predictive value if compared to neuroimaging [4–9] or during intrathecal infusion tests in patients with hydrocephalus [10].

Four recent studies found a significant correlation between ONSD and invasive ICP measurements in patients after severe traumatic brain injury (TBI) [11–14].

This correlation was also found in patients with spontaneous intracranial hemorrhage [15].

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Both ONSD–ICP correlation coefficients and ONSD cut-off points to detect elevated ICP, however, vary throughout these studies.

This literature does not allow to make definitive statements over the reproducibility of ONSD measurements as only one [11] of the previously mentioned studies considers ONSD interobserver variability in a 12-patient subgroup.

More recent observations also underline the significant incidence of artifacts resulting in false ONSD measurements [16].

Finally, to our knowledge, no previous study exists focusing attention on the time needed by ONSD for equilibration after rapid ICP changes.

The primary goal of this investigation is to confirm the reliability of optic nerve ultrasound as a method to detect elevated ICP in intracranial hemorrhage patients and to assess the reproducibility of ONSD measurements.

The secondary goal is to verify that ONSD changes concurrently with rapid ICP variations.

Materials and Methods

Design of the Study

Prospective blind observational study in a 10-bed multi-valent ICU.

Patients

Between April 2007 and March 2009, 63 adult patients with primary intracerebral hemorrhage (29) or subarachnoid hemorrhage (34) requiring ICP monitoring, sedation, and mechanical ventilation were enrolled.

Exclusion criteria were age < 18 years, obvious ocular pathology, no ultrasonographer available.

Either propofol and remifentanyl or propofol and fentanyl infusion was used for sedation.

The study was approved by the local ethics committee and consent was obtained by the closest relative of each patient.

Measurements

Data were collected on day 1, and, if possible, on day 2 after the admission. In 12 patients with ICP > 20 mmHg and intraventricular drain, ONSD was measured before and within 1 min after CSF drainage to bring ICP below 20 mmHg.

Ocular sonography was performed by three experienced operators, each with at least 3 years of experience in scanning and with at least 60 prior ocular scans examining the ONSD. A 7.5-MHz linear probe placed in the gel over

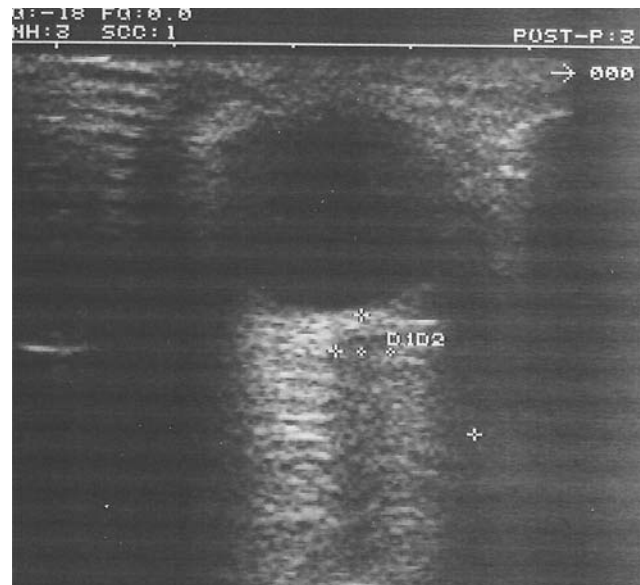


Fig. 1 Optic nerve overview

the upper closed eyelid was used (ultrasound unit: Hitachi EUB 405, Hitachi Medical Corporation, Tokyo, Japan).

According to previous protocols [7, 8, 17, 18], ONSD was measured 3 mm behind the globe (Fig. 1) and two measurements were considered for each ONS (one measurement was taken in the sagittal plane, with the probe being vertical, one in the transversal plane, with the probe being horizontal). The head of the bed was kept at 30–45°.

ICP and hemodynamic parameters were obtained simultaneously to ONSD measurement. Each operator took 2–3 min to perform all the measurements needed to calculate the ONSD. The ICP collected was the average ICP during this time period. The investigators were always blinded to ICP values.

In 39 patients, ICP was measured through an intraventricular drain (Codman EDS 3 CSF External Drainage System), in 24 through an intraparenchymal bolt (Codman MicroSensor Skull Bolt Kit, Codman, Raynham, MA, USA).

Any complication potentially related to the ultrasound probe was collected.

Statistical Analysis

All data are expressed as mean \pm standard deviation, unless otherwise specified. The average ONSD between the two eyes was used for analysis.

A scatterplot was produced to examine ONSD and ICP, and linear regression analysis was carried out.

Elevated ICP was defined as an ICP value steadily > 20 mmHg during the time needed for scanning.

Student's *t*-test was used to compare the study patients and ONSD measurements with ICP greater or less than 20 mmHg. $P < 0.01$ was regarded as significant.

A receiver operator characteristic (ROC) curve was constructed to determine the optimal ONSD cut-off point to detect elevated ICP. Sensitivity, specificity, and 95% CIs were also calculated.

The difference between ONSD measurements in the sagittal plane and measurements in the axial plane was calculated.

Twenty-eight ONSDs were measured consecutively by two ultrasonographers and the difference in each couple of measurements was considered as an index of reproducibility. The measurements of the second observer were not used for ONSD–ICP correlation or ROC curve analysis.

A commercially available program was used for analysis (version 16 SPSS, Chicago, IL, USA).

Results

ICP and hemodynamic parameters are reported in Table 1.

Ninety-four ONSDs were measured. ONSD was 6.16 ± 0.57 mm in case of ICP > 20 mmHg (28 measurements in 26 patients), a significantly higher value than in low ICP measurements (5.0 ± 0.49 mm, $P < 0.01$). CSF drainage to bring ICP below 20 mmHg caused a concurrent ONSD reduction (from 5.89 ± 0.61 to 5 ± 0.33 mm, $P < 0.01$).

As shown in Fig. 2, there was a significant correlation between ONSD and ICP ($r = 0.7042$, $P < 0.0001$, 95% CI for $r = 0.5850$ – 0.7936).

By using ICP as the standard criterion, we created a ROC curve (Fig. 3, graph of sensitivity vs. 100-specificity, AUC = 0.925, 95% CI: 0.852–0.969) to establish the optimal cut-off point to optimize ONSD sensitivity and

Table 1 Optic nerve ultrasound, intracranial pressure, and hemodynamic characteristics

	ICP < 20 ($n = 65$)	ICP > 20 ($n = 29$)	<i>P</i>
ONSD (mm)	5.0 ± 0.49	6.16 ± 0.57	<0.01
ICP (mmHg)	11.6 ± 3.9	32.0 ± 11.8	<0.01
MAP (mmHg)	78.5 ± 18.9	84.5 ± 15.6	NS
CPP (mmHg)	66.6 ± 19.6	50.8 ± 18.2	<0.01
CF(bpm)	84 ± 27	76 ± 34	NS

All the measurements were taken simultaneously. ICP > 20 and ICP < 20 indicate measurements taken with an intracranial pressure greater or less than 20 mmHg, respectively. Intracranial pressure and hemodynamic parameters are the average values registered during scanning

ONSD optic nerve sheath diameter, ICP intracranial pressure, MAP mean artery pressure, CPP cerebral perfusion pressure, CF cardiac frequency

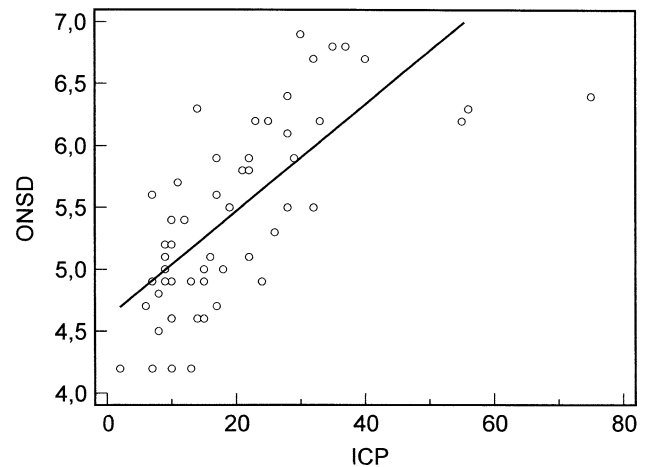


Fig. 2 Scatterplot: ONSD vs. ICP. $R = 0.7042$, $P < 0.0001$, 95% CI for $r = 0.5850$ – 0.7936

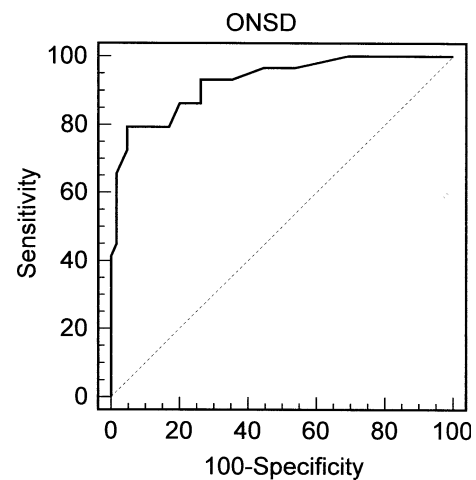


Fig. 3 ROC curve for optic nerve sheath diameter. AUC = 0.925, 95% CI: 0.852–0.969

specificity. An ONSD measurement of 5.2 mm yielded the most favorable balance of test characteristics, with a sensitivity of 93.1% (95% CI: 77.2–99%) and a specificity of 73.85% (95% CI: 61.5–84%).

Of the 28 ONSD measurements taken consecutively by 2 operators, 10 were taken with ICP > 20 mmHg, 18 with ICP < 20 mmHg. The median interobserver difference was 0.25 mm (interquartile range 0.1–0.4 mm).

The measurements taken in the axial plane proved to be slightly higher than the measurements taken in the sagittal plane (median difference 0.15 mm, range 0–0.3 mm).

Optic nerve ultrasound gave no rise to complications.

Discussion

This investigation, considering 94 simultaneous ONSD and ICP measurements, confirms the reliability of ONSD

measurement for the evaluation of patients with spontaneous intracranial hemorrhage.

In a previous study analyzing 53 ONSD measurements taken before ICP monitoring placement, ONSD–ICP correlation coefficient was 0.69. In this study, the 5.2 mm cut-off point showed a 94% sensitivity and a 76% specificity [15].

Similarly, two recent studies by Geeraerts et al. [11, 13] found a 0.68 and a 0.69 correlation coefficient, respectively, whereas the ONSD cut-off value was 5.9 and 5.86 mm, respectively. These authors found a 0.27 mm mean standard deviation for repeated measurements of the same patient performed by 2 observers in a 12-patient subgroup [11].

Harbison Kimberly et al. [12] calculated a 0.59 ONSD–ICP correlation coefficient in a 15-patient sample. They considered an optimal ONSD upper limit of 5 mm to predict ICP > 20 mmHg, which is the same cut-off point of the studies comparing ONSD to neuroimaging in adult patients [6–9].

Soldatos et al. [14] found a 0.68 correlation coefficient and an optimal ONSD cut-off point of 5.7 mm in 32 patients with severe TBI.

The number of measurements of the same patients, anathomy, absolute values of ICP, delay between ONSD and ICP measurements may have influenced these results, and may explain the different findings in these studies.

Given the biologic characteristics of the ONS, we do not expect a purely linear correlation between ONSD and ICP measurements for higher or lower (< 10 mmHg) ICP values, as in these cases the ONS reaches its maximum distensibility or adheres to the optic nerve, respectively [6].

The occurrence of artifacts may affect ONSD measurement as well. The transbulbar sound direction and the incidence of the ultrasound beam on the lamina cribrosa [16] or the dura mater [19] may produce acoustic shadows behind the globe. The incidence of these artifacts grows greater if the probe has a frequency of < 7.5 MHz.

Interestingly, in our sample, the measurements taken in the axial plane are slightly higher than the measurements in the sagittal plane. Since the ONS is a tubular structure, we assume that this difference is due to the more frequent occurrence of artifacts as the probe is horizontal.

Considering the mean of four diameters (two in the axial and two in the sagittal plane) reduces the impact of those artifacts on the final measurement, so our analysis showed an acceptable interobserver variability of repeated measurements with the same ultrasound unit.

Furthermore, a previous study found a good correlation between optic nerve ultrasound and magnetic resonance imaging of the ONS [20].

To our knowledge, no previous study exists, calculating the time needed by ONSD for equilibration during ICP

changes. Since the ONSD is actually the average of four measurements, real-time variations of ONSD during rapid ICP changes cannot reliably be detected. Our 12-patient subgroup analysis, however, suggests that ONSD variations occur almost concurrently with CSF pressure variations.

Small sample size is the major limitation of our study and may limit the generalizability of our results. A second limitation for our previously mentioned 12-patient subgroup analysis is that the ultrasonographer, though being blinded to absolute ICP values, was aware of CSF drainage. For the other measurements, however, we managed to keep the observer blinded both to ICP and to therapeutic interventions.

Conclusions

Since ONSD measurements may be operator dependent and ONSD–ICP correlation is suboptimal, ultrasonography may not be considered as a substitute of invasive ICP monitoring in a critical care setting.

However, it proves to be a reliable means for the evaluation of patients with intracranial hemorrhage, and to have a good reproducibility.

Ultrasonography is safe, easily available and feasible in a critical care setting. Moreover, it may be assumed that ONSD changes almost concurrently with rapid ICP variations.

In comatose patients, ultrasonography may be useful for differential diagnosis.

In patients with known intracranial hemorrhage, it may help monitoring clinical evolution when ICP monitoring is not feasible.

Future studies are needed to assess the optimal cut-off point to predict elevated ICP and to better confirm the accuracy of this method in larger groups of observers.

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