

Comparing ultrasonographic optic nerve sheath diameter to head computed tomography scan to predict intracranial pressure elevation

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Abstract

Introduction: Intracranial hypertension is an emergency condition that needs to be recognized as soon as possible. Lumbar puncture, the gold standard diagnostic procedure for intracranial hypertension, is contraindicated in some conditions while brain imaging procedures may be too difficult to be performed on critically ill patients. To solve this problem, this study aims to assess an alternative method to detect intracranial hypertension by measuring optic nerve sheath diameter using ocular ultrasound and optic nerve sheath diameter difference in each etiology.

Methods: This cross-sectional study was conducted at the Emergency Department of Dr Iskak Tulungagung General Hospital. Sixty-nine patients who visited the emergency room for the first onset of intracranial pathology were included for optic nerve sheath diameter measurement by ultrasound. Subjects were divided into elevated and non-elevated intracranial pressure groups based on head computed tomography scan findings. The optic nerve sheath diameter results were compared and analyzed.

Result: There were 29 subjects in the elevated intracranial pressure group and 40 subjects in the non-elevated intracranial pressure group. The mean of optic nerve sheath diameter in the elevated and non-elevated intracranial pressure groups was 0.63 ± 0.06 and 0.57 ± 0.06 cm, respectively ($p = 0.000$). Based on receiver operating characteristics analysis, 0.58 cm was the most optimal cut-off value.

Conclusion: Ultrasonographic optic nerve sheath diameter can be used to predict elevated intracranial pressure in suspected patients who are contraindicated to invasive intracranial pressure measurement or critically ill. There were significant differences between elevated and non-elevated intracranial pressure groups in stroke and trauma subjects.

Keywords

Intracranial hypertension, intracranial pressure, optic nerve sheath diameter, ocular ultrasound

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Introduction

According to Monroe–Kellie doctrines, elevated intracranial pressure (ICP) can be caused by the increase of one or more components of the intracranial compartment (i.e. brain, blood, and cerebrospinal fluid).¹ The epidemiology of elevated ICP is unknown, but the most discussed etiologies are traumatic brain injury and stroke. The number in Indonesia may be high due to the increasing cases of stroke based on the Indonesian Ministry of Health data.²

Intracranial hypertension is an emergency condition defined by ICP of higher than 20 mmHg, which is measured

by lumbar puncture.¹ Lumbar puncture, as the gold standard of ICP measurement, cannot always be conducted due to some contraindications, such as (1) space-occupying lesion with mass effect, (2) mass at the posterior fossa, (3) Arnold–Chiari

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malformation, (4) current use of anticoagulant, (5) coagulopathy and uncorrected bleeding diathesis, (6) infection at the puncture site, and (7) congenital spine abnormality. The contraindications must be excluded to prevent complications (e.g. brain herniation, hemorrhage), usually by brain imaging (computed tomography (CT) scan or magnetic resonance imaging (MRI)).³ But even brain imaging may be too difficult to carry out for critically ill patients. Therefore, an ancillary diagnostic procedure is needed for these difficult presentations.

Ultrasound (US) is growing to be an essential diagnostic tool for many specialties due to its rapid, real-time, and non-invasive diagnostic ability, hence it is widely used in emergency conditions. US is also free of radiation exposure and costs less than brain imaging. Due to its benefits, we used US to measure optic nerve sheath diameter (ONSD) in order to determine the ICP conditions of our patients. Optic nerve sheath is the continuation of meningeal layers. The logic in measuring ONSD is that the meningeal layers and optic nerve sheath stretch as the ICP elevates.⁴

There are several research measuring ONSD and its relation to intracranial hypertension with different cut-off values in different populations, but similar studies are still scarce in Indonesia and no one has attempted to find the cut-off value of US ONSD for diagnosing intracranial hypertension. This study aims to analyze ultrasonographic ONSD to determine elevated ICP and the difference in each case presentation, especially in the Indonesian population.

Materials and methods

Design

This was a cross-sectional study conducted in the Emergency Department of Dr Iskak Tulungagung General Hospital, East Java, Indonesia from October 2020 to December 2020. Data were collected by emergency medicine specialists and general practitioners who had been trained to measure ONSD using the ocular US. To ensure similar comparison, elevated ICP is determined using head CT scan and defined when fulfilling at least one of these conditions: (1) massive intracranial hemorrhage (defined as hemorrhage of at least 3 cm in the largest dimension in the cerebral hemisphere or at least 1.5 cm in the largest dimension in the brainstem), (2) intraventricular extension of subarachnoid hemorrhage (SAH), (3) basal cistern compression, (4) ≥ 0.5 cm of midline shift, and (5) acute hydrocephalus. The head CT scan criteria for subject categorization were adapted from previous studies.^{5,6} Head CT scan expertise was provided by radiology specialists in Dr Iskak Tulungagung General Hospital. The examiners were not blinded to the head CT scan result.

The sample size was calculated using the following formula

$$n = \frac{Z\alpha^2 \text{sens}(1 - \text{sens})}{d^2 P} = 35.28 \approx 36$$

where n is the total number of subjects; $Z\alpha$ is the standard alpha (1.96); *sens* is the expected sensitivity; d is precision; and P is prevalence (considered to be 0.5 because of no prior prevalence studies on intracranial hypertension).

Patient

We included all patients aged ≥ 18 years old who were admitted with the first onset of intracranial pathology and underwent a head CT scan (with or without contrast) to determine whether they would enter the elevated ICP or the non-elevated ICP group. Exclusion criteria included severe orbital or facial trauma, chronic hydrocephalus, history of ocular disease (especially in the optic nerve or orbital cavity), history of hyperthyroidism with exophthalmos, lid lag, and history of glaucoma. Verbal consent was obtained from the patient or patient's family after we informed them of the study protocol. Patients or patients' representatives were informed about the purpose of this study, the procedure, and that refusal would not cause different treatment.

Procedure

US examination was performed within 2–3 h of admission. Patients were examined in a supine position with 20°–30° head elevation. US probe with gel was applied transversally to the patient's relaxed closed eyes and perpendicularly to the optic nerve axis (B mode). USG GE Healthcare Venue 40 Anesthesia was used for measurement. By using the linear probe, the optic nerve is discovered 3 mm behind the globe. Three measurements were taken: (1) optic nerve diameter, (2) internal ONSD (the distance between the inner border of dura mater), and (3) external ONSD (the distance between the outer border of dura mater). Unit of optic nerve diameter, internal ONSD, and external ONSD will be in centimeters (cm).^{4,7} Figure 1 is an example of ONSD measurement.

Statistical analysis

Statistical package for the Social Sciences (SPSS) 20 was used for data analysis. Categorical data were presented in cross tables. Numerical data were assessed for their normality. Normally distributed data were presented as mean \pm standard deviation, while non-normally distributed data were presented as median (minimum–maximum value). Parametric comparisons were performed using the *T*-test or Mann–Whitney test. The threshold and diagnostic values were explored using receiver operating characteristics (ROC) analysis.

Result

There were 69 subjects included in this study and their baseline characteristics are presented in Table 1. There was no significant difference in either age or gender between the two study groups. In both groups, stroke contributed the most cases followed by trauma. The types of stroke in this

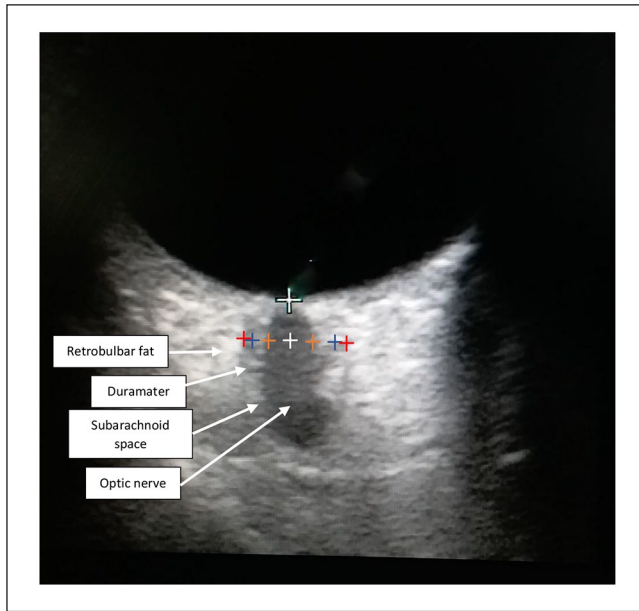


Figure 1. A picture of ocular B-scan that was taken during data collection. Markers were edited and colored for clarity; they did not reflect real-time measurement. Measurement was taken 3 mm behind the globe (the distance between white crosses). ONSD external to dura mater/external ONSD (the distance between red crosses). ONSD internal to dura mater/internal ONSD (the distance between blue crosses). Optic nerve diameter (the distance between orange crosses). ONSD: optic nerve sheath diameter.

study were ischemic stroke, hemorrhagic stroke, and/or SAH. Cases that were included in the “Other” category were metabolic abnormalities.

Optic nerve and ONSDs are presented in Table 2. There was no significant difference in all optic nerve diameter (OND) measurements between the two groups. However, all ONSD measurements were statistically significant between the groups. Since the measurements of the right and left eyes were almost identical, the subsequent analysis will only include mean ONSD.

We made ROC curves of mean internal and external ONSD and measured their area under the curve (AUC) to determine their diagnostic ability for predicting elevated ICP. Figure 2 shows that external ONSD (AUC 0.78 [95% CI 0.67–0.89]) is more accurate than internal ONSD (AUC 0.68 [95% CI 0.55–0.81]) in predicting intracranial hypertension. From the ROC curve coordinates, the best cut-off value to predict elevated ICP is 0.58 cm.

Using external ONSD as the indicator, we compared whether they would be significantly different in each case presentation. Tumor and metabolic cases were not included due to the limited number of subjects. Table 3 shows that external ONSD is significantly different in stroke and trauma cases.

Discussion

We found that internal and external ONSDs are significantly different between subjects with elevated ICP and non-elevated

Table 1. Baseline characteristics of subjects.

Baseline Characteristics	Elevated ICP (n=29)	Non-elevated ICP (n=40)	p value
Age (median; min–max)	54 ± 14.18	56 ± 18.01	0.434
Gender, male (%)	17 (58.6)	23 (57.5)	0.926
Etiology			–
Stroke (%)	17 (58.6)	21 (52.5)	
Trauma (%)	8 (27.6)	16 (40.0)	
Tumor (%)	4 (13.8)	1 (2.5)	
Other (%)	0 (0)	2 (5.0)	

ICP: intracranial pressure.

ICP. Compared with internal ONSD, external ONSD yielded a more accurate prediction of intracranial hypertension. External ONSD could also detect elevated ICP in stroke and trauma subjects.

ONSD measurement using ocular US for detecting ICP elevation recently gained its fame and had been researched widely, yet research in Indonesia is still limited. Bedside ocular US for ONSD measurement has many advantages due to its noninvasiveness, portability, lower cost (relative to brain imaging), absence of ionizing radiation, and repeatability.⁸ It can be considered especially in conditions where invasive devices to measure ICP are unavailable or when the patients are too critically ill to be mobilized for radio-imaging. Wang et al.⁹ also found that ONSD measurement could be conducted for follow-up after therapy administration. Thus, it opened another possibility of qualitative ICP monitoring using ocular ultrasonography.

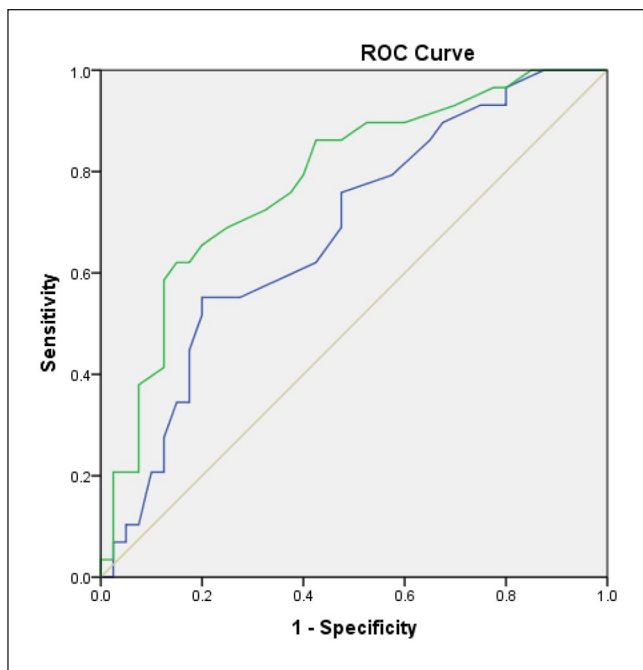
Previous ultrasonographic ONSD studies showed results similar to this research. Wang et al.¹⁰ found that a cut-off value of 5.48 mm was associated with an ICP of >13 mmHg, while a cut-off value of 5.83 mm was associated with an ICP of >22 mmHg in patients with traumatic brain injury. The study results were similar to ours in terms of a significant difference in external ONSD in trauma subjects. Munawar et al.¹¹ found that ONSD of >0.58 cm was associated with elevated ICP in stroke patients with mass effect. We also found significantly different external ONSD in stroke subjects. Another research by Jeon et al.¹² found that ONSD measurement of 5.6 mm was the best cut-off to detect elevated ICP in mixed cases of intracranial hypertension cases (e.g. stroke, tumor, and hydrocephalus). Zoerle et al.,¹³ however, mentioned that US ONSD was not related to intracranial pressure in SAH. This study included some subjects with SAH in addition to intraventricular hemorrhage and/or intracranial hemorrhage, which makes this study incomparable to that of Zoerle et al. The negative result of Zoerle et al. may be (or may not be, which will need further research) salvaged by the use of A-mode that will be discussed in a later paragraph.

The cut-off differences between the studies above may be caused by different procedures. Stevens et al.¹⁴ found discrepancies in ONSD measurement in several studies that include marker depth and anatomical interpretation. Markers should be placed 3 mm posterior to the papillae. ONSD should be measured from the transition of retrobulbar fat to

Table 2. Measurements of optic nerve diameter and optic nerve sheath diameter.

Measurement	Elevated ICP (n=29)	Non-elevated ICP (n=40)	p value
Right OND (cm)	0.27 (0.18–0.45)	0.26 (0.15–0.35)	0.639
Left OND (cm)	0.27 ± 0.06	0.27 ± 0.04	0.758
Mean OND (cm)	0.28 ± 0.05	0.27 ± 0.03	0.477
Right internal ONSD (cm)	0.46 (0.40–0.62)	0.44 (0.30–0.93)	0.016
Left internal ONSD (cm)	0.47 ± 0.06	0.44 ± 0.05	0.008
Mean internal ONSD (cm)	0.49 (0.40–0.62)	0.43 (0.21–0.66)	0.011
Right external ONSD (cm)	0.63 (0.51–0.84)	0.57 (0.41–0.82)	0.000
Left external ONSD (cm)	0.65 (0.52–0.78)	0.56 (0.45–0.75)	0.000
Mean external ONSD (cm)	0.63 ± 0.06	0.57 ± 0.06	0.000

ICP: intracranial pressure; OND: optic nerve diameter; ONSD: optic nerve sheath diameter.
 Bold value indicates the statistical significance of $P < .05$.

**Figure 2.** ROC curve for mean internal ONSD (blue line) and external ONSD (green line).

dura mater or the outer border of subarachnoid space. The differences may also be caused by variable cases or ethnicities that may affect ONSD measurement, which should be studied further.

ONSD measurements in this study were conducted using B-mode. B-mode has some disadvantages, such as low reliability in measuring small structures and blooming effect that may overestimate the measurement. A-mode may be more advantageous because it is free of blooming effect and able to distinguish increased subarachnoid fluid from intracranial hypertension (by performing a 30 test).^{15,16} But in neurology and emergency medicine, B-mode may be more advantageous because some patients may present with decreased consciousness, which cannot be examined using A-mode that needs full cooperation from the patient.¹⁷

Table 3. Measurements of external ONSD in stroke and trauma subjects.

Etiology	Elevated ICP	Non-elevated ICP	p value
Stroke	0.63 ± 0.06	0.58 ± 0.07	0.038
Trauma	0.63 ± 0.08	0.54 ± 0.04	0.002

ONSD: optic nerve sheath diameter.

This study has several limitations. The sample size calculation should involve power analysis since the addition of subjects may strengthen the study results. This study did not use the gold standard tool for determining ICP elevation. Quantitative ICP measurement may yield a more accurate comparison. We could not compare the external ONSD of causes other than stroke and trauma due to the small number of subjects. For upcoming studies, we suggest measuring external ONSD in different etiologies of intracranial hypertension to explore the possibility of different ONSD cut-off values and blinding the examiners to prevent observer bias. More studies will be needed to compare A-mode and B-mode in measuring ONSD to predict intracranial hypertension. We also hope other researchers in Indonesia would be interested to conduct a similar study to find the best fitted ONSD cut-off value for the Indonesian population.

Conclusion

External ONSD measured by the ocular US is associated with elevated ICP. The best ONSD cut-off with ocular US measurement to determine elevated ICP in this study is 0.58 cm. Therefore, ocular ultrasonography can be used to predict elevated ICP in suspected patients who are contraindicated to invasive ICP measurement or too critically ill for radio-imaging procedures.

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Author contributions

S.N.S., H.A.N., and B.P. contributed to the study concept and design; H.A.N. and B.P. contributed to the training of data acquisition; H.A.N., B.P., S.N.S., and F.K. contributed to data acquisition; S.N.S. contributed to data analysis and manuscript drafting; H.A.N. and B.P. contributed to critical revision of the manuscript and clinical expertise.

Availability of data and materials

All materials which were taken from other sources are clearly cited.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

This study was conducted in the emergency department of Dr Iskak Tulungagung General Hospital after receiving the approval of the ethics committee. Ethical approval was granted by the Ethics Committee for Medical Research of Dr Iskak Tulungagung General Hospital on 17 November 2020 (Ethical number: 070/0233/407.206/2020).

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Informed consent

Verbal informed consent was obtained from all subjects or legally authorized representatives before the study. The reason for verbal informed consent was because this study was conducted at the beginning of COVID-19 pandemic where papers and other patient-related documents were restricted to nurse stations. Patients or patients' representatives were informed about the purpose of this study, the procedure, and that refusal would not cause indifferent treatment. Upon submitting our research proposal, we explained our method for obtaining informed consent, hence the approval of the Research Ethics Committee of Dr Iskak Tulungagung General Hospital. Study subjects or subjects' families were informed about the study protocol prior to data acquisition. Verbal consent was obtained from those who agreed to participate in this study for their anonymized information to be published in this article.

Human rights

Our work does not infringe on any rights of others, including privacy and intellectual property rights. There is no human rights violation in our manuscript.

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