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Diagnostic Accuracy of Optic Nerve Ultrasonography and Ophthalmoscopy in Prediction of Elevated Intracranial Pressure

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Abstract

Introduction: Elevated intracranial pressure (ICP) is a major and potentially lethal disorder in patients admitted to the emergency department (ED). Several methods are being used to investigate for elevated ICP. Here we assessed and compared the diagnostic accuracy of two existing tools of ophthalmoscopy and optic nerve ultrasonography in detection of elevated ICP. **Methods:** 131 participants with probable elevation of ICP referred to the emergency department of Al-Zahra Hospital, Isfahan, Iran, from 2012 to 2014, were enrolled. Brain computed tomography (CT) scan, ultrasonography of optic nerve sheath, and ophthalmoscopy were performed for them. The optic nerves sheath with diameter more than 5 millimeters was considered as elevated ICP. Widening of optic nerve, ocular venous engorgement, blurring, hemorrhage over optic disk, elevation of optic disk, and retinal venous tortuosity were recorded as evidences of ICP rising in ophthalmoscopy. Diagnostic accuracy of the two tools in prediction of ICP rising were compared with the results of brain CT scan as a gold standard. **Results:** The mean age of participants was 46.29 ± 10 years (77% male). The number of diagnosed elevated ICPs with ophthalmoscopy and ultrasound were 98 (74.8%) and 102 (77.9%) cases, respectively. The calculated sensitivity and specificity of ophthalmoscopy and ultrasonography in detection of ICP rising were 100.0% (95% CI: 88.6-100.0) and 35.4% (95% CI: 26.0-46.2), 100.0% (95% CI: 84.0-100.0) and 31.9% (95% CI: 23.0-41.7), respectively. **Conclusion:** The present study revealed that bedside ultrasonography of optic nerve sheath and ophthalmoscopy have enough accuracy for the screening of patients with probable elevation of ICP. Of course, it should be considered that despite the high sensitivity of both tools, their specificity is low.

Key words: Ultrasonography; ophthalmoscopy; diagnostic tests, routine; physical examination; optic disk

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Introduction:

Increased intracranial pressure (ICP) is a major and potentially lethal disorder in patients admitted to the emergency department (ED) (1-3). A normal ICP varies from zero to 15 millimeters of water (mmH_2O), while in a case of head trauma it rises up to 20 mmH_2O or higher, leads to severe damage to the intracranial structures (4). Brain parenchyma, cerebrospinal fluid (CSF), and blood circulation are three main components in the skull that may cause an increased ICP if their balance is disturbed (5). However, regardless of the etiology, elevated ICP usually presents common signs and symptoms. Patients with increased ICP are often presented by headache, nausea, vomiting, and progressive decline in their consciousness. The well-known Cushing triad defined as hypertension, bradycardia, and respiratory depression is the end-stage presentation in these patients (5). More precise and reliable methods are being used to diagnose patients with elevated ICP (3). To label a patient definitely with elevated ICP, a direct and invasive sampling of the CSF, also known as spinal tap, is required. The measured pressure is then considered as the golden standard of ICP (3, 6). It has been established that not all patients are eligible for such procedure and in cases of high ICP levels, as the result of space-occupying lesions, spinal tap is contra indicated; therefore, the need for more applicable ICP screening methods have yet existed. CT scan is an excellent way to study intra cranial

structures. Several imaging findings in CT scan are indicative of elevated ICP, including cerebral edema, midline structural shift, ventricular collapse, and ventricular enlargement (7). ophthalmoscopy has also been used to promptly interpretation of ICP status through ocular examination (8). Another way to determine whether a patient has elevated ICP is using the sonographic optic nerve sheath diameter (ONSD). In this method, the optic nerve sheath diameter larger than 5 millimeters is the indirect indicator of elevated ICP (3, 9, 10). Based on the above-mentioned, the present study aimed to evaluate the diagnostic accuracy of ophthalmoscopy and ultrasonography of optic nerve sheath in compare to brain CT scan in prediction of elevated ICP.

Methods:

In the present diagnostic trial, we consecutively enrolled 131 patients suspected to ICP elevation and referred to the emergency department of Alzahra Hospital, Isfahan, Iran, from 2012 to 2014. The protocol of this study was reviewed and approved by ethic committee of Isfahan University of Medical Sciences. The study was designed and conducted according to the Helsinki declaration and after complete explanation of the procedure for patients, written informed consent was obtained from all studied participants.

All included subjects were positive for signs of elevated ICP in their history and examination including nausea, vomiting, altered consciousness, and a compatible chief complaint for related diagnoses such as head trauma. In addition, age less than 18, direct trauma to the eye, ophthalmic diseases, and treatment with medications affecting intracranial pressure were defined as exclusion criteria. By considering the sensitivity of 0.9 and prevalence of 30% (11), $\alpha = 0.05$, and precision of 10% (d = 0.1), a minimum sample size with 117 patients was considered to be appropriate. After the patients' hemodynamic state was stabilized in the ED, ophthalmoscopy and brain CT scans were performed and findings recorded. Cerebral edema, midline structural shift, ventricular collapse, ventricular enlargement, and cistern compression were desired signs of ICP rising in brain CT scan. Widening of optic nerve disk, ocular venous engorgement, blurring, hemorrhage over optic nerve disk, elevation of optic disk, and retinal venous tortuosity were recorded as the signs of ICP rising in ophthalmoscopy. In addition, ONSD more than 5 millimeters was considered as the sonographic sign of ICP elevation. All CT scans were interpreted and reported by a skilled radiologist and direct ophthalmoscopy performed by ED physicians during the bedside examinations, too. CT scans were obtained by a helical CT scan machine (Siemens SOMATOM Emotion 16-slice CT system) and the images taken from the entire skull at a transverse view.

For measurement of sonographic diameter of optic nerve, participants were asked to close their eyes. The ultrasonography was done by the method described by Amini et al. (12). Briefly, a 7.5 mega Hertz probe linear transducer (HS2000, Honda, Korea), sized 5.5 × 1 centimeter, was placed on the center of each eye. Participants were asked to keep their eyes in supine position if they were looking ahead to minimize the rotation of imaging. Each optic nerve was measured three times and the mean number recorded. The mean value of two right and left optic nerve sheaths were entered in the analysis. Any patient who had an optic nerve with diameter greater than 5 millimeters was considered to have elevated ICP. Ultrasonography was performed before awareness from the result of brain CT and the operator was blind to the patient's clinical condition to prevent diagnostic suspicion bias.

Statistical analysis

Data were analyzed using STATA version 11.2 statistical software. Brain CT was defined as a gold standard. Receiver operating characteristic (ROC) and computing of the area under curve (AUC) were used to confirm the adequacy of model and select the optimum cut off for ophthalmoscopy. With assessing five ophthalmic signs in the present study, we designed a six score model (zero = no abnormal finding; five = five abnormality) for measurement of diagnostic accuracy of ophthalmoscopy. Finally, sensitivity, specificity, positive and negative predictive value, and positive and negative likelihood ratio of ultrasonography and ophthalmoscopy in prediction of ICP rising were calculated.

Table 1: Baseline characteristics of patients

Variable	Number (%)
Gender	
Male	101 (77.1)
Female	30 (22.9)
Diagnosis	
Pseudo-tumor cerebri	26 (20.2)
Epilepsy	15 (11.4)
Cerebral vein thrombosis	13 (9.9)
Loss of conciseness	11 (8.4)
ICH and IVH	11 (8.4)
Subarachnoid hemorrhage	10 (7.6)
Hydrocephaly	6 (4.6)
Other	39 (29.5)
CT scan results	
Normal	93 (71.0)
Elevated ICP	38 (29.0)
Ophthalmoscopy	
Widening of optic nerve	91 (69.5)
Blurring of optic disk	22 (16.9)
Elevation of optic disks	84 (64.6)
Hemorrhage over optic disk	3 (2.3)
Retinal venous tortuosity	14 (10.8)

CT scan: Computer tomography scan; ICP: Intracranial pressure; IVH: Intraventricular hemorrhage; ICH Intracerebral hemorrhage.

Table 2: Diagnostic accuracy of ultrasonography and ophthalmoscopy in prediction of elevated ICP

Diagnostic value (%)	Test (95% confidence interval)	
	Ultrasonography	Ophthalmoscopy
Prevalence	29.0 (21.6 - 37.8)	29.0 (21.6 - 37.7)
True positive	37.2 (28.0 - 47.4)	38.8 (29.3 - 49.2)
True Negative	100.0 (85.4 - 100.0)	100.0 (87.0 - 100.0)
False positive	62.7 (52.6 - 71.9)	61.2 (50.8 - 70.7)
False negative	0.0 (0.0 - 14.6)	0.0 (0.0 - 13.0)
Sensitivity	100.0 (88.6 - 100.0)	100.0 (88.6 - 100.0)
Specificity	31.2 (22.2 - 41.7)	35.5 (26.0 - 46.2)
Positive predictive value	37.3 (28.0 - 47.4)	38.8 (29.3 - 49.2)
Negative predictive value	100.0 (85.4 - 100.0)	100.0 (87.0 - 100.0)
Positive likelihood ratio	0.6 (0.4 - 0.8)	0.6 (0.5 - 0.9)
Negative likelihood ratio	NaN	NaN

The entry "NaN" in any of the above cells means that the calculation cannot be performed because entered values include one or more instances of zero; ICP: Intracranial pressure.

Results:

We enrolled 131 patients with positive ophthalmoscopy signs of ICP rising (mean ± standard deviation of patients age 46.29 ± 10.0 years; 77.1% male). Pseudo-tumor cerebri (20.2%), epilepsy (11.4%), cerebral vein thrombosis (9.9%), loss of conciseness (8.4%), intraventricular and intracerebral hemorrhage (8.4%), subarachnoid hemorrhage (7.6%), and hydrocephaly (4.6%) were the frequent etiology of ICP rising. Brain CT scan confirmed 38 (29.0%) cases of ICP rising (Table 1).

AUC of ophthalmoscopy was 0.68 (95% CI: 0.63-0.73). Based on ROC analysis, presence of at least one sign in ophthalmoscopy was defined as elevated ICP. Therefore, the number of diagnosed elevated ICPs with this criterion was 98 (74.8%) cases. The calculated sensitivity and specificity of ophthalmoscopy, with presence of at least one of the above-mentioned ICP rising signs, were 100.0% (95% CI: 88.6-100.0) and 35.4% (95% CI: 26.0-46.2), respectively (Figure 1). Ultrasound examination revealed that mean right and left ONSD were 5.5 ± 0.9 (range: 3.8 - 8.7) and 5.5 ± 1.0 (range: 2.0 - 8.6) millimeters, respectively. ROC analysis of ultrasound examination revealed that AUC of this method was 0.75 (95% CI: 0.66 - 0.84) (Figure 2).

Considering the cutoff point of 5 millimeters, finally 102 patients (77.9%) were categorized in the elevated ICP group, based on ONSD. Sensitivity and specificity of ultrasonography in prediction of elevated ICP were 100.0% (95% CI: 84.0 - 100.0) and 31.9% (95% CI: 23.0 - 41.7), respectively (Table 2).

Discussion:

Elevated ICP is one of the main reasons of mortality in patients referred to the ED. Regardless of its etiology, the immediate diagnosis and treatment of this condition can strongly improve the prognosis of the patients (2, 3). Several methods are being used to evaluate patients with

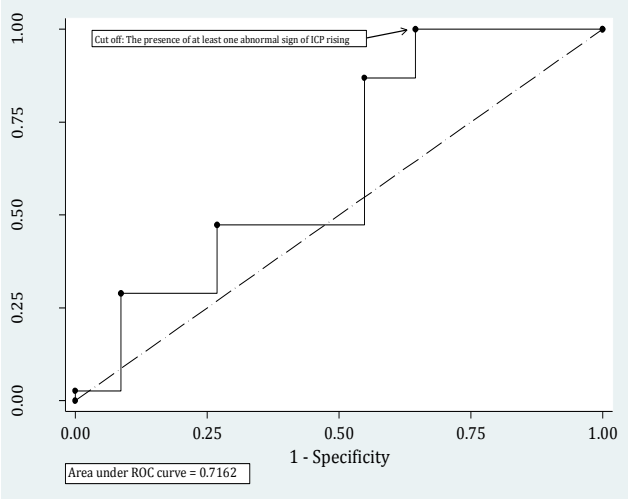

Figure 1: Receiver operating characteristic (ROC) of ophthalmoscopy in detection of elevated intracranial pressure.

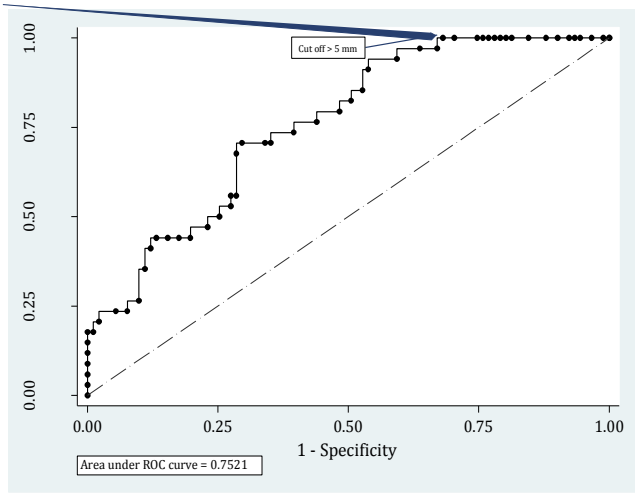

Figure 2: Receiver operating characteristic (ROC) of ultrasonography in detection of elevated intracranial pressure.

probable elevated ICP, including clinical assessment and use of physical examination, laboratory studies, inspection of the ocular signs of increased ICP, and imaging studies (7, 13, 14). Based on the results of the present study, sensitivity of ultrasonography in prediction of ICP elevation was 100.0%, while its specificity was low (23.7%). Meanwhile, the diagnostic accuracy of ONSD was similar to ophthalmoscopy (sensitivity=100.0; specificity=35.5). Ophthalmodynamometry has been shown to be efficient for ICP assessment, while for continuous monitoring of ICP other measurements should be taken (15). In two of their studies, Amini et al. demonstrated that ultrasonography examination of optic nerve sheath could be considered as an available, accurate, and noninvasive screening tool for determining the elevated intracranial pressure in cases with head trauma or cerebrovascular accident (12, 16). In contrast, Caffery et al. showed that sensitivity of optic nerve sheath diameter in detection of elevated ICP is 75%. These authors concluded that it is not an adequate screening tool for detection of non-traumatic causes of ICP elevation (17). One explanation for the differences between our results and the findings of Caffery et al. may be methodological. They only examined non-traumatic causes of ICP rising, but we assessed patients with all causes. The meta-analysis suggested that ultrasonography of optic nerve had a good level of diagnostic accuracy for detecting ICP rising. It may aid in clinical decision-making and triage of patients for transferring them to specialized centers (11). Rajajee et al. suggested that optic nerve diameter, equal to or greater than 0.48 centimeter, has the greatest accuracy in diagnosis of raised ICP (18). The present study revealed that presence of at least one of the ophthalmoscopy abnormalities, including widening of optic nerve disk, ocular venous engorgement, blurring, hemorrhage over optic disk, elevation of optic disk, and retinal venous tortuosity might predict the presence of ICP elevation. Similar to this results, Mena et al. demonstrated that the rise in ICP leads to marked hemorrhage within the optic nerve sheath as well as intra- and preretinal hemorrhages (19). Nevertheless, association of raised intracranial pressure with ophthalmic findings was not fully understood. Therefore, further study is recommended to investigate and explain its exact mechanism. One limitation of our study was the fact that we used helical CT scan, which has less accuracy than spiral ones. Moreover, the studied patients had various etiologies of ICP rising including head trauma, subarachnoidal hemorrhage, space-occupying lesions, hydrocephalous, metabolic disorders, and electrolyte imbalance that could affect the outcomes.

Conclusion:

The present study revealed that bedside ultrasonography of optic nerve sheath and ophthalmoscopy have enough accuracy for the screening of patients with probable elevation of ICP. Of course, it should be considered that despite the high sensitivity of both tools, their specificity is low.

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Conflict of interest:

None

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