Research Square

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Clinical Value of Optic Nerve Sheath Diameter Assessment in Prognosis of Comatose Patients with Supratentorial Lesions

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Abstract

Background and objective

Optic nerve sheath diameter (ONSD) and ONSD/ eyeball transverse diameter (ETD) ratio have been proved to be related to intracranial pressure. This study aimed to evaluate ONSD and ONSD/ETD ratio in comatose patients with supratentorial lesions and determine the relationship of these two indexes with the prognosis of these patients.

Methods

A total of 54 comatose patients with supratentorial lesion and 50 cases of normal controls were retrospectively included in this study. ONSD and ETD was messured on un-enhanced computed tomography(CT). The difference of ONSD, ONSD/ETD ratio between the two groups was compared. The prognosis of comatose patients were scored unsing Glasgow outcome scale (COS) at 3-month follow-up and classified into good (score ≥ 3) and poor (score < 3) prognosis. The differences of ONSD and ONSD/ETD ratio between good and poor prognosis of comatose patients were compared statistically.

Result

ONSD and ONSD / EDT in the comatose group were 6.30 ± 0.60 mm and 0.27 ± 0.03, respectively, both were significantly greater than that in normal controls (5.10 ± 0.47 mm, t = 11.426, P < 0.0001 ; 0.22 ± 0.02, t = 11.468, P < 0.0001 ; respectively). ONSD in poor prognosis was siginificantly greater than that in good prognosis (6.40 ± 0.56 mm vs. 6.03 ± 0.61 mm, t = 2.197, P = 0.032). ONSD / EDT raito in poor grognosis was significantly higher than that in good gronosis (0.28 ± 0.02 vs 0.26 ± 0.03, t = 2.622, P = 0.011). The area under the responder operating charateristic curve to predict prognosis of comatose patients were 0.650 (95% *CI*: 0.486–0.815, *P* = 0.078) for ONSD and 0.711(95% *CI*: 0.548–0.874, *P* = 0.014) for ONSD/ETD ratio, respectively.

Conclusions

ONSD and ONSD / EDT raito increased in comatose patients. ONSD / EDT raito may be more valuable than ONSD in evaluation for prognosis of comatose patients with Supratentorial lesions.

Background

Coma is the worst form in disturbance of consciousness with a high mortality rate. There are many reasons for coma, such as hypoxic ischemic encephalopathy (HIE), traumatic brain injury (TBI), cerebrovascular disease, brain tumor, infection, inflammatory, etc [1]. At present, many methods have been used to predict the prognosis of comatose patients. The wildly used methods include electroencephalogram, somatosensory evoked potential, transcranial Doppler ultrasound, serology, clinical behavior score, etc.

Supratentorial lesions refer to diseases above the tentorium of cerebellum that might elevate Intracranial pressure (ICP). Supratentorial lesions typically cause coma by mass effect, tissue shift, and herniation [1]. The common pathophysiological mechanism for death is brain hernia caused by increased ICP. ICP may be directly related to the prognosis of comatose patients with supratentorial lesions. Therefore, monitoring ICP is important for comatose patients with Supratentorial lesions, through which clinical information can be obtained for decision-making of operation opportunity and therapeutic regimen.

The commonly used methods to evaluate ICP are extraventricular drainage and subdural puncture. These monitoring methods are accurate, but invasive and costly, which may lead to a series of complications, such as intracranial infection, induce or aggravate cerebral hemorrhage, and therefore have limited application value clinically.

Non-invasive ICP monitoring methods have been gradually developed in recent year. As optic nerve sheath communicates with the intracranial subarachnoid space [2], and ICP level can be indirectly determined by the optic nerve sheath diameter, measuring ONSD has become an emerging non-invasive technique in recent years. At present, there are three methods to measure ONSD, i.e., ultrasound, magnetic resonance imaging, and computed tomography. Of these methods, CT is more suitable for comatose patients with intracranial diseases, because it can quickly determine the cause of coma and evaluate the development of the disease. Previous studies have shown that ONSD is well correlated with ICP; when ICP increases, ONSD widens, and when ICP decreases, ONSD narrows [3-6]. In many studies, ONSD also provided prognostic information [3,5,7,8]. Meanwhile, it was reported that ONSD strongly correlated with eyeball transverse diameter (ETD) in healthy people [9]. The ONSD/ETD ratio was regarded as a less variable index than ONSD, and has a better predicting value than ONSD in ICP monitoring [8].

The purpose of this study was to describe the ONSD and ONSD/ETD ratio in comatose patients with Supratentorial lesions, and determine the relationship between these two indexes with the prognosis of comatose patient.

Patients And Methods

Study design and clinical setting

This retrospective study was approved by the ethics committee of Peking University International Hospital. Comatose patients with supratentorial lesions who was admitted to the neurological Intensive Care Unit (NICU) of Peking University International Hospital (Beijing, China) from August 2015 to November 2020 were the candidates of the study group. The inclusion criteria were as follows: 1) Patient's age≥18 and ≤ 80 years old; 2)supratentorial lesions demonstrated by CT, including acute cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage(SAH), and TBI; 3) coma on admission with Glasgow coma scale(GCS) scores ≤ 8. The exclusion criteria include: 1) previous history of glaucoma, thyroid associated ophthalmopathy, optic nerve diseases; 2) combined ocular and optic nerve injuries at admission; 3)serious complications that affecting life expectancy, such as hematopathy, tumor, etc.

We also recruited 50 cases of normal control group from our hospital. All cases were confirmed by head CT without intracranial lesions. The clinical data of all the subjects were reviewed and collected. Data collected for analysis included age, sex, weight, body mass index (BMI), mean arterial pressure (MAP). Primary disease, clinical history, GCS score, Operations during hospitalization that may affect ICP, such as hematoma clearance and decompressive craniectomy were also recorded in comatose group.

Measurement of ONSD and ETD

All comatose patients took head CT on the first day of coma onset for etiology assessment. The CT scans were performed on spiral scanner (64 row, Siemens, Germany), with tube voltage of 120kv, tube current of 200-300mAs, slice thickness of 2mm, slice interval 3mm, and the pitch 1. Two experienced radiologists who were blinded to clinical data and interpreted CT images independently. The ONSD and ETD were measured at a fixed mediastinal window (width 300, level 35) for the same contrast and brightness. The direction of optic nerve was identified by CT three-dimensional reconstruction, and the ONSD was measured in its vertical direction 3 mm behind the eyeball [3]. ETD was measured from one side of the retina behind the lens to the other for the maximum diameter. The values measured by the two radiologists were averaged. All measurements of ONSD and ETD were performed bilaterally and the averaged value was taken to calculate ONSD/ETD ratio.

Outcome assessment

The comatose patients were assessed with GOS score at the 3-month follow-up by telephone or face-to-face. According to GOS, the patients were divided into two groups: good prognosis group (GOS 3, severe disability; GOS 4, moderate disability; GOS 5, return to normal life) and poor prognosis group (GOS 1, dead; GOS 2, vegetative state;).

Statistical analysis

SPSS23.0 statistical software (IBM, Armonk, NY, USA) was used for analysis. Continuous variables were expressed as mean ± standard deviation. Non-normal distributions were expressed as medians with interquartile range. Categorical variables were presented as counts and percentages. Chi-square test was used to compare the data including sex, GCS, etiology and clinical history. Independent-Samples T Test was used to compare the data including age, weight, BMI, ONSD and ONSD/ETD ratio. Nonparametric tests were used to compare height and MAP. The area under receiver operating characteristic (ROC) curve was used to assess the prognostic value of the ONSD and ONSD/ETD ratio. All tests were two-sided and P-value <0.05 was considered statistically significant.

Results

Clinical characteristics

A total of 54 comatose patients with Supratentorial lesions and 50 cases of normal control group were selected for this study. The median GCS score at admission in coma group was 3.5 (3, 6). The main

causes of coma were: Acute cerebral infarction (n=12), Cerebral hemorrhage (n=19), SAH (n=13), and TBI (n = 10). The demographic characteristics of the study group and the control group were described and compared (Table 1).

Table 1 Baseline Characteristics of the comatose patients and the control group

Characteristic	Study group (n=54)	Control group (n=50)	c^2/t /z value	P value
Age [yr/d, mean (SD)	58.8 (17.4)	54.9 (17.0)	1.155	0.251
Gender, male[n (%)]	27 (50.0)	24 (48.0)	0.042	0.847
Height [cm, mean (SD)]	165.7±7.5	164.0 (7.5)	-1.442	0.150
Weight [kg, mean (SD)]	66.2±13.9	67.3±12.1	-0.424	0.672
BMI [mean (SD)]	23.5(4.8)	24.9(3.4)	-1.753	0.083
MAP [mean (SD)]	86.2±20.6	90.6±15.5	-2.392	0.016

SD= standard deviation, BMI = body mass index, MAP= mean arterial pressure

ONSD and ONSD/ETD ratio between the comatose patients and the control group

ONSD in the study group and control group were 6.30±0.60mm and 5.10±0.47, respectively (t=11.426, P<0.0001); the ONSD/ETD ratio in comatose group and in control group were 0.27±0.03 and 0.22±0.02, respectively (t=11.468, P<0.0001).

Outcome of comatose patients and the associated factors

At 3-month follow-up, 17patients (31.5%) had good outcomes, 37 patients (68.5%) had poor outcomes. Table 2 presents the results of comparison between good prognosis group and poor prognosis group. There were significant differences in GCS score (c2 =28.834, P<0.0001), ONSD (t= 2.197, P=0.032), and ONSD/ETD ratio (t= 2.622, P=0.011) between the two groups. There was no difference in age, gender, height, weight, BMI, MBP, etiology, past history and surgical operation.

Table 2 Comparison of good prognosis group and poor prognosis group

Characteristic	Good prognosis (*n*=17)	Poor prognosis (*n*=37)	c^2/t /z value	*P*-value
Age, yrs[mean (SD)]	52.8(21.4)	61.6 (14.8)	1.544	0.136
Gender-male [n (%)]	9(52.9)	18(48.6)	0.086	1.000
Height [cm, mean (SD)]	167.4(7.3)	164.9 (7.6)	-1.398	0.165
Weight [kg, mean (SD)]	68.5(13.2)	65.1(14.3)	-0.830	0.410
BMI [mean (SD)]	23.4(6.70)	23.5(3.8)	0.061	0.952
MAP[mean (SD)]	93.8(22.1)	82.7 (19.2)	-1.491	0.138
GCS score [n(%)]			28.834	<0.0001
3	0	27		
4	2	2		
5	4	4		
6	4	0		
7	2	2		
8	5	2		
Etiology [n(%)]			6.270	0.093
ACI	3	9		
CH	9	10		
SAH	1	12		
TBI	4	6		
Clinical history				
Hypertension	7	14	0.055	1.000
Diabetes	3	7	0.012	1.000
CHD	3	4	0.482	0.665
Stroke	4	4	1.493	0.243
ONSD [mm, mean (SD)]	6.03(0.61)	6.40(0.56)	2.197	0.032
ONSD/ETD, [mean (SD)]	0.26(0.03)	0.28(0.02)	2.622	0.011

Operation [n(%)]	8（47.1）	10（27.0）	2.103	0.215

SD= standard deviation, BMI = body mass index, MAP= mean arterial pressure, GCS= Glasgow coma scale, CHD=coronary heart disease, ACI= acute cerebral infarction, CH= cerebral hemorrhage, SAH= subarachnoid hemorrhage, TBI=traumatic brain injury, ONSD= optic nerve sheath diameter, ETD= eyeball transverse diameter

Predict efficiency of ONSD and ONSD/ETD ratio on outcome

The efficiency of ONSD and ONSD/ETD ratio in detecting poor prognosis were showed in Figure 1. The area under the curve (AUC) for ONSD predicting poor prognosis was 0.650 (95% *CI*: 0.486–0.815, *P*=0.078), with a sensitivity of 54.1% and specificity of 76.5% at a cutoff value of 6.4 mm; the AUC for ONSD/ETD ratio predicting poor prognosis was 0.711(95% *CI*: 0.548–0.874, *P*=0.014) at a cutoff value of 0.25 , with a sensitivity of 94.6% and specificity of 52.9%.

Discussion

The results of this study showed that ONSD in comatose group was 6.30 ± 0.60 mm against 5.10 ± 0.47 mm in normal control group. ONSD / EDT ratio in comatose group was 0.27 ± 0.03 against 0.22 ± 0.02 in normal control group. ONSD and ONSD / ETD ratio were significantly higher in comatose patients with Supratentorial lesions than normal controls, which indirectly confirmed the relationship between ONSD and ICP. There was significant higher ONSD and ONSD / ETD ratio in poor prognosis group than in good prognosis group. However, to predict outcome of comatose patients, the ONSD/ ETD ratio was demonstrated better performance than the ONSD.

Monitoring ICP has important clinical significance for the prognosis and therapeutic schedule of comatose patients. As a noninvasive monitoring method of ICP, ONSD has been used for 20 years and expected to be an effective technique to predict the prognosis of patients. Some researches suggest that ONSD increases with the increase of intracranial pressure, and the increase of ICP has a significant correlation with the poor prognosis of neurological function [7, 10–12]. It was found that ONSD increased in 95% of patients with CT indicated ICH or SAH, and the pathological ONSD was 6.6 ± 0.8 mm, ONSD/ETD ratio was 0.29 ± 0.05 against normative 0.19 ± 0.02. They also found the presence of ONSD greater than a threshold of 5.5 mm was significantly suggestive of elevated ICP and warranted for invasive measurement[5]. Our study showed that ONSD in comatose group was significantly higher than that in normal control group. The results of the current study complement the ONSD data in comatose patients with supratentorial lesions.

Some scholars had made exploration on prognostic value of ONSD in patients with TBI and HIE [3, 7, 13–15]. Shahan Waheed *et al.* found that in patients with blunt brain injury, ONSD of deathes was higher than that of survivals [7]. Another study found that ONSD was a good predictor of mortality (AUC: 0.805) and the cutoff ≥ 7.3 had a sensitivity of 86.4% and a specificity of 74.6%[13]. In hypoxic-ischemic

encephalopathy, ONSD correlated closely with the neurologic outcome[14, 15]. Other scholars found that ONSD showed potential prognostic value for a poor neurological outcome in patients after hemicraniectomy [16]. At present, some studies found that ONSD / ETD is more valuable than ONSD in predicting intracranial pressure[8, 17]. Therefore, it can be inferred that ONSD / ETD may also be more valuable in predicting prognosis. Some researchers found that the changes in ONSD/ETD ratio compared to the baseline was predictive for late malignant progression in patients with malignant middle cerebral artery infarction [18].In cases with traumatic head injury without hemorrhage, there was an inverse correlation between ONSD/ETD ratio and the GOS [19].Our study found that ONSD/ ETD is more valuable in predicting the prognosis of comatose patients, which may be related to the small variability of ONSD / ETD. The prognostic value of ONSD / ETD needs to be further confirmed

In the process of measuring ONSD, we found that the “mediastinal” window was the best window to observe optic nerve, while most previous studies used “spine” window[5, 6, 9], or "abdomen" window[20], or unspecified window when measuring ONSD. In addition, diverse distance and anatomical marks in the processes of measurement may lead to a great variability of results in studies on ONSD. In this case, due to individual differences, monitoring ONSD may be of great value to determine abnormality of ICP and predict prognosis. Therefore, it is very important to establish an unified method to measure ONSD and the range of normal ONSD values .

Whether ONSD is related to age, height, weight, BMI, MBP and other factors has not been determined. Many studies have shown that ONSD has no correlation with the above factors [7, 21, 22]. Like other nerves in the human body, optic nerve fibers are lost with age. However, the average diameter of axons increased with age [23]. At the same time, dural thickness increased with age [24]. Therefore, some scholars believe that ONSD is approximately constant during a lifetime[9]. Our study showed that these factors were not significantly different between comatose patients and normal controls except MBP, which is related to hemodynamic instability of coma group.

There are some limitations in our study. First, this is a retrospective analysis with a small sample size, which may lead to inevitable bias. Second, only a few of our cases had invasive intracranial pressure monitoring, so we cannot directly link ONSD with ICP. Third, the comatose patients in our study had different etiologies, which may also cause some bias. Multi-center studies with larger sample are needed to further evaluate ONSD in comatose patients with a specific etiology and to determine the relationship of ONSD and ONSD/ETD ratio with prognosis of comatose.

In conclusion, our study showed that ONSD was significantly increased in comatose patients with supratentorial lesions, which indicating an increase of ICP. The ONSD in comatose patients with poor prognosis is higher than those with good prognosis, which means that ONSD measurement could be used as a new method to evaluate the prognosis of comatose patients with supratentorial lesions. Well-designed study with larger sample is needed to further clarify.

Abbreviations

ONSD: Optic nerve sheath diameter; ETD: eyeball transverse diameter; GOS: Glasgow outcome scale; CT : computed tomography ; HIE : hypoxic ischemic encephalopathy; TBI: traumatic brain injury; ICP: Intracranial pressure; SAH: subarachnoid hemorrhage; GCS: Glasgow coma scale; BMI: body mass index; MAP :mean arterial pressure; ROC: receiver operating characteristic; CHD: coronary heart disease; ACI: acute cerebral infarction; CH: cerebral hemorrhage

Declarations

Ethics approval and consent to participate: The research protocol was approved by the ethics committee of Peking University International Hospital.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions:

Sha Zhu: designed, collected data, wrote

Chao Chen: measuring ONSD and ETD

Dianjiang Zhao: measuring ONSD and ETD

Yuanli Zhao: guidance

Xianzeng Liu guidance and manuscript review

Jun Zhang: guidance and manuscript review

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Figures

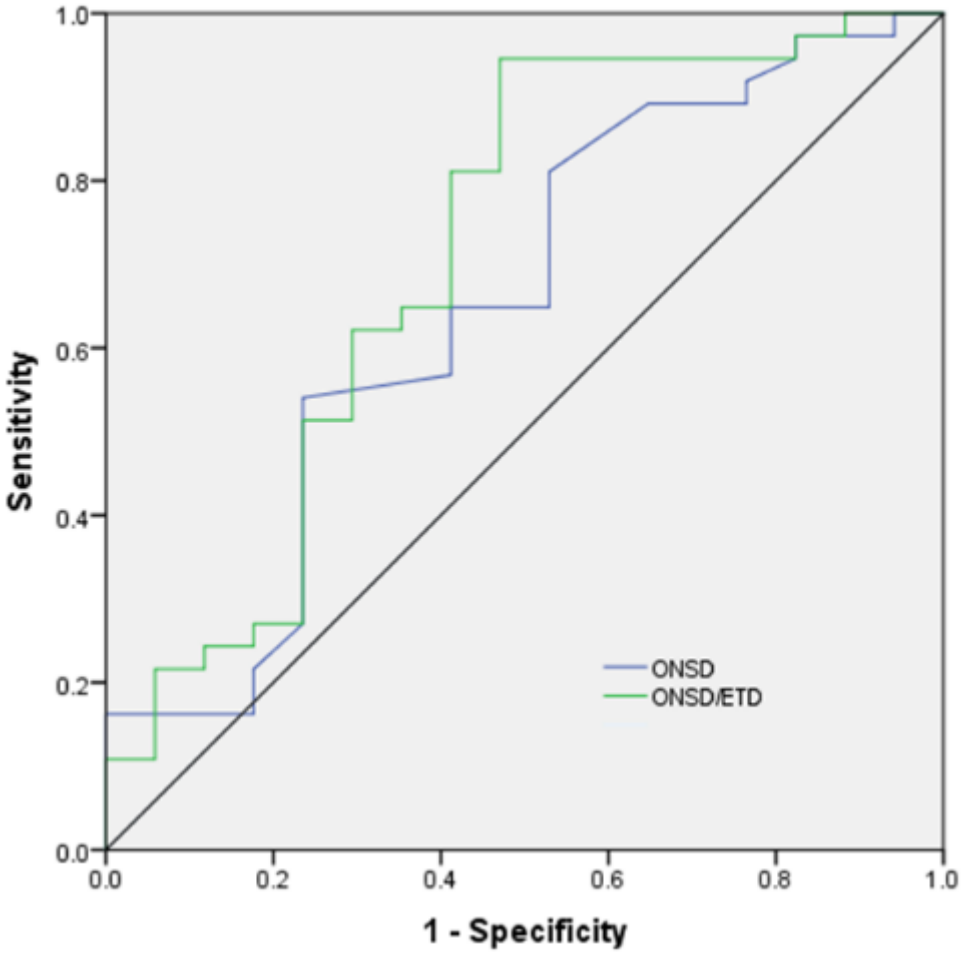

Figure 1

ROC curves of the performance of ONSD and ONSD/ETD ratio to predict poor prognosis