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Original Research

Can optic nerve sheath diameter assessment be used as a non-invasive tool to dynamically monitor intracranial pressure?

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Abstract

This study aims to detect whether the optic nerve sheath diameter (ONSD) can be used to dynamically monitor intracranial pressure (ICP). Adult patients undergoing invasive ICP monitoring on the day of admission are included in this study. For each patient, the ONSD is first measured in the supine position and then in the 30° head-up position. Subsequently, a dynamic test is conducted on 16 patients. The ONSD is measured in the supine position once a day for three consecutive days starting on the day of admission. There is a strong correlation between the ONSD and ICP values in the supine position on admission (r = 0.799), and when patients are changed from the supine to the 30° head-up position, the ICP and ONSD values decrease correspondingly. However, the change in ICP is not strongly correlated with the change in ONSD (r = 0.358). In the dynamic test, a good agreement between the ICP and ONSD only exists in three patients (18.8%), and three patients have completely different profiles for ICP and ONSD. These results suggest that the changes in the ONSD and ICP values are not closely correlated after dynamic observation. Therefore, measurement of the ONSD may not be a suitable tool to dynamically monitor ICP.

Keywords: Optic nerve sheath diameter; Intracranial pressure; Ultrasonography; Dynamic method; Position

1. Introduction

Several neurological comorbidities (e.g., head injury, hydrocephalus and subarachnoid haemorrhage) can result in increased intracranial pressure (ICP) [1,2]. ICP is typically measured in mmHg or cmH_2O (1 mmHg = 1.36 cmH_2O) and ranges from 5 to 15 mmHg while supine, but it is not static. Increased ICP can result in a pressure gradient among compartments and a shift in brain structures causing changes in consciousness, bilateral ptosis, pupillary dilatation and impaired upgaze, all of which can lead to cerebral ischemia, brain herniation and even death [3,4]. The monitoring of ICP is regarded as a crucial component in the management of patients with high ICP. Currently, monitoring methods are invasive and include intra-parenchymal sensors and subarachnoid bolts [5,6], which are both reference standards for ICP measurements. Although accurate and highly sensitive, these invasive techniques require strict neurosurgical settings and cause side effects that must be managed (i.e., haemorrhage, infection and brain lesions) [7,8]. Therefore, non-invasive ICP estimation would be beneficial.

Various non-invasive ICP estimation methods have been proposed, with different advantages and limitations; however, none have been sufficiently accurate to replace invasive ICP measurement [9–11]. Measurement of the optic nerve sheath diameter (ONSD) by magnetic resonance imaging, computed tomography or ultrasonography are promising non-invasive ICP estimation methods [12,13]. The diameter of the optic nerve sheath (ONS) is linked to the cerebrospinal fluid (CSF) pressure [14], and the meningeal envelope around the ONS is a continuation of the dural and subarachnoid spaces. An increase in ICP can lead to a shift of CSF into the ONS, resulting in an increase in its diameter, mainly in the anterior part; it can also cause an increase in the diameter of the nerve itself due to the accumulation of CSF among the fibres and result in papilledema [15]. Previous studies have demonstrated that the assessment of ONSD is associated with ICP. Chen *et al.* [1] studied 84 patients and found that the relative real-time changes in ICP could be reflected by the ONSD measured via ultrasound. Hanafi *et al.* [16] analysed data from 112 patients with traumatic headaches and found that the ultrasonic measurement of ONSD was sensitive and specific for the detection of patients with high ICP. A prospective study by Robba *et al.* [7] indicated that ONSD was the best non-invasive method to estimate ICP and suggested the following formula to estimate ICP using ONSD: $nICP_{ONSD}$ = 5.00 × ONSD – 13.92 mmHg [7]. However, a recently published study revealed that the ultrasonic measurement of ONSD could not accurately estimate ICP in patients with

subarachnoid haemorrhage [12] because the elasticity of the ONS may be impaired after a subarachnoid haemorrhage [12]. Kavi's study also indicated that the measurement of ONSD was not a reliable method to monitor ICP, as the expansion in the ONSD could persist even after the ICP was controlled [17]. Therefore, the application of the assessment of ONSD in the dynamic monitoring of ICP remains controversial.

This study aims to assess whether the ONSD can be used to dynamically monitor ICP. Two studies are conducted to achieve this goal. First, the correlation between the changes in ONSD and ICP values when patients changed from the supine to the 30° head-up position is calculated. Second, the changes in ONSD and ICP values are dynamically observed from day one to day three of the patients' admission.

2. Patients and methods

2.1 Patients

This prospective study was performed in the Department of Neurology of the Third Hospital of Hebei Medical University from May 2019 to June 2021. The study protocol was approved by the Institutional Review Board of the Third Hospital of Hebei Medical University (No. K2019-010-1). All patients enrolled in the study signed informed consent.

The inclusion criteria were as follows: (1) $\geq$18 years old, (2) requiring ICP monitoring and undergoing invasive ICP monitoring on the day of admission and (3) a Glasgow Coma Scale (GCS) = 3–12. Patients with a known history of ophthalmological disorders or optic nerve trauma were excluded from this study.

2.2 Invasive intracranial pressure monitoring

Two invasive methods were used to detect ICP: an intra-parenchymal fibreoptic transducer (Camino Laboratories, Integra Lifesciences, CA, USA) and a catheter inserted into the brain ventricles that was connected to an external pressure transducer (Codman, Johnson & Johnson Medical Ltd., New Brunswick, NJ, USA). The instruments were operated by neurosurgeons with routine clinical practice in the operating room. ICM+ software (ICM, Cambridge, UK) was used to monitor the data collection and the real-time calculation of ICP values.

2.3 Optic nerve sheath diameter assessment

The ONSD assessment was performed in B-mode using the iU22 ultrasound system (Philips, Amsterdam, Netherlands) and a 6–13 MHz linear array transducer (Philips, Amsterdam, Netherlands) using the lowest possible acoustic power to measure ONSD to avoid damage to the retina and the lens [18]. The patients were placed in the supine position or the 30° head-up position with the head in the middle and the eyelids closed. The probe was covered with ultrasonography gel and carefully placed on the closed upper eyelid without exerting pressure on the eye. The optic nerve image was a low-echo strip structure located in the front and rear of the eyeball. The simultaneous appearance of the lens and optic nerve meant that the ultrasound probe was on the best plane. After removing the probe, the optic nerve and the sheaths on its two sides were visible with distinct margins [19]. The ONSD was measured at 3 mm behind the optic disc. Two measurements were performed for each optic nerve: one in the transverse plane with the probe in a horizontal position and one in the sagittal plane with the probe in a vertical position [20]. Each eye was assessed twice in each position. The final ONSD value for each position was the mean of all eight values. The ONSD assessment was conducted by an operator with 30 years of experience in ultrasound examination. The operator was blinded to the actual ICP and had no knowledge of the patient's medical history.

2.4 Data collection

All patients were carefully managed in accordance with international guidelines [12,13]. Mechanical ventilation was used as necessary to maintain adequate oxygenation (SaO_2 >90%) and normocapnia ($PaCO_2$ = 35–40 mmHg). The clinical data for each patient were collected, including gender, age, the GCS score upon admission, the Acute Physiology and Chronic Health Evaluation II (APACHE II) score upon admission, height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (calculated as $1 \div 3 \times \text{SBP} + 2 \div 3 \times \text{DBP}$). For each patient, the ONSD was first measured in the supine position and then in the 30° head-up position. The ICP value was recorded in each position.

To further detect whether the ONSD values increased or decreased in response to the ICP changes, a dynamic test was conducted in 16 of the 49 patients. The ONSD was measured in the supine position once a day for three consecutive days, starting on the day of admission. The ICP values were recorded each day (see Fig. 1).

2.5 Statistical analysis

The data were analysed using SPSS 22.0 software (IBM Corp., Armonk, NY, USA). The quantitative data were described as mean $\pm$ standard deviation (SD) or median and range. Categorical data were described as numbers and percentages. The Pearson correlation analysis was used to detect the correlation between the ONSD and ICP in different positions and the correlation between the changes in ONSD and ICP from the supine position to the 30° head-up position. In the dynamic test, because of the different units of measurement for ONSD and ICP, the values were standardised using Z-scores (produced in consideration of the intra-patient mean and SD). The Z-scores were calculated at three time points (D1, D2 and D3) and graphically described as points connected by a line. For each patient, if the two lines were parallel, the ONSD and ICP showed good

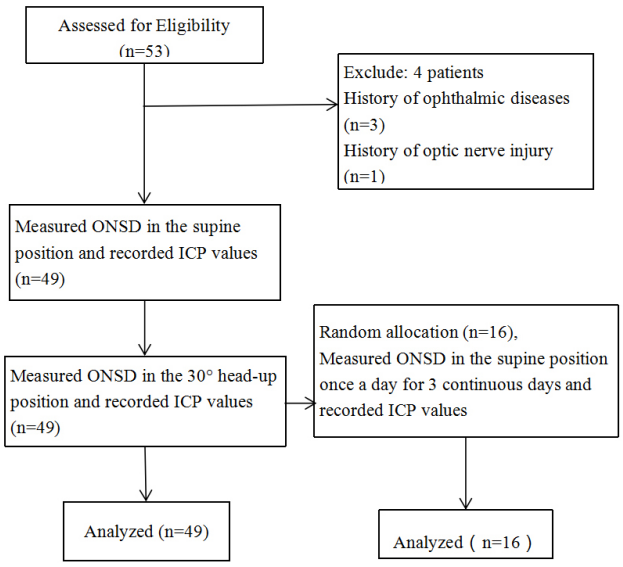

Fig. 1. CONSORT patient flow diagram.

agreement. Conversely, if the two lines were divergent, the agreement was incomplete or absent [12]. Statistical significance was indicated by $p < 0.05$.

3. Results

3.1 Patient characteristics

A total of 53 patients were screened for this study, and four patients were excluded because they had histories of ophthalmological disorders or optic nerve trauma. Finally, 49 patients with a median age of 61 (18–75), including 38 men (77.6%) and 11 women (22.5%), requiring ICP monitoring upon admission were enrolled in this study. With respect to the reasons for requiring ICP monitoring, 27 patients (55.1%) had a hypertensive cerebral haemorrhage, six patients (12.2%) had an aneurysmal subarachnoid haemorrhage, 13 patients (26.5%) had a traumatic brain injury and three patients (6.1%) underwent ICP monitoring for other reasons. In terms of the method of ICP monitoring, 27 patients (55.1%) were monitored using an intraparenchymal fibreoptic transducer, and 22 patients (44.9%) were monitored using an external ventricular drainage system. The median GCS score at admission was 6 (3–12), and the median APACHE II score at admission was 19 (17–24). Among the enrolled patients, three (6.1%) were complicated with intracranial infection, eight (16.3%) with cerebral hernia and one (2.0%) with sepsis.

The characteristics of the 49 patients included in the study are shown in Table 1.

Of the 49 patients, 16 underwent dynamic tests, including 12 men (75.0%) and four women (25.0%) with a median age of 62 (34–75). Of the 16 patients, 13 (81.3%) underwent ICP monitoring via the intraparenchymal fibreoptic transducer and three (18.8%) via the external ventricular drainage system. The median GCS score of these 16 patients upon admission was 7 (3–11), and the median APACHE II score was 18.5 (17–22).

Table 1. Patient characteristics.

Characteristics	N (%) or median (range)
Total number	49 (100)
Male/female	38 (77.6)/11 (22.4)
Age (years)	61 (18–75)
Height (cm)	174 (160–180)
Weight (kg)	70 (50–95)
GCS score at admission	6 (3–12)
APACHE II score at admission	19 (17–24)
SBP (mmHg)	132 (99–202)
DBP (mmHg)	74.5 (34–100)
MAP (mmHg)	93 (59–126)
ICP measurements	
Intraparenchymal fiberoptic transducer	27 (55.1)
External ventricular drainage system	22 (44.9)
Diagnosis	
Hypertension cerebral hemorrhage	27 (55.1)
Aneurysmal subarachnoid hemorrhage	6 (12.2)
Traumatic brain injury	13 (26.5)
Others	3 (6.1)
Complications	
Intracranial infection	3 (6.1)
Cerebral hernia	8 (16.3)
Sepsis	1 (2.0)

Note: GCS, Glasgow Coma Scale; APACHE, Acute Physiology and Chronic Health Evaluation; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial blood pressure.

3.2 The effect of position on the intracranial pressure and the optic nerve sheath diameter

In the supine position, the mean ICP of the enrolled patients was 18.30 ± 6.71 mmHg. Thirty patients (61.2%) presented with an ICP ≥20 mmHg, and the mean ONSD was 6.39 ± 0.66 mm. On admission, the ONSD was strongly correlated with ICP in the supine position (r = 0.799, 95% confidence interval (CI): 0.668–0.882, $p <$ 0.001).

In the 30° head-up position, the mean ICP of the enrolled patients was 16.36 ± 6.16 mmHg. Fifteen patients (30.6%) presented with an ICP ≥20 mmHg, and the mean ONSD was 6.17 ± 0.58 mm. The Pearson correlation coefficient between the ONSD and ICP values obtained in the 30° head-up position was 0.686 (95% CI: 0.502–0.81, $p <$ 0.001).

When patients changed from the supine position to the 30° head-up position, the ICP and ONSD values decreased correspondingly (see Fig. 2). The mean changes in the ICP and ONSD were 4.27 ± 1.98 mmHg (0–8.00 mmHg) and 0.46 ± 0.34 mm (0.01–1.39 mm), respectively. However, the Pearson correlation analysis showed that the change in the ICP was not strongly correlated with the change in the

ONSD (r = 0.358, 95% CI: 0.086–0.58, p = 0.012). The most obvious lack of correlation was seen in one patient who had a change in ICP of 7 mmHg and a change in ONSD of 0.037 mm.

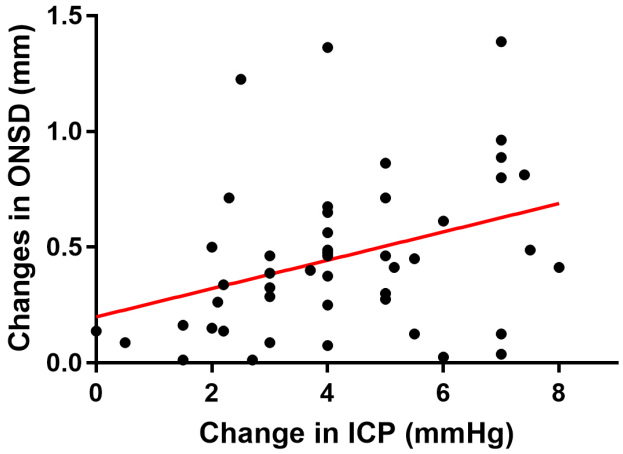

Fig. 2. Correlation between change in ICP and change in ONSD when patients changed the position. The change in ICP was not strongly correlated with the change in ONSD, with an r of 0.358 (95 % CI, 0.086–0.58; p = 0.012). ICP, intracranial pressure; ONSD, optic nerve sheath diameter. The correlation among the changes of ONSD and ICP from the supine position to the 30° head-up position was evaluated with a Pearson correlation analysis.

3.3 The analysis of the dynamic test

The dynamic test was performed on 16 patients. As a result of the different units of measurement for the ONSD and ICP, the values were standardised using Z-scores. The Z-scores at D1, D2 and D3 for the ICP and ONSD for each patient are presented in Fig. 3. In terms of the changes in ICP, of the 16 patients, eight (50.0%) demonstrated a decrease from day one to day three, three (18.8%) demonstrated a decrease from day one to day two and an increase from day two to day three, five (31.3%) had an increase from day one to day two and a decrease from day two to day three, one (6.3%) demonstrated a decrease from day one to day two and an increase from day two to day three and one (6.3%) demonstrated an increase from day one to day three.

In terms of the changes in ONSD, of the 16 patients, five (31.3%) demonstrated a decrease from day one to day three and nine (56.3%) had an increase from day one to day two and a decrease from day two to day three.

The lines on the graph representing the changes in ICP and ONSD were completely parallel in three patients (patients 11, 13 and 16), indicating a good agreement between the ICP and ONSD during the dynamic test for these three patients (18.8%). However, in three patients (patients 1, 2 and 7) the profiles for the ICP and ONSD were completely different.

4. Discussion

The results of the present study indicate that in a longitudinal test, the variation in the ICP was not strongly correlated with the variation in the ONSD when patients changed from the supine to the 30° head-up position. In addition, in the dynamic test, only three of the 16 patients (18.8%) demonstrated a good agreement between the ICP and ONSD, indicating that ONSD is not an accurate tool to dynamically estimate ICP.

Although non-invasive methods for assessing ICP are not accurate enough to substitute for invasive methods, non-invasive ICP estimation may be helpful and could be used as a method to identify patients at high risk for developing intracranial hypertension who require specific monitoring and surveillance or as a diagnostic tool in patients with an unexplained alteration of consciousness outside the ICU [11,21]. The ONSD measured by ultrasonography is an important non-invasive tool to estimate ICP and can be used to screen patients with high ICP while avoiding the placement of intracranial probes and the associated risks of bleeding and infection [12]. Previous studies have demonstrated the accuracy of the ONSD for measuring ICP [7,22]. Chen *et al*. [1] found that the relative real-time changes in ICP could be reflected by the ONSD measured by ultrasound. Hanafi *et al*. [16] found that ultrasonic measurement of the ONSD was sensitive and specific for the detection of patients with high ICP. In a prospective study, Robba *et al*. [7] indicated that ONSD was the best non-invasive method to estimate ICP. In a meta-analysis, Robba *et al*. [13] demonstrated that the ultrasonographic measurement of the ONSD had a high accuracy in the diagnosis of intracranial hypertension. A recently published meta-analysis enrolled 779 patients from 22 studies and suggested that the ONSD had high sensitivity and specificity in diagnosing patients with high ICP [23]. Consistent with these studies, this study revealed that the ONSD and ICP values obtained in the supine position on admission were strongly correlated (r = 0.799), indicating that the ONSD can accurately reflect the ICP.

The head-up position has been used for decades in the treatment of patients with high ICP, as this position decreases ICP quickly [24]. In this study, when patients changed from the supine position to the 30° head-up position, the ICP and ONSD decreased by 4.27 $\pm$ 1.98 mmHg and 0.46 $\pm$ 0.34 mm, respectively. However, the change in ICP was not strongly correlated with the change in ONSD (r = 0.358). Kerscher *et al*. [25] detected the dynamic changes in the ONSD and ICP after therapy to decrease the ICP, and no correlation was found between the changes in ICP and ONSD. Kavi found that ONSD expansion could persist even after ICP was controlled. Therefore, the assessment of ONSD throughout the acute phase of neurologic injury may not be a reliable method to monitor the ICP [17]. Bäuerle

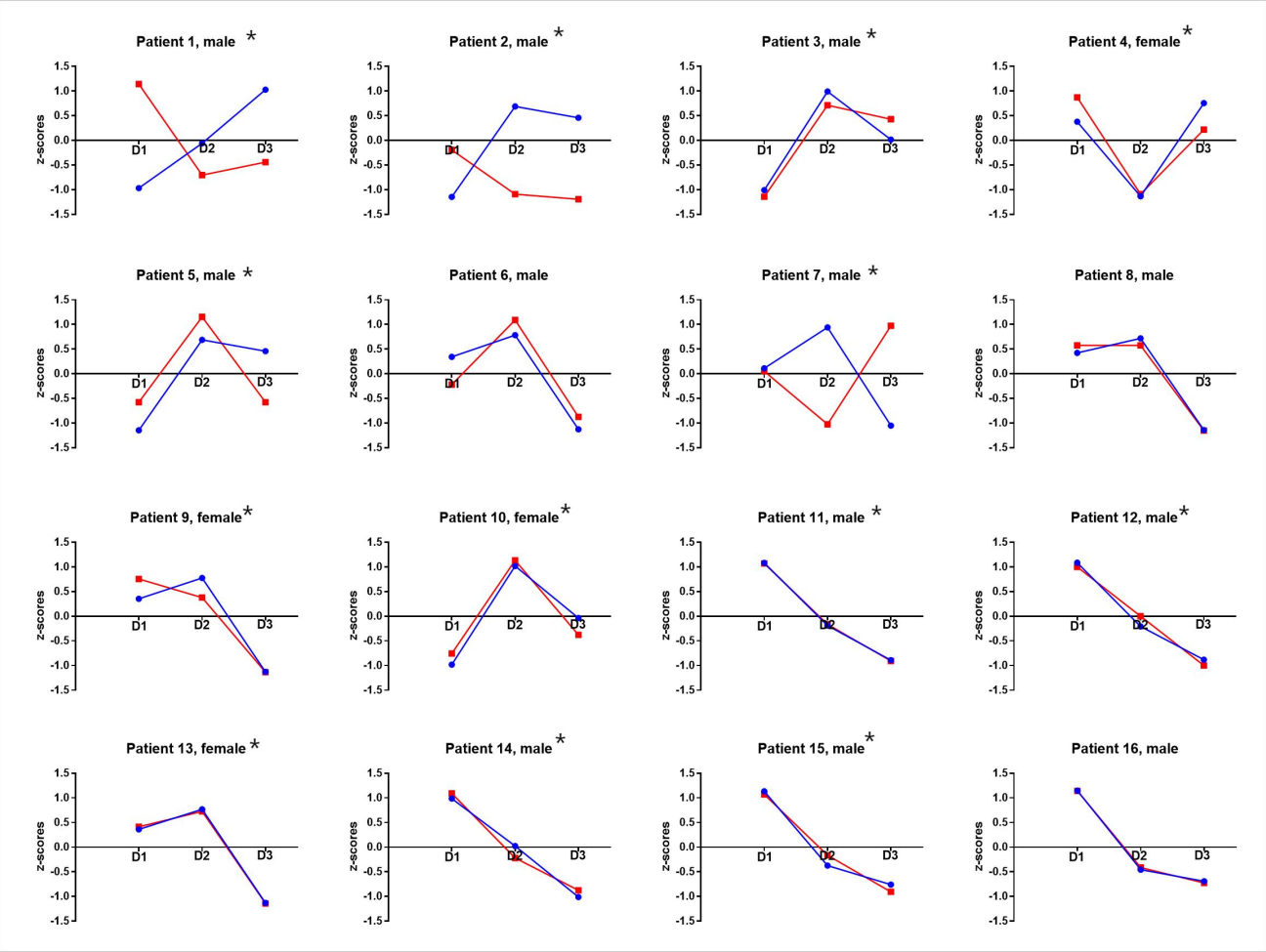

Fig. 3. ICP and ONSD z-scores during dynamic test. In 3 patients (patient 11, 13, and 16), the lines of ICP and ONSD showed completely parallel. Three patients had completely different profiles for ICP and ONSD (patients 1, 2, and 7). ICP, red line; ONSD, blue line; ICP, intracranial pressure; ONSD, optic nerve sheath diameter. * indicated that the patient used intraparenchymal fiberoptic transducer to monitor ICP. The values of ONSD and ICP were standardized using Z-scores (produced in consideration of the intra-patient mean and SD). The Z-scores were calculated at three time points (D1, D2, and D3) and graphically described as points connected by a line. For each patient, if two lines (representing ONSD and ICP) were parallel, the ONSD and ICP would have good agreement. Conversely, if the two lines were divergent, the agreement was incomplete or absent.

et al. [26] reported a similar finding: the ONSD remained high after the normalisation of ICP in 27 patients with subarachnoid haemorrhage after an aneurysm rupture. This result is most likely related to the impairment of the retraction capability of the ONS. Zoerle *et al*. [12] explored the changes in the ONSD at the time of rapid changes in ICP after CSF drainage. The changes in ONSD were poorly correlated with the changes in the ICP. The impairment of the ONS elasticity after subarachnoid haemorrhage may have contributed to this result [12].

The impairment of the ONS elasticity could be used to explain the results of the present study. Usually, high ICP results in the transfer of CSF into the ONS, causing an enlargement of the ONSD [13]. When the ICP decreases, the CSF will move back into the intracranial subarachnoid space, and the ONS will shrink to its initial diameter. However, these changes require normal ONS elasticity [12]. Hansen *et al*. [27] isolated human optic nerve preparations to explore the elastic properties of the ONS and found that the reversibility of the ONSD may be impaired after episodes of prolonged intracranial hypertension [27]. In this study, when the patients changed from the supine position to the 30° head-up position, the ICP immediately decreased. However, in some patients, intracranial hypertension impaired the elasticity of the ONS, and as a result, the ONSD did not decrease rapidly. Therefore, ONSD may not be suitable to dynamically monitor ICP.

This hypothesis was further confirmed by the dynamic test performed in the present study. From day one to day three, a good agreement between the ICP and ONSD only existed in three patients (18.8%). In addition, three patients had completely different profiles for the ICP and ONSD.

This result demonstrates that the ONSD may not be suitable for dynamically monitoring the ICP. However, Wand *et al*. [20] indicated that ONSD measurements are a useful tool for dynamically evaluating ICP and found that changes in ICP and ONSD values were correlated ($r = 0.669$) from admission through follow-up. In addition, Wang *et al*. [20] had a long follow-up period (one month) and the maximum ICP value was only 400 mmH_2O (29.41 mmHg). The impairment of ONS elasticity may have recovered during the long follow-up period. Therefore, additional studies are needed to clarify this issue.

The present study had several limitations. First, it was limited by its small sample size, especially in the dynamic test (16 patients). Larger multicentre studies should be conducted to confirm this study's findings. Second, the follow-up time was too short, as the dynamic test was only conducted from the day of admission until day three after admission. A study with a longer follow-up time should be performed to determine if ONSD can be used to dynamically monitor ICP. Third, in this study, the reasons for the ONSD being unsuitable for dynamically monitoring ICP were not clarified. The impairment of ONS elasticity and whether it contributed to the findings should be investigated further. Fourth, this study may have been subject to bias (e.g., spectrum bias was likely as most patients had intracranial haemorrhage). Finally, this study did not focus on the difference in the ONSD measurements for each eye or the variance in ONSD measurements in the transverse and sagittal axes. For ONSD measurement, a consensus was not reached regarding the axis to be measured or the eye to be used [28]. These issues should be investigated in future studies.

5. Conclusions

In the present study, the ONSD and ICP values obtained in the supine position on admission were strongly correlated. However, the change in ICP was not strongly correlated with the change in ONSD when patients changed from the supine to the 30° head-up position. In addition, in the dynamic test, only three of the 16 patients showed a good agreement between the ICP and ONSD. These results suggest that changes in the ONSD and ICP values are not strongly correlated during dynamic observation. The ONSD may not be a suitable tool to dynamically monitor ICP. The impairment of ONS elasticity could be used to explain the results of the present study, however, further studies are needed to confirm this hypothesis.

Author contributions

GBW, JT, JYG conceived of the study, and XBL and ZYW participated in its design and coordination and JYG helped to draft the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The Third Hospital of Hebei Medical University.

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Conflict of interest

The authors declare no conflict of interest.

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