Original Article
Clinical value of bedside ultrasound measurements of inferior vena cava diameter and its rate of change in early fluid resuscitation in patients with severe traumatic brain injury

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Abstract: Objective: To explore the clinical value of inferior vena cava diameter (IVCD) detection in guiding early fluid resuscitation in patients with severe traumatic brain injury (sTBI). Methods: Eighty patients with sTBI admitted to our hospital from October 2018 to October 2021 were retrospectively enrolled and divided into an observation group (n=40) and control group (n=40) according to the different monitoring methods used for treatment. The cerebrospinal fluid (CSF) lactate level, coagulation function, neurological function, and functional impairment, organ, cognitive, living ability and physical condition, Glasgow score, and adverse reactions in two groups were compared. Results: The differences in CSF lactate level and serum levels of PT, APTT and TT between both groups before resuscitation were not significant (all P>0.05). After resuscitation, all these indexes decreased in both groups, so that patients in the observation group had significantly lower CSF lactate level and serum levels of PT, APTT and TT than those in the control group (all P<0.05). Differences in the levels of neurological function factors such as GFAP, NSE, MBP, and S-100B and the scores of NIHSS, SOFA, MMSE, APACHE II and Barthel were not significant between both groups before treatment (all P>0.05). The levels of neurological function factors, NIHSS, SOFA and APACHE II scores decreased in both groups after treatment (all P<0.05) with lower scores in the observation group than the control group (all P<0.05). The MMSE and Barthel scores increased after treatment, and the scores were significantly higher in the observation group than those in the control group (all P<0.05). The GOS scores of patients in the observation group were higher than those in the control group at 1 month after treatment. The incidence of adverse reactions in the observation group (10%) was significantly lower than in the control group (30%). Conclusion: Monitoring IVCD to guide fluid resuscitation in patients with sTBI can reduce cerebrospinal fluid lactate levels, better protect patients’ vital organs and neurological function, reduce the occurrence of adverse effects, improve patients’ quality of life, and improve prognostic outcome.

Keywords: Bedside ultrasound, inferior vena cava diameter, sTBI, fluid resuscitation

Introduction
Traumatic brain injury (TBI) is a serious injury caused by violence or trauma to the head. TBI incidence is second only to that of extremity injuries, but ranks first in the rate of disability and mortality, posing a huge burden to society, economy and healthcare [1]. Among cranioencephalocranial injuries, 20% are severe traumatic brain injury (sTBI) [2]. With the continuous improvement in medical technology and exploration of mechanisms of sTBI, the disability and mortality rate of sTBI have been significantly reduced, but the mortality is still as high as 35%, and the survivors also suffer from cognitive and physical impairment, which affects the quality of life and increases the burden on families [3].

Approximately 50%-70% of patients with sTBI experience significant intracranial hypertension, which can cause secondary brain injury such as inadequate perfusion of brain tissue, cerebral hypoxia, and ischemia [4]. As patients’ intracranial pressure rises, cerebral perfusion...
pressure decreases and cerebral vessels are compressed, leading to regional ischemia and loss of cerebral vascular autoregulation, aggravating the cerebral pressure-flow relationship [5]. Efficiently relieving intracranial hypertension and reducing cerebral edema is particularly important for helping patients with sTBI.

Fluid resuscitation techniques maintain proper perfusion of the patient’s end organs by rehydration to treat hypovolemic shock, and proper assessment of the patient’s blood volume is essential for fluid resuscitation in patients with sTBI [6]. Fluid resuscitation can improve the effective circulating blood volume, increase the perfusion of human tissues and organs, and ensure cardiac output [7]. It was shown that effective fluid resuscitation and volume monitoring in the early stages of sTBI can reduce the intracranial pressure of patients as well as serious complications such as hypovolemia and heart failure caused by too much or too little effective circulation [8]. Research on fluid resuscitation, has clinically shown that aggressive fluid resuscitation in patients with sTBI may cause cerebral edema, aggravate cerebral hypoxia and ischemia, and increase the incidence of complications, morbidity, and mortality [9].

Currently, indicators commonly used to assess blood volume include intrathoracic volume index, central venous pressure (CVP), pulse index continuous cardiac output (PICCO), floating a catheter in the pulmonary artery, heart rate variability, end-diastolic volume and invasive arterial blood pressure monitoring. However, these are mostly invasive, complex, expensive, and are associated with many complications, and therefore not suitable for clinical application [10]. It is crucial to develop an accurate and less invasive way of blood volume assessment to guide fluid resuscitation in patients with sTBI.

Inferior vena cava ultrasound has been widely used to guide volume management in critically ill patients due to its simplicity, noninvasiveness, and reproducibility. However, for fluid resuscitation in patients with TBI, its specific advantages over CVP have not been clearly elaborated. The aim of this study was to monitor blood volume using inferior vena cava diameter (IVCD) during early fluid resuscitation in patients with sTBI, aiming to explore its clinical application value in early fluid resuscitation in patients with sTBI, and to lay a foundation for reducing the risk and cost of clinical operation for blood volume assessment.

Materials and methods

General information

In this retrospective analysis, 40 patients with severe cranioencebral injury admitted to our hospital from October 2018 to October 2021 who had fluid resuscitation guided by CVP detection were included in the control group, and another 40 coma patients with severe cranioencebral injury who had fluid resuscitation guided by IVCD detection from October 2018 to October 2021 were included in the observation group. The study was approved by the ethics committee of Affiliated Kunshan Hospital of Jiangsu University (Ethical Review No. 2017-04-005).

Inclusion criteria: Patients with severe cranioencebral injury confirmed by CT examination; patients with Glasgow Coma Score (GCS) of 3-12; patients without combined injuries.

Exclusion criteria: Patients with organic lesions of heart, liver, kidney, and other important organs; patients complicated by acute and chronic infectious diseases; patients with immune deficiency diseases; or patients with malignant tumor.

Methods

Patients in both groups were routinely given supportive therapy to maintain mean arterial pressure (MAP) at 80-100 mmHg (1 mmHg =0.133 kPa).

In the control group, the CVP was measured to guide fluid resuscitation. The patient was placed in a supine position, and the CVP was detected at the 5th intercostal space at midclavicular line. The upper limit of CVP was set at 8 mmHg. When CVP <8 mmHg, a rapid intravenous infusion of 250 ml of 0.9% NaCl solution was administered until CVP ≥8 mmHg. If the MAP was still below 80 mmHg at this time, norepinephrine was added with a starting dose of...
10 μg/min and subsequent increments of 2 μg/min, until the MAP goal was reached.

In the observation group, the IVCD was monitored to guide fluid resuscitation. Patients were placed in a supine position, and the ultrasound probe was placed on the right side of the patient’s xiphoid process so that the ultrasound beam was parallel to the long axis of the patient’s trunk. The IVCD was measured at 2 cm where left hepatic vein merges into the distal end. The upper limit of IVCD was set at 2.5 cm and the upper limit of IVCCI was set at 50%. When the IVCD <2.5 cm and IVCCI ≥50%, a rapid intravenous infusion of 250 ml, 0.9% NaCl solution was administered until IVCCI ≤50%. If the MAP was still below 80 mmHg at that time, norepinephrine was added, and the starting drip rate was set at 10 μg/min, with subsequent increments of 2 μg/min, mmHguntil the MAP goal was reached.

Data extraction

Data were extracted from our record in an Excel spreadsheet (Microsoft, Redmond, WA). Full text and charts were reviewed in detail for data on study design, study population, and relevant information, complications during hospital admission, including CSF lactate level, coagulation function, neurological function, visceral, cognitive, and daily abilities and physical status, Glasgow score and adverse reactions.

CSF lactate level: Blood lactate is a key marker of ischemia and hypoxia, and can be used in critically ill patients in severity grading. When the patient’s 48-h sustained blood lactate level is higher than 4 mmol/L, the patient’s mortality rate can be up to 80% [11]. However, since this represents the patient’s systemic lactate level and lacks specificity, Katsnelson et al. proposed that CSF lactate level is more sensitive and can better reflect the ischemia and hypoxia of the patient’s brain tissue [12]. Before and after the intervention, 1-2 mL of cerebrospinal fluid was collected using lumbar puncture [13], and the lactic acid level in the patient’s cerebrospinal fluid was measured using a lactic acid kit (Rondox, UK).

Coagulation function: Five mL of venous blood was drawn from patients before and 2 d after resuscitation. 3.2% trisodium citrate was used as the anticoagulant. The blood was placed in an anticoagulation tube for 1 h at 4°C, and the supernatant was obtained by centrifugation. The patient’s coagulation indexes, including prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT) were determined using Sysmex CS-5100 automatic coagulation analyzer (Japan) [14].

Neurological function and functional impairment: Five mL of fasting venous blood was drawn from patients before and after treatment, and the supernatant was obtained after blood clotting, and the levels of neurological function factors such as GFAP, NSE, MBP and S-100B in the serum were measured by ELISA. The NIHSS scale was used to compare the neurologic impairment of the two groups before and 1 month after treatment, and the higher the NIHSS score, the more severe the neurological impairment [15].

Visceral, cognitive, and daily abilities and physical status: The SOFA scale, including 6 domains (respiratory, cardiovascular, hepatic, coagulation, renal, and neurological systems, with 40 points in total), was used to evaluate the organ function of patients before and 1 month after treatment. The higher the score, the worse the organ function.

The MMSE scale was used to evaluate the degree of cognitive dysfunction of patients before and 1 month after treatment. A score of 27-30 represents normal, 21-26 represents mild cognitive dysfunction, 10-20 represents moderate cognitive dysfunction, and 0-9 represents severe cognitive dysfunction.

The APACHE II scale was used to evaluate the physical condition of patients before and 1 month after treatment. The APACHE II scale contains 13 items such as physiology, age and chronic diseases, and higher scores represent poorer physical condition.

The Barthel Index is an ordinal scale used to measure performance in activities of daily living (ADL). A score of 60 or more means the patients can take care of themselves; a score of 40-60 means the patients need some assistance from others in daily life; a score of 20-39 means the patients need frequent assistance from others; and a score of less than 20 means
the patients are completely dependent on others.

Glasgow score: The GOS scale was used to evaluate the prognosis of patients 1 month after treatment, with a score of 5 representing good recovery, 4 representing mild disability, 3 representing severe disability, 2 representing vegetative survival, and 1 representing death [16].

Adverse reactions: The incidence of adverse reactions such as epilepsy, hydrocephalus, acute cerebral bulging, cerebrospinal fluid leakage, subdural effusion, and intracranial infection during the treatment was compared between both groups.

The data collected above are routinely recorded in clinical TBI patients, so were easy to obtain.

Statistical analysis
All data were processed and analyzed using the statistical software SPSS 20.0. The mean ± standard deviation was used to express the measured data; paired sample t-test was used for intragroup comparison. The independent sample t-test was used for intergroup comparison. Chi-square test was used to compare the counted data (%). P<0.05 indicated a difference was statistically significant.

Results
Comparison of baseline data
The two groups did not differ significantly (all P>0.05) in terms of gender, age, BMI, time of injury, or GSC score, indicating the comparability between both groups (Table 1).

Table 1. Comparison of baseline data (X±s)/[n (%)]

<table>
<thead>
<tr>
<th></th>
<th>Control group (n=40)</th>
<th>Observation group (n=40)</th>
<th>P</th>
<th>t/χ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26</td>
<td>27</td>
<td>0.194</td>
<td>0.660</td>
</tr>
<tr>
<td>Female</td>
<td>14</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>57.82±7.10</td>
<td>54.12±15.39</td>
<td>0.531</td>
<td>0.653</td>
</tr>
<tr>
<td>BMI</td>
<td>6.95±0.96</td>
<td>6.86±0.33</td>
<td>0.442</td>
<td>0.935</td>
</tr>
<tr>
<td>Time from injury (h)</td>
<td>5.32±2.10</td>
<td>5.28±2.93</td>
<td>0.375</td>
<td>0.832</td>
</tr>
<tr>
<td>GSC score</td>
<td>6.43±0.98</td>
<td>7.10±0.65</td>
<td>0.247</td>
<td>0.53</td>
</tr>
</tbody>
</table>

CSF lactate levels before and after intervention
The difference in CSF lactate level between the two groups before resuscitation was not significant (P>0.05); however, immediately after resuscitation, the CSF lactate level of patients in the observation group was significantly lower than that of control group (P<0.05), and the number of patients who achieved lactate clearance rate of 50-70% and >70% in the observation group were 16 and 10 cases, respectively, which were higher than 8 and 2 cases in the control group (Figure 1).

Coagulation function in both groups
The differences in PT, APTT, and TT before resuscitation were not significant between both groups (all P>0.05); however, the levels of PT, APTT, and TT decreased in both groups at 2 d after resuscitation, and the levels of PT, APTT and TT were significantly lower in the observation group than the control group (all P<0.05) (Figure 2).

Neurological function and functional impairment
The differences in the levels of neurological function indices such as GFAP, NSE, MBP, S-100B and NIHSS scores between the two groups before treatment were not significant (all P>0.05). However, the levels of these indices decreased in both groups immediately after treatment, and the levels of these indices in the observation group were significantly lower than those in control group (all P<0.05) (Figure 3).

Organ, cognitive, living ability and physical condition of patients after treatment
The SOFA, MMSE, APACHE II, and Barthel scores did not differ significantly before treatment (all P>0.05). The SOFA and APACHE II scores of patients in both groups decreased at 1 month after treatment, and the scores of the observation group were significantly lower than those of the control group (all P<0.05). The MMSE and Barthel scores were increased in both groups after treatment, and the scores
Figure 1. Comparison of CSF lactate levels before and after intervention. A: Before resuscitation, the difference in CSF lactate levels between the two groups was not significant \((P>0.05)\); after resuscitation, the cerebrospinal fluid lactate levels of patients in the observation group were significantly lower than in the control group \((P<0.05)\); B: The lactate clearance rate in patients in the observation group was significantly higher than in the control group \((^*P<0.05\) before and after resuscitation, \(^{#}P<0.05\) between groups).

Figure 2. Comparison of coagulation function. (A) PT, (B) APTT, and (C) TT in both groups after 2 d of resuscitation were lower than before resuscitation, and the PT, APTT, and TT in observation group were significantly lower than of the control group \((P<0.05)\) \((^*P<0.05\) before and after resuscitation, \(^{#}P<0.05\) between both groups).

Glasgow scores of patients in two groups

At 1 month after treatment, the number of patients in the observation group scored for 5, 4, 3, 2 and 1 were 13 (32.5%), 8 (20%), 10 (25%), 6 (15%) and 3 (7.5%), respectively, while those in the control group were 8 (20%), 5 (12.5%), 7 (17.5%), 11 (27.5%) and 9 (22.5%), respectively. The prognosis of patients in the observation group was significantly better than that of the control group (Figure 5).

Incidence of adverse reactions in both groups

The incidence of adverse reactions in the observation group (10%) was significantly lower than that (30%) of the control group \((P<0.05)\) (Figure 6).

Discussion

TBI is one of the most common traumatic emergencies worldwide and has a high rate of disability and mortality, which can bring a deep burden to society and patients' families. Patients with sTBI should be evaluated as soon as possible and given the most effective resusciti-
Figure 3. Comparison of neurologic function factor levels and functional impairment. The differences in neurologic function factor levels and NIHSS score were not significant between both two groups before treatment ($P>0.05$). The levels of (A) NSE, (B) GFAP, (C) MBP, and (D) S-100B were decreased in both groups after treatment, and the level of each indicator in the observation group was significantly lower than in the control group ($P<0.05$). One month after treatment, the (E) NIHSS scores in both groups were decreased after treatment, and the NIHSS score of patients in the observation group was significantly lower than that of the control group ($P<0.05$) ($^*P<0.05$ before and after treatment, $^#P<0.05$ between both groups).

Bedside ultrasound for inferior vena cava diameter

Clinical measures of hydration are not always reliable, and invasive methods such as measurement of CVP cannot be used routinely. In a previous study, IVCD was used to assess fluid status in children undergoing hemodialysis, and the results validated the applicability of VCD in the estimation of hydration status. The combination of clinical values and measurement of IVCD can enable a more accurate evaluation of hydration of children on hemodialysis [19]. Therefore, this study sought to determine whether the use of IVCD to guide fluid resuscitation in patients with TBI has a better effect.

The inferior vena cava, which runs anteriorly to the right of the human spine and superiorly along the right side of abdominal aorta, is the largest vein that collects venous blood from the lower abdomen and lower extremities. Bilginet
al. showed that IVCD can be used as a noninvasive index to monitor blood volume and that the variability of IVCD with respiration during positive pressure ventilation reflects volume responsiveness [20, 21]. Determination of IVCD by ultrasound can guide fluid resuscita-
Bedside ultrasound for inferior vena cava diameter

Figure 6. Comparison of the incidence of adverse reactions. The incidence of adverse reactions was 30% in (A) the control group and 10% in (B) the observation group after treatment.

Figure 7. Bedside ultrasound monitoring allows accurate observation of the inferior vena cava in patients and is the key for the development of therapeutic measures.

In this study, we compared the clinical effects of using central venous pressure (CVP) to guide fluid resuscitation and using IVCD and its rate of change to guide fluid resuscitation in patients with sTBI. The results showed that the difference in cerebrospinal fluid lactate level before resuscitation was not significant between the two groups, and the level of cerebrospinal fluid after resuscitation was significantly lower in the observation group than the control group. This may be because the cellular metabolic function of sTBI patients subjected to mechanical trauma can be disturbed, causing damage to the mitochondrial inner membrane and inhibiting aerobic metabolism of brain cells, which induces lactic acid accumulation when anaerobic metabolism predominates. Talving et al. showed by monitoring 216 patients with sTBI that patients with high CSF lactate levels and low pH had a poor prognosis, while patients whose CSF lactate could be quickly normalized had a good prognosis [24]. In this study, patients in the observation group had significantly lower post-resuscitation CSF levels and higher CSF clearance rate than the control group, suggesting that the use of IVCD and its rate of change to guide fluid resuscitation is more appropriate and can rapidly reduce patients' CSF lactate levels and improve their postoperative outcomes. Coagulation dysfunction caused by sTBI has been considered as one of the important factors affecting the prognostic outcome of patients [25]. A large amount of coagulation substances and neurohormones is released, resulting in a hypercoagulable state, accompanied by shock, infection and other symptoms, and the body will rapidly activate the coagulation system, promoting coagulation dysfunction and increasing the risk of death [26, 27]. In this study, the differences in PT, APTT, and TT in both groups before resuscitation were not significant, and PT, APTT, and TT in the observation group were significantly lower than in the control group after 2 d of resuscitation. This proved that the use of IVCD and its rate of change to guide fluid resuscitation can effectively improve the coagulation index, prevent patients from developing coagulation dysfunction, and improve the prognosis. Studies have shown that the levels of neurological function factors such as GFAP, NSE, MBP, and S-100B can reflect the severity of TBI and assess the prognosis of patients. When patients' brain cells are damaged, a large amount of neurological function factors are released, leading to an increase in serum neurological function factors, and this high level correlates with a worse prognosis [28, 29]. In this study, the levels of neurofunctional factors such as GFAP, NSE, MBP, and S-100B were reduced in both groups after treatment, and the levels of these factors were significantly lower in the observation group than the control group. This shows that the use of IVCD and its rate of change to guide fluid resuscitation can...
Figure 7. Bedside ultrasound. Differences in inferior vena cava diameter, rate of change, volume responsiveness, inferior vena cava hemofiltration, and blood flow spectrum were seen among different patients. A: Inferior vena cava diameter of 1.28 cm with a change rate of 48% suggests volume deficit and volume responsiveness. B: Inferior vena cava diameter of 1.71 cm, change rate of 16%, suggests volume unresponsiveness. C: Inferior vena cava diameter of 1.79 cm, change rate of 28%, suggests volume responsiveness. D (left): inferior vena cava hemofiltration spectrum; D (right): inferior vena cava flow spectrum.

better reduce serum neurofunctional factor levels and reduce neurological impairment. Moreover, NIHSS scores of patients in the observation group were significantly lower than in the control group, indicating significantly improved neurological function in the patients guided by IVCD. After treatment, the SOFA and APACHE II scores of both groups were lower than those before treatment, but were significantly lower in the observation group than the control group. MMSE and Barthel scores of patients in both groups increased after treatment, and were significantly higher in the observation group than the control group. GOS scores of patients in the observation group were significantly higher than those in control group. The incidence of adverse reactions was significantly lower than that of the control group. These findings show that the use of IVCD and its rate of change to guide fluid resuscitation can better protect vital organ functions, reduce the degree of cognitive dysfunction and postoperative adverse reactions, improve patients’ living ability, and improve their physical condition and outcome.

In conclusion, monitoring IVCD and its change rate to guide fluid resuscitation in patients with stTBI can rapidly reduce patients’ CSF lactate levels, PT, APTT, and TT, better protect patients’ vital organ function,
reduce the occurrence of adverse reactions, substantially improve patients’ quality of life, and better facilitate postoperative recovery.

**Disclosure of conflict of interest**

None.

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**References**


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