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The shape change index (SCI) of inferior vena cava (IVC) measuring by transabdominal ultrasound to predict the presence of septic shock in intensive care unit (ICU) patients

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Abstract. – OBJECTIVE: This study is designed as prospective and observational research of patients with sepsis. It was carried out in the intensive care unit (ICU). We investigated the shape change index (SCI) of inferior vena cava (IVC) measured with trans-abdominal ultrasound to detect the signs of septic shock. The aim of this research was to find the most effective tool in predicting shock in patients compared with that of other parameters such as brain natriuretic peptide (BNP), lactate, variation index of inferior vena cava IVC-VI, and extravascular lung water index (EVLWI).

PATIENTS AND METHODS: We suppose that SCI can be used as the safest and most sensitive tool in the early recognition of septic dysfunction. The observational study was conducted in the Department of ICU, Shandong Provincial Hospital Affiliated to Shandong University from January 2016 to December 2017. SCI of IVC, serum lactate, BNP, IVC-VI, and EVLWI concentrations were measured in 30 sepsis patients. All studied biomarkers were analyzed and contrasted according to the score of the Sequential Organ Failure Assessment (SOFA). Pearson correlation analysis was analyzed to statistic the relationship between variables.

RESULTS: We showed the correlation of BNP value, lactic acid value, IVC-VI, EVLWI, and SCI of IVC in sick patients suffering septic shock. Positive correlation was observed in the BNP value, lactic acid value, IVC-VI, EVLWI, and SCI of IVC (r=0.447, p=0.013; r=0.484, p=0.007; r=0.423, p=0.023; r=0.638, p<0.001; r=0.599, p<0.001; respectively). However, the SCI and EVLWI showed a stronger correlation with the SOFA than the others. SCI of IVC, as estimated by transabdominal ultrasound, was more accurate than the other commonly used non-invasive predictors. EVLWI, as an accurate and classical predictor, was an invasive predictor. SCI of IVC was faster, more convenient and safer than the other.

CONCLUSIONS: SCI of IVC was faster, more convenient and safer than the other commonly used non-invasive predictors. Early recognition and diagnosis of sepsis may improve patient outcome.

Key Words:
Septic shock, Shape change index of inferior vena cava (SCI of IVC), Transabdominal ultrasound, Sequential organ failure assessment (SOFA), Correlation analysis.

Introduction

The major causes of morbidity and mortality in patients entering the intensive care unit (ICU) are severe sepsis and septic shock[1]. In cellular metabolism level, septic shock can lead to seriously low blood pressure and other abnormalities[2]. Bacteria, fungi, viruses or parasites normally cause infection[3]. These pathogens can be located in any section of the body, especially in pulmonary, myocardial, cerebral, hepatic, or renal[4]. Most commonly, these can lead to multiple organ failure or death[5]. The mortality caused by septic shock reaches up to 50% in many countries[6]. Early detection and prediction of septic shock may be helpful to re-

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duce the mortality rate. Thus, there is an urgent need to explore effective means to prevent deaths. In ICU, initial physical examination findings are not enough in detecting septic shock. The Sequential Organ Failure Assessment (SOFA) score is an authenticated score to assess the number of impaired organs and the severity of the disease[7]. Brain Natriuretic Peptide (BNP) and arterial lactate have been used as biochemical markers for serious septic shock, both of which are sensitive and specific[8]. Ultrasound (US) as a non-invasive and fast tool to visualize muscles, tendons and internal organs, as well as to capture the structure and lesions with real-time images[9]. Computerized tomographies (CT) are more sensitive than US; however, they are invasive and time-consuming[10]. In addition, because of an increase in invasive devices and septic shock patients, there has been an increasing rate of deaths in recent decades[11]. However, the evidence is not also presented on the effectiveness of automated systems for early sepsis alert in septic shock. At present, there has been no comparable research on the effect of detection on early sepsis. Moreover, there is still a lack of consensus on the detection on early sepsis[12].

This is a prospective observational study of patients with sepsis. The accuracy of the shape change index (SCI) of inferior vena cava (IVC) was measured with the trans-abdominal US to detect septic shock in patients to determine the utility of effective tool in predicting shock in patients compared with that of other parameters such as serum lactate, serum Brain natriuretic peptide (BNP), variation index of inferior vena cava (IVC-VI), and Extravascular Lung Water Index (EVLWI). We speculate that SCI can be used as a sensitive instrument in the early identification of septic dysfunction early recognition as well as diagnosis of sepsis may improve patient outcome.

Materials and Methods

Clinical Samples

30 patients with septic shock were enrolled in this research. All patients were hospitalized at the Department of ICU, Shandong Provincial Hospital Affiliated to Shandong University from January 2016 to December 2017. A prospective search for eligible patients was accomplished using the hospital information system. Septic shock was defined on the basis of the standard guidelines published by Jiang et al[2]. In this work, there were 19 males and 11 females from 15 to 81 with a median of 54.93 ± 18.55 years. Data were obtained from the medical record database. Vital signs, serum bio-markers (lactate and BNP level) were measured; the variation index of inferior vena cava (IVC-VI) and shape change index of inferior vena cava (SCI) diameter were calculated by Ultrasound (US). We have been relying on severity scores such as acute physiology and chronic health evaluation II (APACHE II) and SOFA for predicting disease course and outcome.

Inclusion and Exclusion Criteria

The criteria for ICU transfer in patients with severe sepsis/septic shock were as follows:

1) despite adequate fluid resuscitation, sustained shock requiring norepinephrine 0.1 μg/kg/min;
2) acute respiratory failure (respiratory rat > 30/min, PaO_2 < 60 mmHg in room air or $PaCO_2$ > 50 mmHg);
3) acute heart failure or pulmonary edema;
4) acute renal failure needing hemodialysis;
5) drowsy mentality.

ICU transfer was required when at least one of these conditions occurred in hospitalized patients with severe sepsis/septic shock. Death imminent within 6 hours, and APACHE II score <15 were ruled out.

Informed consent was obtained from patients or their relatives. This research was approved by the Ethics Committee of the Shandong Provincial Hospital (clinical trial registry number: Chinese Clinical Trial Registry (ChiCTR)-IPC-14005596).

Study Assessments

The records were reviewed for demographic data, laboratory test results, and US results. Serum NT-proBNP measurements were made using a two-site (sandwich complex) immunoassay with a cutoff value ≥ 125.0 pg/mL considered as abnormal. Concentrations of NT-proBNP were analyzed as early as possible after ICU admission, using a Cobas® e 602 (Roche Diagnostics, Mannheim, Germany). Plasma concentrations of lactate were analyzed as early as possible, using ABL800 (Radiometer Medical, Copenhagen, Denmark). The normal range of lactate was 0.5-2.0 mmol/L. A cutoff value of ≥ 2.0 mmol/L was considered abnormal. An Acuson P300 ultrasound machine with a 1-3.5-MHz frequency cardiac probe was used to detect the diameter of IVC (Acuson P300, Erlangen, Germany). The maximal diameter (MXD) and the minimal diameter (MID) were measured transversely from the subcostal area

and right mid-axillary. The measurements were taken by qualified ultrasound radiologists. The IVC was detected 2.0 cm caudal to the junction point of the hepatic vein and IVC, selecting 2-D mode every 10.0 s (and including 2-3 respiratory cycles). To measure the vein lumen at one respiratory cycle, from one interior wall to the opposite wall, the inspiratory (IVCi) and expiratory (IVCe) were detected. The IVC provided respiratory variation was IVC-VI (IVC-VI=[(IVCe–IVCi)/IVCe] ×100%). To investigate the SCI of IVC measured from the subcostal area and right mid-axillary line through ultrasonography lays the foundation for future research about SCI. The maximal diameter (MXD) and the minimal diameter (MID) were measured transversely from the subcostal area and right mid-axillary line. The SCI of IVC was calculated by MXD/MID×100%[13]. Transpulmonary thermodilution and calculation of EVLWI were measured by this method. A 5-French thermistor-tipped catheter was placed into the femoral artery and a central venous catheter was inserted into a central vein (jugular or subclavian vein); both were connected to pulse indicator contour cardiac output (PiCCO) system.

Thermodilution technique measured the cardiac output (CO) and volumetric parameters, and was obtained after injection of 15 mL of cold isotonic saline 0.9% (<8°C) *via* the central venous catheter. This mean of three consecutive injections was recorded.

Table I. Clinical features and characteristics of the patients.

Characteristics	
Number of patients	30
Age (years)	
Range	15-81
Median	58
Mean	54.93 ±18.55
Gender	
Male	19(63.3%)
Female	11(36.7%)
Reason for admission	
Medical	20(66.7%)
Surgical	10(33.3%)
Source of sepsis	
Pulmonary	17 (56.7%)
Gastrointestinal	11(36.7%)
Genitourinary	2 (6.7%)
SOFA	
Range	1-13
Median	7
Mean	6.57±2.92
Controlled mechanical ventilation	12(40.0%)
18(60.0%)	
Spontaneous breath	12(40.0%)

Data are presented as median, mean and number (n) of patients (%). SOFA, sequential organ failure assessment.

Statistical Analysis

Statistical Package for Social Sciences Version SPSS 18.0 (version 18.0 for Microsoft Windows: SPSS Inc., Chicago, IL, USA) was used to set up a database of the patients. The data were expressed as the mean ± standard deviation and range. Pearson correlation analysis analyzed the relationship between variables. Two-tailed values of ≤ 0.05 were regarded as significant.

Results

Basic Patients' Characteristics

This study included 30 patients with septic shock, all of whom met the inclusion criteria of the study. The clinical features and characteristics of the patients are presented in Table I. We reviewed the medical records of all patients, which included medical history, clinical presentation, laboratory test results and US results. There were 17 patients (56.7%) with the pulmonary source, 11 patients (36.7%) with gastrointestinal source and 2 patients (6.7%) with the genitourinary source.

Table II summarizes the laboratory characteristics in patients. The concentrations of serum NT-proBNP were measured as early as possible after entering the ICU. The concentrations of serum NT-proBNP at the respective time-points were 8954.23 ± 8549.87 pg/mL. The lactic acid value at the respective time-points was 3.98 ± 1.47 mmol/L.

Table III summarizes the ultrasonic characteristics in patients. The IVC-VI at the respective time-points were 0.42 ± 0.09. The EVLWI at the respective time-points were 12.38 ± 3.33. The SCI of IVC at the respective time-points were 2.22 ± 0.46.

Correlation Analysis

Figure 1 shows the correlation of BNP value, lactic acid value, IVC-VI, and SCI of IVC in patients. Positive correlation was observed in the BNP value, lactic acid value, IVC-VI, EVLWI, and SCI of IVC (r=0.447, p=0.013; r=0.484,

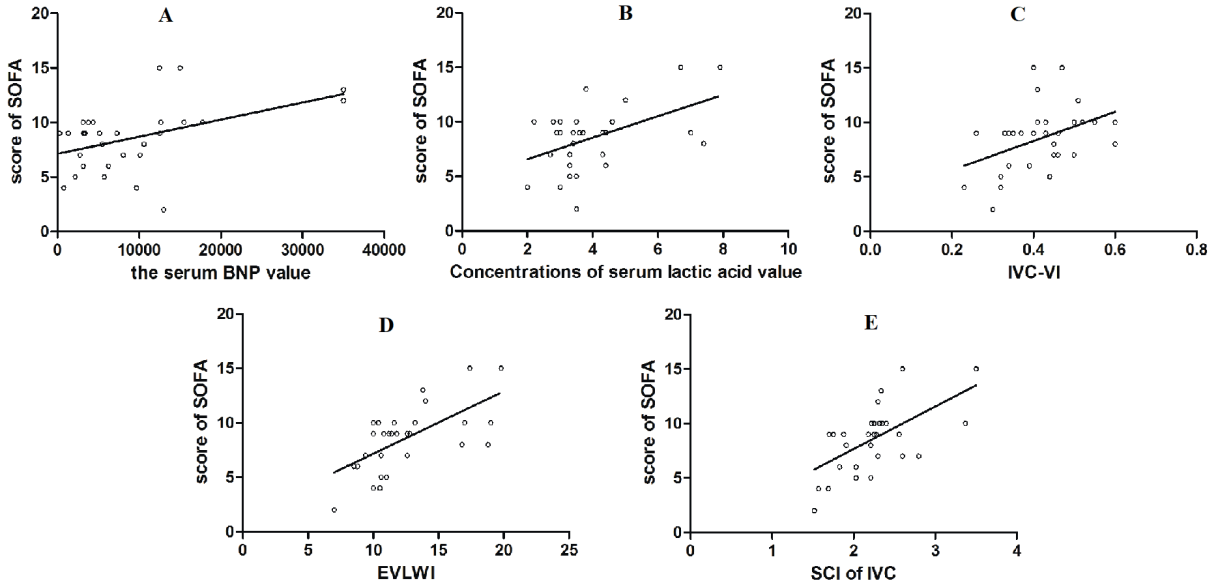

Figure 1. Correlation of BNP value, lactic acid value, IVC-VI, EVLWI, SCI of IVC and SOFA score in patients with septic shock. ***A,*** Correlation of BNP value and SOFA score in patients with septic shock. ***B,*** Correlation of lactic acid value and SOFA score with septic shock. ***C,*** Correlation of IVC-VI and SOFA score in patients with septic shock. ***D,*** Correlation of EVLWI and SOFA score in patients with septic shock. ***E,*** Correlation of SCI of IVC and SOFA score in patients with septic shock.

p=0.007; r=0.423, p=0.023; r=0.638, p<0.001; r=0.599, p<0.001, respectively). However, the SCI of IVC and EVLWI showed a stronger correlation with the SOFA than the others.

Discussion

Septic shock and multiple organ dysfunction syndromes remain a treatment challenge for both primary care physicians and intensivists[14]. Septic shock is characterized by hypotension unresponsive to fluid resuscitation, and is a subset of severe sepsis[15]. With more emphasis on noninvasive tools, nowadays, simpler methods are developing for fluid assessment. In the present work, we evaluated the efficacy of ultrasonographically SCI of IVC in comparison to other assessments in early warning fluid responsiveness in patients with septic shock. To clarify the best correlation in predicting fluid responsiveness, we detected BNP value, lactic acid value, IVC-VI, EVLWI, and SCI of IVC in patients with septic shock. SCI of IVC, measured by ultrasound, was the most accurate predictor in commonly used invasive and non-invasive predictors. Our data demonstrated that, compared with BNP value, lactic acid value, IVC-VI, SCI showed a stronger correlation with the SOFA in patients with septic shock.

Table I summarizes the main clinical features of the enrolled patients. Table II and III summarize the laboratory and ultrasonic characteristics in patients. The concentrations of serum NT-proBNP at the respective time-points were 8954.23 ± 8549.87 pg/mL. The lactic acid value at the respective time-points were 3.98 ± 1.47 mmol/L. The IVC-VI at the respective time-points were 0.42 ± 0.09. The EVLWI at the respective time-points were 12.38 ± 3.33. The SCI

Table II. Laboratory characteristics.

Characteristics	Median	Mean
Serum NT proBNP	5981.00	8954.23±8549.87
Lactic acid value	3.50	3.98±1.47

Data are presented as medians.

Table III. Ultrasonic characteristics.

Characteristics	Median	Mean
IVC-VI	0.42	0.42±0.09
EVLWI	11.3	12.38±3.33
SCI	2.24	2.22±0.46

Data are presented as medians.

of IVC at the respective time-points were 2.22 ± 0.46.

As shown in Figure 1, SCI showed a stronger correlation with the SOFA in patients with septic shock compared with BNP value, lactic acid value, IVC-VI. The ideal diagnostic method should be fast, non-invasive, sensitive, and specific. Several studies[16,17] in related fields proved that early detection and diagnosis is the most effective way to reduce the mortality with the increasing incidence of sepsis and its complications; rapid and detailed research has become more and more important[18]. To clarify the best correlation in predicting fluid responsiveness, we detected BNP value, lactic acid value, IVC-VI, and SCI of IVC in patients. We found that the detection of SCI could decrease mortality rate as previously reported[17]. We observed that the traditional measurements (shock index, BNP index, and lactate level, EVLWI) have an inferior predictive value.

The incidence of sepsis and its complications is increasing, despite the evolution of scientific technology. Plasma concentration of both these peptides can be measured and have comparable diagnostic and prognostic accuracy[19]. The protocol for SCI of IVC is not well described in several medical literature. Other studies[20,21] have shown that IVC-VI diameter with respiration is helpful in predicting fluid responsiveness BNP is a 32-amino acid polypeptide secreted by the ventricles of the heart, and it produces the active BNP and the inactive amino-terminal (NT) pro BNP molecules[22]. The previous investigations[23-25] revealed that the concentration of BNP peptide can be used as a reliable indicator for sepsis-induced myocardial inhibition. However, unlike the previous trial, BNP has limitations in an emergency condition in our research. In contrast, the measurement of lactic acid can provide useful information in an extremely short time during emergency treatment[26]. The results of this work conformed with the previous results[27]. Like most other studies[28-29], a possible explanation for the limitation is that BNP was measured at presentation before intravenous fluid resuscitation, or after intravenous fluid resuscitation in ICU. This is a chief knowledge gap, because no research has incorporated cardiac biomarkers into prognostic tools. At present, no sepsis prognostic scoring system considers myocardial damage or cardiac biomarkers.

Lactate is measured to estimate the severity and the effect of treatment in patients with severe septic shock[30]. The research data suggest that the content of lactate was a superior predictor than BNP alone. Nevertheless, it is plausible that the elevating lactate is simply an activity of significant organ dysfunction or shock, especially refractory hypotension. The most important problem is the "washing out effect" (the lactic acid that accumulates in the tissues after the perfusion is improved into the circulatory system, and the lactic acid may be further elevated), which may be limited in clinical application[31]. Lactate is a potentially useful biomarker in patients with severe sepsis. However, initial lactate was associated with mortality independent of clinically shock in patients before intravenous fluid resuscitation with severe sepsis.

Unlike our study, a previous research[32-34] showed that the distensibility index of IVC (IVC-DI) in mechanically ventilated patients with sepsis provided encouraging results, being able to accurately predict volume responsiveness in sepsis or septic shock. Unlike the previous work, our study group included a high proportion of patients with advanced disease. This difference in patients groups may account for the different results. Our study showed IVC-VI is not particularly useful in shock assessment. Equally, recent studies[35] particularly recruiting patients with spontaneously breathing have failed to show the identical predictive value. Lu et al[36] also found the IVC-VI could not play predictive value in the patient with suspected hypovolemia. IVC collapsibility index (IVC-CI) is affected by intrathoracic pressures and right heart dysfunction similar to central venous pressure (CVP)[37]. More invasive techniques became popular with time. However, marked inter-rater variability and lack of expertise in carrying out ultrasonographic (USG) IVC assessment further add to the drawbacks of this method. Since the concept of the ICUs in the 1950s, the hemodynamic monitoring has traveled a long way but is still at crossroads, because CVP is unable to predict accurate volume status, and failed to make clinical decisions.

In recent times, the pendulum has swung toward noninvasive, simple, and fast techniques[38]. Our results showed that the SCI of IVC is valuable for fluid resuscitation in patients of septic shock. Similarly, EVLWI, as an accurate and classical predictor, was an invasive predictor[39,40]. Compared with the other commonly used predictors, the measurement of SCI of IVC was more accurate, convenient, and safer

Ultrasound assessment of SCI of IVC might be recommended as a noninvasive and continuous method to predict fluid responsiveness in mechanically ventilated patients with septic shock. Early recognition and appropriate treatment of shock have been shown to decrease mortality[2-4]. The difference in patients groups may account for the different results[41-43].

With the increasing incidence of sepsis and its complications, rapid and detailed research has become more and more important. Our work contributes significantly to the knowledge of early detection in septic shock. This is the first clinical study to assess the effect SCI of IVC for fluid resuscitation in patients. Secondly, our findings confirmed that SCI of IVC stabilized hemodynamics significantly and decreased mortality rate as previously reported[41-43].

This work showed that measurement SCI of IVC had a strong and independent prognostic importance for all patients with septic shock. Compared with traditional impact parameters, such as lactic acid, BNP and IVC-VI, the SCI of IVC in this setting is more valuable. Larger investigations with longer follow-up are needed to evaluate circulation more precisely and to explore its effect on clinical outcomes.

Conclusions

Our study adds to the accumulating evidence that SCI of IVC, derived by ultrasound graphically, is potentially useful for evaluating volume status in septic shock patients. These findings are important for performing serial measurements to further prospective SCI of IVC. Larger sample size and enough statistical powers are needed to clarify current issues regarding the use SCI of IVC in the field of septic shock.

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Conflict of Interest

The Authors declare that they have no conflict of interest.

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