Letter to the Editor

Correlation of Inferior Vena Cava Respiratory Variability Index with Central Venous Pressure and Hemodynamic Parameters in Ventilated Pigs with Septic Shock

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Septic shock is a common critical condition, for which effective early fluid resuscitation is the therapeutic focus. According to the 2008 international guidelines for management of severe sepsis and septic shock, resuscitation should achieve a central venous pressure (CVP) of 8-12 mmHg within the first 6 h[1]. However, it is still uncertain about the sensitivity and specificity of CVP in reflecting the cardiac preload. Ultrasonography is a simple, rapid, non-invasive, and repeatable method for the measurement of sensitivity and specificity of CVP and has thus gradually attracted the increasing attention of physicians. It was reported that ultrasonography can show the inferior vena cava diameter, respiratory variability index, and blood volume in patients with sepsis or heart failure[2-3]. In this study, the relation of pulse-induced contour cardiac output (PiCCO) hemodynamic parameters with the maximum inferior vena cava diameter (IVCmax), minimum inferior vena cava diameter (IVCmin), inferior vena cava respiratory variability index (IVCrvi), and CVP was studied in pigs with septic shock.

Ten juvenile pigs (5 males and 5 females) weighing 30.28±1.80 kg were anesthetized by intraperitoneal injection of 3% pentobarbital sodium (30 mg/kg), intravenous injection of fentanyl (25 μg/kg) and rocuronium bromide (0.6 mg/kg) through an indwelling ear vein catheter and maintained by intravenous infusion of 3% pentobarbital sodium (5-10 mL/h) and fentanyl (10 μg/kg/h). The animals were placed at the supine position, tracheal intubation was performed, followed by mechanical ventilation in SIMV mode, with a tidal volume of 10-15 mL/kg, a respiratory rate of 12 breaths/min, an inspiration of 21% oxygen, a positive end-expiratory pressure of 3 cm H_2O, an inspiratory:expiratory ratio of 1:1.5-1:2.0. A 6F-diameter catheter was inserted into the internal jugular vein for monitoring of CVP a PiCCO sensor and a PiCCO plus monitor for monitoring of temperature. A femoral artery was isolated into which a PiCCO thermodilution catheter was inserted and connected to the PiCCO plus monitor. An animal model of septic shock was established by injecting 50 mL of diluted *E. coli* endotoxin into the internal jugular vein (100 μg/kg). Septic shock was induced when the mean arterial pressure (MAP) decreased to 70% of the baseline value. The fluid resuscitation was carried out 6 h after the establishment of septic shock model.

PiCCO hemodynamic parameters were measured before, during, 1 and 6 h after the establishment of septic shock model. The cardiac index (CI), global end-diastolic volume (GEDV), intrathoracic blood volume (ITBV), stroke volume variation (SVV), CVP, IVCmax, IVCmin, and IVCrvi were recorded. The IVCmax and IVCmin were measured at the end of inspiration and expiration respectively with a portable ultrasound machine. The IVCrvi was calculated according to the formula: (IVCmax – IVCmin) / IVCmax × 100%. The data are expressed as mean±SD (n=3) and analyzed using the SPSS 15.0 software. Relevant parameters before and after fluid resuscitation were compared by repeated ANOVA. The relation between different parameters was analyzed by Pearson correlation analysis. P<0.05 was considered statistically significant.

The IVCmin was significantly different from the IVCrvi (P<0.001), but not from the IVCmax (P=0.097) before and after fluid resuscitation. The CVP, CI, GEDV, ITBV, and SVV were also significantly different before and after fluid resuscitation (P=0.016, P=0.040, P=0.002, P=0.001, and P<0.001, Table 1).

The CVP was significantly correlated with the CI, GEDV, ITBV, SVV, IVCmax, IVCmin, and IVCrvi (r=0.922, r=0.707, r=0.734, r=-0.653, r=0.433, r= 0.816, r=-0.719; P<0.001, P<0.001, P<0.001, P<0.001, P=0.00, P<0.001, P<0.001, Figure 1). The IVCmax was significantly correlated with the SVV (r=-0.362, P=0.022), but not with the CI, GEDV, or ITBV (r=0.135,

doi: 10.3967/0895-3988.2013.06.012
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r=0.029, *r*=0.035; *P*=0.405, *P*=0.858, *P*=0.829). The IVCmin and IVCrvi were significantly correlated with the CI, GEDV, ITBV, and SVV (*r*=0.724, *r*=0.665, *r*=0.697, *r*=-0.796, *r*=-0.820, *r*=-0.869, r=-0.864, r=0.771; *P*<0.001, *P*<0.001, *P*<0.001, *P*<0.001, *P*<0.001, *P*<0.001, *P*<0.001, *P*<0.001, Figure 2).

Table 1. CI, GEDV, ITBV, SVV, IVCmax, IVCmin, IVCrvi, and CVP before and after Fluid Resuscitation

	CI (L/min/m^2)	GEDV (mL)	ITBV (mL)	SVV (%)	IVCmax (cm)	IVCmin (cm)	IVCrvi (%)	CVP (mmHg)
Baseline value	3.55±0.57	251.60±36.04	322.80±39.52	11.60±2.37	1.11±0.14	0.86±0.11	22.10±4.86	5.25±0.65
Shock	1.71±0.49	125.00±38.75	164.10±46.88	24.00±5.19	0.90±0.17	0.35±0.11	59.30±17.75	2.15±0.59
1 h after fluid resuscitation	2.91±0.44	204.30±38.77	260.50±46.00	17.70±2.98	0.99±0.15	0.66±0.07	32.70±7.45	4.11±0.59
6 h after fluid resuscitation	3.25±0.35	226.90±34.86	292.60±42.38	14.10±2.33	1.03±0.15	0.79±0.08	23.50±5.74	4.64±0.63
F	11.74	18.96	21.58	25.54	9.38	21.71	25.38	14.03
P	0.040	0.002	0.001	<0.001	0.097	0.001	<0.001	0.01

Note. CI: cardiac index, GEDV: global end-diastolic volume, ITBV: intrathoracic blood volume, SVV: stroke volume variation, IVCmax: maximum diameter of inferior vena cava, IVCmin: minimum diameter of inferior vena cava, IVCrvi: inferior vena cava respiratory variability index.

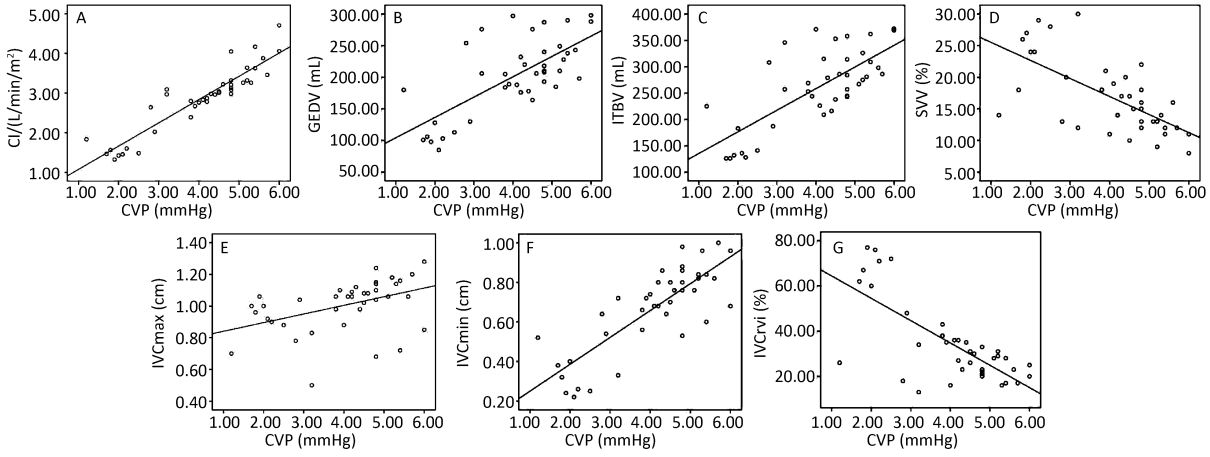

Figure 1. Scattered diagrams of CVP (X-axis) and CI (Y-axis) (A), CVP (X-axis) and GEDV (Y-axis) (B), CVP (X-axis) and ITBV (Y-axis) (C), CVP (X-axis) and SVV (Y-axis) (D), CVP (X-axis) and IVCmax (Y-axis) (E), CVP (X-axis) and IVCmin (Y-axis) (F), CVP (X-axis) and IVCrvi (Y-axis) (G).

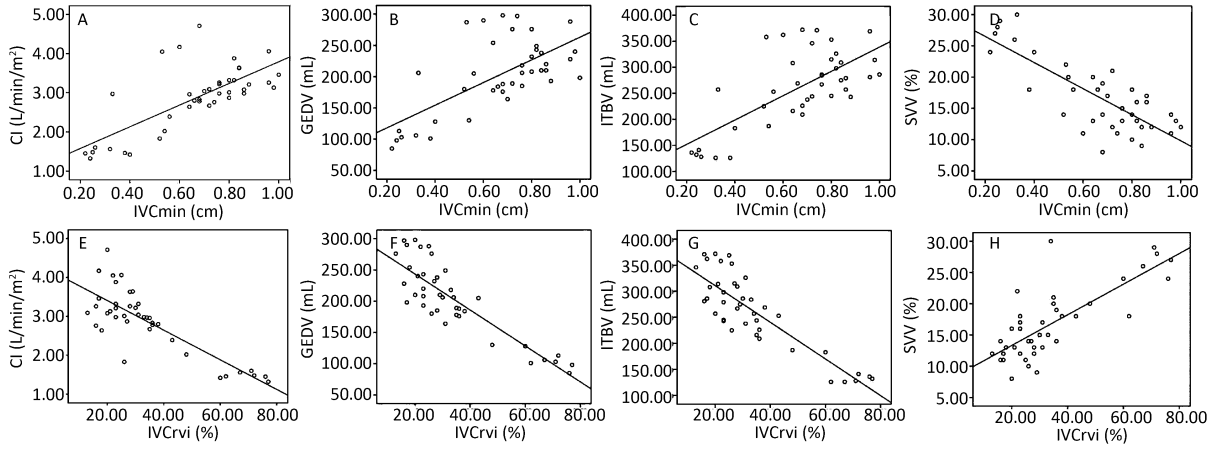

Figure 2. Scattered diagrams of IVCmin (X-axis) and CI (Y-axis) (A), IVCmin (X-axis) and GEDV (Y-axis) (B), IVCmin (X-axis) and ITBV (Y-axis) (C), IVCmin (X-axis) and SVV (Y-axis) (D), IVCrvi (X-axis) and CI (Y-axis) (E), IVCrvi (X-axis) and GEDV (Y-axis) (F), IVCrvi (X-axis) and ITBV (Y-axis) (G), IVCrvi (X-axis) and SVV (Y-axis) (H).

Septic shock can result in end-organ hypoperfusion with tissue hypoxia, hypotension and blood lactate concentration ≥4 mmol/L, thus requiring active fluid resuscitation. It was reported that fluid resuscitation should maintain the CVP at 8-12 mmHg during the initial 6 h[1]. It is therefore necessary to establish the central venous access and monitor the CVP during fluid resuscitation in patients with septic shock. However, it is a traumatic procedure to establish the central venous access, which may cause complications, such as pneumothorax and arterial puncture. It is not easy to establish the central venous access in some patients because of variations in anatomical structures. Rapid assessment of blood volume is therefore a challenge for the fluid resuscitation.

PiCCO, a commonly used minimally-invasive hemodynamic monitoring technology, employs thermodilution to accurately determine the indicators of cardiac preload and function such as MAP, ITBV, GEDV, SVV, and CI, and is widely used to monitor various critically ill patients[4]. According to the international guidelines for management of severe sepsis and septic shock, one of the aims of treatment is to maintain the CVP at 8-12 mmHg. However, whether CVP can accurately reflect the cardiac preload and is an appropriate indicator for guiding fluid resuscitation is still controversial[5]. It was reported that CVP is poorly correlated with blood volume, and therefore cannot be used to predict the responses to fluid therapy[6]. In contrast, this study demonstrated that the CVP was significantly correlated with the CI, GEDV, ITBV, and SVV in patients with septic shock, suggesting that CVP can reflect the cardiac preload and function.

Ultrasonography is a simple, rapid, non-invasive and repeatable method for the detection of cardiac preload and function, and has attracted the increasing attention of physicians[7]. The diameter of inferior vena cava changes with respiration and is influenced by blood volume which decreases with the decreasing diameter of inferior vena cava. Measurement of inferior vena cava diameter with bedside ultrasonography contributes to the assessment of blood volume. Sefidbakht et al.[8] investigated 88 trauma patients and found that the diameter of inferior vena cava is significantly shorter in patients with shock than in those without shock and is negatively correlated with shock. Wiwatworapan et al.[9] investigated 47 critically ill patients and concluded that the diameter of inferior vena cava is well correlated with the CVP in Thai-population. Ferrada et al.[10] defined the FLAT inferior vena cava as the diameter of inferior vena cava less than 2 cm and the patients with FLAT IVC respond to fluid challenge. In this study, the IVCmin and IVCrvi were significantly correlated with the CI, GEDV, ITBV, and SVV, indicating that ultrasonography is a non-invasive and rapid method to measure the diameter of inferior vena cava in pigs with septic shock reflecting their cardiac preload and function.

In summary, the IVCmax, IVCmin, and IVCrvi are significantly correlated with the CVP and PiCCO hemodynamic parameters in pigs with septic shock, thereby reflecting their cardiac preload and function, and providing the experimental evidence for the repeated, rapid, non-invasive evaluation of blood volume by ultrasonography in patients with septic shock.

ACKNOWLEDGEMENTS

The authors declare that they have no competing financial interests.

ZHANG Guo Qiang contributed to the study design and provided technical support of ultrasound. LIU Xiao Lei performed ultrasonography, collected the data and drafted the manuscript. TAO Yong Kang, YAN Sheng Tao and QI Zhi Wei established and managed the animal model of septic shock. LU Hai Tao and WANG Hai Feng monitored the hemodynamic parameters. GU Cheng Dong processed the data. The authors sincerely thank all colleagues in the Clinical Research Center of China-Japan Friendship Hospital for their support and cooperation in the study.

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Received: December 24, 2012;

Accepted: May 7, 2013

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