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Inferior vena cava diameter variation compared with pulse pressure variation as predictors of fluid responsiveness in patients with sepsis

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ABSTRACT

Background: Currently, physicians employ pulse pressure variation (PPV) as a gold standard for predicting fluid responsiveness. However, employing ultrasonography in intensive care units is increasing, including using the ultrasonography for assessment of fluid responsiveness. Data comparing the performance of both methods are still lacking. This is the reason for the present study.

Materials and methods: We conducted a prospective observational study in patients with sepsis requiring fluid challenge. The PPV, inferior vena cava diameter variation (IVDV), stroke volume variation (SVV), and the other hemodynamic variables were recorded before and after fluid challenges. Fluid responders were identified when cardiac output increased more than 15% after fluid loading.

Results: A total of 29 patients with sepsis were enrolled in this study. Sixteen (55.2%) were fluid responders. Threshold values to predict fluid responsiveness were 13.8% of PPV (sensitivity 100% and specificity 84.6%), 10.2% of IVDV (sensitivity 75% and specificity 76.9%) and 10.7% of SVV (sensitivity 81.3% and specificity 76.9%). The area under the curves of receiver operating characteristic showed that PPV (0.909, 95% confidence interval [CI], 0.784-1.00) and SVV (0.812, 95% CI, 0.644-0.981) had greater performance than IVDV (0.688, 95% CI, 0.480-0.895) regarding fluid responsiveness assessment.

Conclusions: The present study demonstrated better performance of the PPV than the IVDV. A threshold value more than 10% may be used for identifying fluid responders.

1. Introduction

Fluid administration is a part of initial resuscitation in most patients with sepsis admitted to the intensive care unit (ICU) [1,2]. Early fluid resuscitation is important for optimizing cardiac output (CO) and restoring organ perfusion [2]. Approximately 50% of patients with sepsis had fluid responsiveness defined by an increase of CO by 10% to 15% [3-11].

To predict fluid responsiveness, we use many parameters, such as pulse pressure variation (PPV) [3,10,12-21], stroke volume variation (SVV) [6,14,19-26], systolic pressure variation [3,5,27,28], and ultrasound-derived parameters [7-9,29]. Several studies supported the accuracy of these parameters. However, the PPV seems to be the most accurate parameter to predict fluid responsiveness [18]. Michard et al [3] have demonstrated the great performance of the PPV since the year 2000 with very high sensitivity and specificity with the area under the receiver operating characteristic (ROC) curve of 0.98. The PPV was also used in various scenarios in either medical or surgical conditions and in addition, the studies by Marik et al [18], Biais et al [23], and Monge Garcia et al [30] showed the best performance compared with other parameters. However, the PPV needs arterial line insertion, which was reported to have complications [31,32]. In some circumstances, we may need to use totally noninvasive tools, such as ultrasound, to avoid complications.

Portable ultrasonography is widely used for many purposes in critical care units because it is entirely noninvasive, easy to record, and requires only a short period of training [33]. In 2004, Vieillard-Baron et al [7] proposed using the superior vena cava collapsibility index assessed by transesophageal approach. They demonstrated superior vena cava collapsibility as a good parameter of fluid responsiveness in mechanically ventilated patients with sepsis. Regarding transthoracic echocardiography (TTE), Feissel et al [8] showed inferior vena cava (IVC) diameter variation as also being a good predictor of fluid responsiveness. Also, Barbier et al [9] confirmed the good performance of the IVC-derived variable, namely the IVC distensibility index by TTE.

However, data are lacking about the comparison between the PPV and IVC parameters concerning fluid responsiveness. Therefore, we aim to compare the performance between 2 techniques, namely the PPV and inferior vena cava diameter variation (IVDV) by TTE regarding fluid responsiveness. We used the increase of CO of more than 15% after fluid challenge (FC) measured by the Vigileo monitor as the gold standard to identify fluid responders [34].

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2. Methods

2.1. Patients

We prospectively conducted this study in an 8-bed medical intensive care unit (MICU) of Ramathibodi Hospital, Thailand from November 2012 to December 2013. The study protocol was approved by the institutional ethics committee and informed written consent was obtained from the next of kin of each patient. The patients were enrolled with the following inclusion criteria: (1) age older than 18 years old; (2) admission from emergency department or general ward with severe sepsis or septic shock defined by the International Sepsis Definitions Conference [35] (3) on controlled mechanical ventilation and requiring intravenous FC for resuscitation based on clinical characteristics of patients [36]. The exclusion criteria were as follows: (1) cardiac arrhythmia; (2) ascites; (3) preexisting severe valvular heart disease and/or intracardiac shunt; and (4) contraindication for sedative agents and/or neuromuscular blocking agents.

All patients were temporarily sedated and paralyzed and on fully controlled mechanical ventilation using the Puritan Bennett 840 system. No spontaneous breathing effort was detected on the mechanical ventilator waveform monitor ensuring that the respiratory changes in arterial pressure reflected only the effects of positive pressure ventilation. Modes of ventilation were selected to volume or pressure controlled ventilation, depending on the decision of the primary physicians. A tidal volume was set to not less than 8 $mL\ kg^{-1}$ (predicted body weight). The preset respiratory rate was set at 16 breath/min. Positive end expiratory pressure was set between 8 and 10 cm H_2O. The plateau pressure was kept at below 30 cm H_2O.

2.2. Measurement

The hemodynamic measurements were obtained at 2 points, namely before FC and after FC. Mechanical ventilator settings and dosages of inotropic and/or vasopressor agents were kept constant during the study period.

Baseline hemodynamic variables including heart rate (HR), systolic blood pressure, diastolic blood pressure, mean arterial pressure (MAP), SVV, and CO were recorded before and after FC. The minimum pulse pressure (PPmin) and maximum pulse pressures (PPmax) were measured to later calculate PPV.

The Vigileo monitor (Edwards Lifescience, Irvine, CA, USA, Software Ver. 03.01) and the FloTrac sensor (Edwards Lifescience, Irvine, CA, USA) were connected to an arterial line. The arterial pressure was zeroed to atmospheric air at the phlebostatic axis and measurement was initiated. The PPmax and PPmin were determined by arterial waveform tracing along 5 breathing cycles or more [37]. The PPV was calculated by the difference between the PPmax and PPmin divided by the mean pulse pressure and presented in percentages [3]. The maximum stroke volume and minimum stroke volume were obtained. The CO was calculated from SV × HR. The SVV was calculated by the difference between maximum stroke volume and minimum stroke volume divided by the mean stroke volume and was displayed in percentage by the Vigileo monitor [21,24,25].

The IVC was visualized by M turbo (SonoSite, Bothell, Washington) with 5-MHz probe echocardiogram at subxiphoid long-axis view using a 2-dimensional mode. Its diameter during the respiratory cycle was measured 3 times by M-mode perpendicular to the IVC and not more than 2 cm from the right atrium. The average of the 3 values for each parameter was used for analysis. The maximum IVC diameter (IVDmax) and minimum IVC diameter (IVDmin) during the respiratory cycle were measured. The IVDV was calculated by the difference of IVDmax and IVDmin divided by the mean IVC diameter and presented in percentage. The inferior vena cava distensibility index (IVDI) was calculated by the difference between IVDmax and IVDmin divided by the IVCmin and presented in percentage. All IVC diameter measurements were performed by a well-trained operator not involved in the patients' care.

The FC test was performed with 1000 mL of crystalloid (0.9% normal saline) over 1 hour or 500 mL of colloid (6% hydroxyethyl starch 130/0.4, Voluven; Fresenius Kabi, Bad Homburg, Germany) or 5% human albumin over 30 minutes [36]. In accordance with previous trials [3,4,38,39], an increase in CO of 15% or greater after the FC was chosen as a threshold value to define responders and nonresponders.

2.3. Statistical analysis

We used Shapiro-Wilk to test the normality of distribution. Data were presented as the mean ± SD for continuous variables tested to be a normal distribution and as the median with interquartile range for variables not to distribute normally. The comparisons of hemodynamic data before and after FC were assessed using the paired Student *t* test and the comparisons between responders and nonresponders were assessed using the 2-sample Student *t* test for normally distributed variables. The nonparametric tests were used to compare non-normally distributed variables. The ROC curves and the area under the curve (AUC) with 95% confidence interval (CI) of PPV, IVV, and SVV were calculated and compared. The threshold values that allowed the discrimination of the fluid responsiveness were determined by considering the values that yielded the greatest sensitivity and specificity.

We analyzed interobserver and intraobserver reliability in 10 cases of sepsis with intraclass correlations (ICC), presented with correlation coefficient, *P* value, and 95% CI. We assigned 3 operators, including the main operator of this study, not involved in the patient care to perform 2 measurements of IVDV in each patient. The intraobserver reliability was computed from 2 consecutive measurements performed by each of 3 operators. The interobserver reliability was analyzed from 3 independent data measured by the 3 operators.

3. Results

A total of 29 patients were enrolled in the present study. Sixteen patients (55.2%) had positive hemoculture, with bacteremia in 14 patients (48.35), and fungemia in 2 patients (6.9%). The most common infection was pneumonia. The average Acute Physiology And Chronic Health Evaluation II and Sequential Organ Failure Assessment were 30.93 ± 7.34 and 10.93 ± 4.10, respectively. The mean lactate level was 6.71 ± 5 mmol/L. The baseline characteristics are presented in Table 1.

Fluid responders were defined in 16 patients (55.2%). We did not find a difference in the general baseline characteristics between responders and nonresponders. Regarding hemodynamic parameters at baseline, the responders had lower MAP than the nonresponders (58.3 ± 7.3 vs 64.8 ± 7.9 mm Hg, $P < .05$). The former had a markedly higher PPV, as well as SVV, than the latter. We found a difference in IVDV between groups, but not reaching statistical significance (Table 2).

Table 3 shows the performance among the variables of interest. The PPV showed the best parameters of all (Fig. 1). The AUC of ROC, of PPV, IVDV, IVDI, and SVV were 0.909, 0.688, 0.688, and 0.812, respectively. Fig. 2 shows the discrimination ability of PPV and IVDV regarding fluid responsiveness. At a cutoff value of 13.8%, the PPV provided 100% sensitivity and 84.6% specificity to predict fluid responsiveness. The IVDV at a threshold value of 10.2% provided sensitivity and specificity of 75.0% and 76.9%, respectively. The SVV provided 81.3% sensitivity and 76.9% specificity at a threshold value of 12.5. The poor relationship between PPV and IVDV is shown in Fig. 3.

The ICCs regarding intraobserver reliability of each of 3 operators were 0.977 ($P < .001$; 95% CI, 0.912-0.994), 0.952 ($P < .001$; 95% CI, 0.808-0.988), and 0.941 ($P < .001$; 95% CI of 0.761-0.985), respectively. The ICC regarding interobserver reliability among 3 operators was 0.895 ($P < .001$; 95% CI, 0.691-0.972).