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Respiratory variation of central vein diameter in upper body as a surrogate of pulse pressure variation

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ABSTRACT:

Background: Cyclical change in central vein diameter during respiratory cycle can be used for fluid-responsiveness assessment. The purpose of this study is to assess variations in the diameter of central veins in upper body region, specifically internal jugular vein (IJV), subclavian vein (SCV), and brachiocephalic vein (BCV), in mechanically ventilated patients. We hypothesized that variations in the diameter of these veins caused by passive ventilation would be strongly concordant with pulse pressure variation (PPV).

Methods: The study was conducted in mechanically ventilated, critically ill surgical and medical patients. The PPV values were automatically calculated and were recorded. The diameters of the study veins such as the IJV, SCV, and BCV were measured bedside using the ultrasound. Then respiratory variations of venous diameter were calculated into distensibility index, collapsibility index and variability index. The relationships between PPV and ultrasound-derived parameters were assessed. Patients were separated into two groups according to their PPV values (>13 and <10). The test performance and proper cut-off values of ultrasound-derived parameters to distinguish between these two groups were generated by receiver operating characteristic (ROC) curves.

Results: A total of 44 patients were assessed. There were substantial correlations between PPV and ultrasound parameter namely IJV-DI (r=0.652, p<0.001), IJV-VI (r=0.655, p<0.001), SCV-CI (r=0.618, p<0.001), and SCV-VI (r=0.626, p<0.001). While PPV and BCV-CI show moderate correlation (r=0.531, p=0.008). The IJV-DI, IJV-VI, SCV-CI, SCV-VI and BCV-VI values were significantly greater in PPV>13 group than PPV<10 group. All these parameters were effective in distinguishing between PPV>13 from PPV<10 group with AUC 0.983, 0.983, 0.928, 0.928 and 0.826, respectively. The IJV-DI, IJV-VI, SCV-CI, SCV-VI and BCV-VI analysis demonstrated appropriate cut-off values for separating patients with PPV>13 from those with PPV<10 as 16.19% (sensitivity 92%, specificity 96%), 14.98 % (sensitivity 92%, specificity 96%), 9.74% (sensitivity of 93%, specificity of 91%), 12.33% (sensitivity of 87%, specificity of 100%) and 13.71% (sensitivity of 73%, specificity of 100%), respectively.

Conclusions: In critically ill patients, all ultrasound-derived measures such as IJV-DI, IJV-VI, SCV-CI, SCV-VI, and BCV-VI revealed significant correlation with PPV value.

Keywords: pulse pressure variation, internal jugular vein, subclavian vein, brachiocephalic vein, variability index, distensibility index, collapsibility index, respiratory variation

INTRODUCTION

Fluid resuscitation is required for patients with hemodynamic instability to restore intravascular volume, enhance cardiac output, and increase oxygen delivery. Over-resuscitation, on the other hand, leads to fluid overload, which increases morbidity or even risk of death in critically ill patients [1]. Dynamic parameters based on heart-lung interaction are useful to predict fluid responsiveness without additional fluid bolus. Several investigations have confirmed the accuracy of pulse pressure variation (PPV) in mechanically ventilated patients. The use of PPV as a surrogate of fluid responsiveness has the largest amount of evidence [2]. Nevertheless, this method has its limitation and disadvantage such as requirement of invasive arterial catheterization and unsuitable method if any arrhythmia present. Furthermore, it necessitates a sophisticated and expensive monitoring system, which cannot be afforded by many hospitals in Thailand's rural areas.

The cyclical change in central vein diameter during the respiratory cycle result from cyclical change in intrathoracic pressure induced by positive pressure ventilation [10] can be detected at bedside. This approach can be used for predict fluid responsiveness [10]. Advantage of ultrasound-derived dynamic parameters above PPV is not only a noninvasive technique but also its ability to predict fluid responsiveness in an arrhythmic patient [3]. The inferior vena cava (IVC) is the most common vein to which breathing variations are applied [4] but obesity, surgical wound and air in bowel loop all hindered assessment of IVC variation, especially in surgical patients.

Therefore, our research focuses on the internal jugular vein (IJV), subclavian vein (SCV), and brachiocephalic vein (BCV), which are all important veins in the upper body region that anesthesiologists and intensivists potentially utilize to monitoring perioperatively, especially in the case of subdiaphragmatic surgery. We hypothesized that respiratory variation in diameter of these veins will correlated well with PPV value in mechanically ventilated, critically ill patients.

KEY MESSAGES:

- Respiratory variation diameter during invasive mechanically ventilation of IJV, SCV and BCV were show good correlation with PPV values and significantly different between PPV>13 and PPV<10 group of patients.

MATERIALS AND METHODS

This single-center observational study was conducted at medical and surgical intensive care units (ICUs) in Phramongkutklao hospital (a tertiary teaching hospital), Bangkok, Thailand. The study period was from April 2021 to November 2021. The study protocol was approved on March 30, 2021 by Institutional Review Broad, Royal Thai Army Medical Department. Research no. R014h/64 following the Council for International Organization of Medical Science (CIOMS) Guidelines 2012 and Good Clinical Practice of International Conference on Harmonization statement no. IRBRTA 0434/2564.

Participants

Patients who were admitted to medical or surgical ICUs, required invasive mechanical ventilation and had arterial line in place, were screened. The patients who were enrolled were older than 20 years old, ventilated with tidal volume at least 8 ml per predicted body weight (kg) and presented with any signs of hemodynamic instability. The signs of instability hemodynamic defined as mean arterial pressure (MAP) less than 65 mmHg longer than 5 minutes or need vasopressor or inotropic agents to maintain MAP at least 65 mmHg, skin mottling, delayed capillary refill time (> 2 seconds), suspected hyperlactatemia from hypoperfusion, or urine output less than 0.5 ml per body weight (kg) per hour. Due to some limitations of PPV, so we excluded patients who had any of these following conditions: cardiac arrhythmia during examination, contraindication to ventilation with more than or equal to 8 ml per predicted body weight (kg), intraabdominal hypertension, significant valvular heart disease, opened abdomen, opened thorax, patient-ventilator asynchrony, high respiratory effort, right ventricular dysfunction, history of pulmonary hypertension, significant valvular heart disease, respiratory compliance less than 30 ml/cmH_2O. We also excluded patients with previous history of surgery or radiation at neck and upper chest or thrombosis of any study vessel. If any vessel had central venous catheter in place, the ipsilateral brachiocephalic vein and associated tributaries were not included into our study. Demographic data such as age, gender, height, weight, body mass index, co-morbidity, vital signs, acute physiology and chronic health evaluation (APACHE II) score, serum lactate level, tidal volume, positive end expiratory pressure (PEEP) level, dose of vasopressor were collected.

Measurement

Ultrasonographic measurement of central neck vein was performed using linear array transducer probe (GE Logiq v5 for surgical ICU patients and Philips EPIQ 5 for medical ICU patients). Adequate sedation should be evaluated and ensured before the examination was performed. Patient neck position was set in neutral position with head of bed up to 30-degree angle during the examination. First, for examination of internal jugular vein (IJV), the probe was gently placed in transverse position, perpendicular to skin, at level of cricoid cartilage, on sternocleidomastoid muscle. Second, the subclavian vein (SCV) was examined by placing the probe vertically, perpendicular to skin, at just medial to mid clavicular line, closed to inferior border of clavicle. Third, the brachiocephalic vein (BCV) was measured by placing the probe just medial to the sternal head of the clavicle, then pivoting it clockwise around 45 degrees from the vertical line, (Fig. 1a).

To avoid pressure compression on the vein, we suggest using a sufficient amount of ultrasonic gel on the patient's skin to avoid pressure compression on the veins during point-of-care ultrasound imaging.

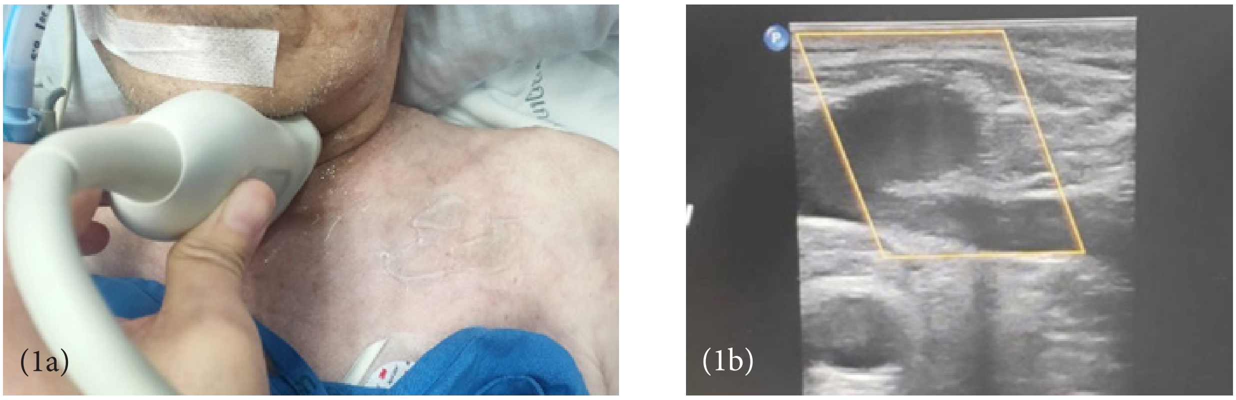

Figure 1. Probe position for evaluating brachiocephalic vein (1a), and ultrasonographic imaging of brachiocephalic vein (junction between internal jugular vein and subclavian vein) in B-mode (1b).

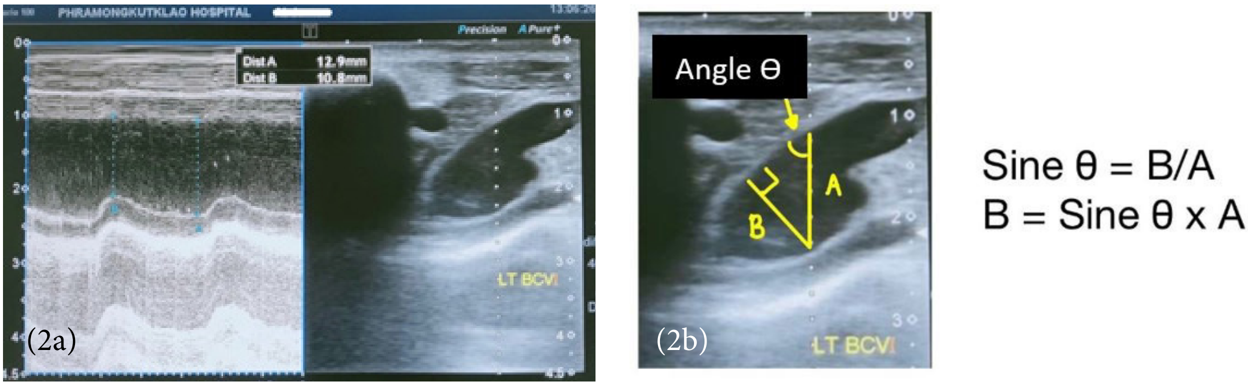

Figure 2. Ultrasonographic imaging of brachiocephalic vein in M-mode (2a) and calculation method of BVC diameter (2b).

The ultrasound imaging in B-mode was evaluated to verify true axial view for IJV and SCV, as well as the position of BCV confirmation, which required identifying the junction between internal jugular vein and subclavian vein (Fig. 1b). Then, the image was converted to M-mode. A diameter of the vein during end inspiration and end expiration were recorded in centimeters. To obtain a BCV diameter, we measured angle and length between wall of the vessel and manually calculated BCV diameter using a trigonometry formula (sine angle). (Fig. 2a, 2b).

We calculated the respiratory variation of the study vessels with 3 following methods:

1. Distensibility index for IJV (IJV-DI) = (maximum diameter-minimum diameter) x100/minimum diameter
2. Collapsibility index for SCV (SCV-CI) = (maximum diameter-minimum diameter) x100/maximum diameter
3. Variability index for IJV (IJV-VI), variability index for SCV (SCV-VI), and variability index for IJV (BCV-VI) = (maximum diameter-minimum diameter) x100/mean diameter

Arterial blood pressure was monitored via radial arterial catheter connected with pressure transducer and the pulse pressure variation (PPV) values were automatically calculated and were displayed on monitor screen (Philips Intellivue Philips, USA).

Our primary outcome is to evaluate the correlation between PPV and ultrasound-derived parameters namely IJV-DI, IJV-VI, SCV-CI, SCV-VI, and BCV-VI. Secondary outcomes are to assess the test performance of each ultrasound variable that show correlation to PPV according to the primary outcome, and to find the optimum cut-off values of these parameters to discriminate patient with PPV>13 from patients with PPV<10.

Statistical analysis

Based on a previous study [5], the correlation of the change in cardiac output after fluid bolus and the change in SCV diameter during respiratory cycle was r = 0.84, with α of 0.05. A sample size of 40 patients was estimated.

Continuous variables were expressed in terms of mean (±standard deviation) or median (interquartile range) and categorical variables were expressed in terms of frequency (n, %). The correlation between PPV and ultrasound-derived variables such as IJV-DI, IJV-VI, SCV-CI, SCV-VI, and BCV-VI were analyzed with Spearman's rho Correlation (r). For secondary outcome analysis, patients were divided into two groups based on their PPV values: patients with a PPV value more than 13 and those with PPV less than 10. Due to gray zone of PPV [2,6], we did not include individuals with a PPV score of 10% to 13% into secondary outcome analysis. The PPV values and ultrasound-derived variables between two groups (PPV <10 vs PPV >13) were compared using Mann-Whitney U test. Receiver operating characteristic (ROC) curve analysis was used to determine the test performance, sensitivity, specificity, and the Youden index was used to identify the optimum cut-off values of ultrasound-derived parameters in order to discriminate patients with PPV >13 from patients with PPV <10. A P-value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS, Version 23.0.

RESULTS

A total of 44 patients were included in this study and were analyzed for primary outcome. Of these, 40 patients were included in secondary outcome analysis. Baseline characteristics and hemodynamic parameters were presented in Table 1. The majority of the patients were males with average age of 63 years, were admitted to the medical ICU. The average APACHE II score was 17.2. Average mean arterial pressure (mean ±SD) was 75.93 ±17.09 mmHg. If any patients had ultrasound-derived parameter results from both left and right side of the vessels, we used mean value of both sides for primary and secondary outcomes analysis.

Spearman's rho correlation between the PPV values and the ultrasound-derived parameters (IJV-DI, IJV-VI, SCV-CI, SCV-VI, and BCV-VI) were presented in Table 2. There were strong correlations between PPV and IJV-DI (r=0.652, p<0.001), IJV-VI (r=0.655, p<0.001), SCV-CI (r=0.618, p<0.001) and SCV-VI (r=0.601, p<0.001). The correlation between PPV and BCV-CI were moderate (r=0.531, p 0.008).

A total of 40 patients included into secondary analysis, there were 17 patients (42.5%) had PPV values higher than 13 (PPV >13 group), and 23 patients (52.5%) had PPV values less than 10 (PPV <10 group). Median of IJV-DI, IJV-VI, SCV-CI, SCV-VI and BCV-VI in PPV >13 group were all significantly higher than in PPV <10 group (Table 3).

Area under the ROC curve were analyzed. All ultrasound parameters were proper for discrimination between PPV >13 group and PPV <10 group with AUC 0.983 for IJV-DI and IJV-VI, AUC 0.928 for SCV-CI and SCV-VI, and AUC 0.826 for BCV-VI (Fig. 3). An optimal cut-off values to distinguish PPV >13 group from PPV <10 group were ≥16.19% for IJV-DI (sensitivity 92%, specificity 96%), ≥14.98% for IJV-VI (sensitivity of 92%, specificity of 96%), ≥9.74% for SCV-CI (sensitivity of 93%, specificity of 91%), ≥12.33% for SCV-VI (sensitivity of 87%, specificity of 100%), and ≥13.71% for BCV-VI (sensitivity of 73%, specificity of 100%).

Table 1. Baseline characteristics.

	Total (N=44)
Age (years)*	63.52 ± 16.84
Study site	
Medical ICU, n (%)	32 (72.7)
Surgical ICU, n (%)	12 (27.3)
Sex	
Male, n (%)	31 (70.5)
Female, n (%)	13 (29.5)
Height (cm)*	163.93 ± 7.42
Actual body weight (kg)*	62.62 ± 12.8
Body mass index (kg/m^2)*	23.27 ± 4.16
APACHE II score	17.21 ± 6.48
Co-morbidity, n (%)	
None	11 (25)
Diabetes mellitus	14 (31.8)
Hypertension	17 (38.6)
Chronic kidney disease	6 (13.6)
Coronary artery disease	7 (15.9)
Other	22 (54.5)
Respiratory rate (per minute)+	17 (14-19)
Heart rate (per minute)*	97.18 ± 19.02
Systolic blood pressure (mmHg)*	119.55 ± 22.35
Diastolic blood pressure (mmHg)*	60.18 ± 11.24
Mean arterial pressure (mmHg)*	75.93 ± 17.09
Norepinephrine dose (mcg/kg/min)*	0.26 ± 0.34
Tidal volume/predicted body weight (ml/kg)*	9.4 ± 1.52
Positive end expiratory pressure (cmH_2O)$^+$	5 (5-7)
Lactate (mmol/L)*	3.73 ± 3.4

*mean ± SD; + median (IQR)
ICU, intensive care unit; APACHE II, Acute Physiology and Chronic Health Evaluation II; RASS, Richmond Agitation Sedation Scale;

Table 2. Spearman's rho Correlation between PPV and ultrasound-derived parameters.

	n	r	p-value
IJV-DI	40	0.652	<0.001*
IJV-VI	40	0.655	<0.001*
SCV-CI	40	0.618	<0.001*
SCV-VI	40	0.626	<0.001*
BCV-VI	24	0.531	0.008*

IJV-DI, internal jugular vein distensibility index; IJV-VI, internal jugular vein variability index; SCV-CI, subclavian vein collapsibility index; SCV-VI, subclavian vein variability index; BCV-VI, brachiocephalic vein variability index

Table 3. Median (interquartile range) of PPV and ultrasonographic parameters compare between PPV<10 group and PPV>13 group.

	PPV <10	PPV >13	p-value
PPV (%)	5 (4-6)	17 (16,21)	<0.001*
IJV-DI (%)	7.69 (3.45-10.29)	24.62 (18.31-39.52)	<0.001*
IJV-VI (%)	7.41 (3.37-9.76)	27.59 (16.67-30.77)	<0.001*
SCV-CI (%)	5.77 (4.85-6.97)	15.38 (12.51-18.76)	<0.001*
SCV-VI (%)	6.11 (4.99-6.67)	17.40 (12.87-19.35)	<0.001*
BCV-VI (%)	5.88 (4.15-9.92)	20.47 (12.05-27.34)	0.008*

PPV, pulse pressure variation; IJV-DI, internal jugular vein distensibility index; IJV-VI, internal jugular vein variability index; SCV-CI, subclavian vein collapsibility index; SCV-VI, subclavian vein variability index; BCV-VI, brachiocephalic vein variability index

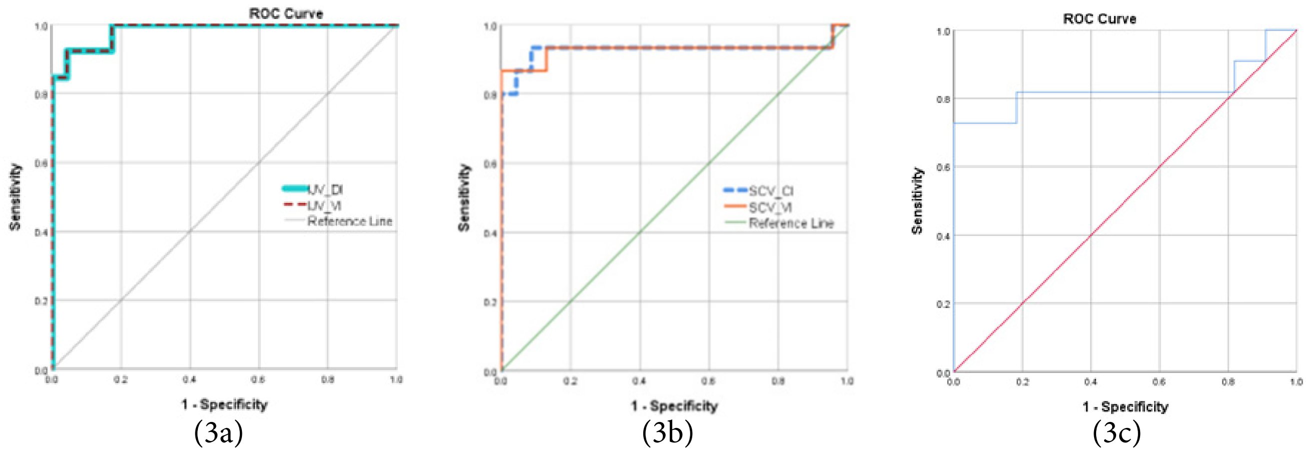

Figure 3. ROC curve of IJV-DI and IJV-VI (3a), SCV-CI and SCV-VI (3b), and BCV-VI (3c)

DISCUSSION

Our study demonstrated the correlation between PPV and respiratory variation in diameter of IJV, SCV, and BCV. Furthermore, we discovered that IJV-DI, IJV-VI, SCV-CI, SCV-VI and BCV-VI have high sensitivity and sensitivity in distinguishing patients with a PPV value greater than 13 from patients with PPV value less than 10. Meta-analysis [6,7] showed ability to predict fluid-responsiveness of PPV with satisfied accuracy. So, our finding implied that these two ultrasound-derived parameters may be used as dynamic parameter for evaluate of fluid-responsiveness, especially in limited resource or in patient whose IVC cannot be assessed.

Our patients were breathing in assisted control mode of mechanical ventilation. To ensure that patient breath without any respiratory effort, before enrollment, we assessed flow-time waveform on ventilator that show smooth decelerating inspiratory flow wave, we also physically examined patients who did not show sign of respiratory distress include nasal flaring and did not using accessory muscle. Our average MAP result was about 76 mmHg, which seem higher than expected in hemodynamic instability patients. Because definition of instability hemodynamic of our study not depend on only MAP and some patient received vasopressor during the examination.

Prior to enrolment, our patients were breathing in an assisted control mode of mechanical ventilation. Assessment of flow-time waveform on ventilator that show smooth decelerating inspiratory flow wave was ensured. And clinical examination to determine the absence of signs of respiratory distress such as nasal flaring or using accessory muscle were confirmed to ensure that the patient breathes without exerting. If IJV collapse was found on inspiratory phase during the examination, active breathing with respiratory effort was suspected, and this patient was excluded. We did not use any neuromuscular blocking agent during study, patient was given only sedative agent.

We found certain challenges during ultrasound examination such as anatomical limitation in assessing the brachiocephalic vein via supraclavicular approach. Our institute usually inserted central venous catheter via IJV as a first choice in critically ill patient. So many of ipsilateral BCV in the same patients had to be excluded from our study.

Guarracino et al. [8] reported IJV distensibility >18% predicted increase cardiac index ≥15% with sensitivity of 80% and specificity of 95%. This result is comparable to our study that found IJV-DI ≥16.19% discriminated between patients with PPV >13 from patients with PPV <10. Recent study of SCV variation by Jouffroy et al. [9] reported interchangeability between PPV and respiratory variation of SCV (ΔSCV) in mechanically ventilated, kidney transplant patients in operating room. A bias value was 1.6% (level of agreement -4% to 8%). The agreement between ΔSCV >13% and PPV >13% was 100%. This research supported our findings, showing a strong correlation between PPV and both SCV-CI and SCV-VI.

There are limitations in our research. First, we did not use fluid loading and cardiac output monitoring to determine fluid responsiveness because we did not want to interfere an attending physician treatment and we did not routinely use cardiac output monitoring in every shock patient in daily practice. Additionally, our primary outcome was to find the correlation between PPV and ultrasound-derived parameters. As previously stated, PPV is a good predictor for fluid responsiveness if we used regarding its limitation. Second, our measurement was performed by one physician who obtained short course in point-of care ultrasound and partially supervised by a certified radiologists in our institutions, we did not evaluate interobserver agreement that need to be investigated in the further. Third, we did not include an arrhythmic patient into our study because of PPV limitation. As a result, the study did not look into the benefit of ultrasound-derived dynamic parameters on arrhythmic patients. Fourth, a disadvantage of ultrasonographic measurement is an operator dependent technique. Finally, we did not blind PPV result during the examination. We recorded PPV just before the ultrasound measurement was performed. This study's findings may not be applicable to all critically ill mechanically ventilated patients. As mention above, an external validity of these technique has to be confirmed. A larger study performed by many physicians need to be investigated further.

CONCLUSION

In critically ill patients, all ultrasound-derived measures such as IJV-DI, IJV-VI, SCV-CI, SCV-VI, and BCV-VI revealed significant correlation with PPV value. The IJV-DI, IJV-VI, SCV-CI, SCV-VI and BCV-VI analysis demonstrated proper cut-off values for separating patients with PPV>13 from those with PPV<10 as 16.19%, 14.98 %, 9.74%, 12.33% and 13.71%, respectively.

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AUTHORS' CONTRIBUTIONS

(I) Conceptualization: N. Phancharoenkit, P. Fuengfoo; (II) Data curation: N. Phancharoenkit; (III) Formal analysis: N. Phancharoenkit, P. Fuengfoo; (IV) Funding acquisition: N. Phancharoenkit; (V) Methodology: N. Phancharoenkit, P. Fuengfoo; (VI) Project administration: N. Phancharoenkit; (VII) Visualization: N. Phancharoenkit; (VIII) Writing – original draft: N. Phancharoenkit, P. Fuengfoo; (IX) Writing – review & editing: N. Phancharoenkit, P. Fuengfoo.

SUPPLEMENTARY MATERIALS

None

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