RESEARCH

Comparison of Inferior Vena Cava Distensibility Index and Pulse Pressure Variation as Predictors of Fluid Responsiveness in Sepsis Patients at the ICU

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ABSTRACT

Background: Sepsis is a major global health challenge with an estimated 49 million incident cases and 11 million deaths each year, which requires appropriate fluid management to improve patient prognosis. This study aims to compare the effectiveness of the inferior vena cava distensibility index (IVC-DI) and pulse pressure variation (PPV) as predictors of fluid responsiveness in sepsis patients in the intensive care unit (ICU).

Methods: This study used an experimental design with a sample of 36 sepsis patients selected through consecutive sampling. Fluid administration of 500 ml RL was carried out for 15 minutes, followed by measurement of IVC-DI and PPV, and evaluation of an increase in stroke volume (SV) > 15% as an indicator of fluid responsiveness.

Results: The study showed that PPV had a sensitivity of 93% and specificity of 90%, with a positive predictive value of 87.5% and a negative predictive value (NPV) of 95%. The overall accuracy of PPV was 91.6%. PPV showed a very strong correlation with SV increase > 15% ($r = 0.832$, $p < 0.001$). On the other hand, IVC-DI had a sensitivity of 80% and specificity of 71%, with a positive predictive value of 66% and a NPV of 83%. The overall accuracy of the IVC-DI was 75%. The IVC-DI showed moderate correlation with SV increase > 15% ($r = 0.507$, $p = 0.002$). Inter-observer agreement in IVC-DI measurements also showed excellent results with a Kappa value of 1.00, indicating perfect agreement. From the results of this study, PPV proved to be more accurate in predicting fluid responsiveness compared to IVC-DI in sepsis patients in the ICU. These two methods, although equally useful, showed different levels of effectiveness in this clinical context.

Conclusion: PPV showed better performance than IVC-DI in predicting fluid responsiveness in mechanically ventilated sepsis patients in the ICU. PPV demonstrated higher accuracy, sensitivity, specificity, and a stronger correlation with SV improvement, indicating that PPV may serve as a more reliable predictor in this clinical setting.

Keywords: fluid responsiveness; inferior vena cava distensibility index; intensive care unit; pulse pressure variation; sepsis

INTRODUCTION

Sepsis is a life-threatening pathological condition resulting from an exaggerated immune response to infection, which can cause organ damage and be fatal if left untreated. With 49 million cases and 11 million deaths each year, sepsis often requires fluid and vasoconstrictor therapy, especially if it progresses to septic shock, which can be fatal if not treated appropriately.[1] Appropriate fluid therapy management in sepsis patients involves careful clinical and hemodynamic assessment to determine fluid requirements, fluid type, and patient response. The use of monitoring tools, such as echocardiography and central venous pressure monitoring, can help minimize the risk of complications and increase the chances of a successful recovery.[2]

Pulse pressure variation (PPV) is an effective dynamic parameter for assessing fluid responsiveness in critically ill patients, particularly those undergoing mechanical ventilation. By utilizing physiological changes during the respiratory cycle, PPV provides a real-time assessment of the patient's volume status, more accurate than static parameters such as central venous pressure. In a meta-analysis conducted by Yang et al in 2013, PPV demonstrated high sensitivity and specificity in predicting response to therapy.[3] As PPV is affected by the respiratory cycle, accurate results are highly dependent on consistent tidal volumes. In cases where patients breathe spontaneously or are ventilated with low tidal volumes <6- 8 ml/kg predicted body weight, the accuracy of PPV may be reduced, especially in patients undergoing mechanical ventilation. Although the artery line monitoring procedure is invasive, with proper training and equipment, this technique can be applied even in type C hospitals for rapid and appropriate decision-making in the intensive care unit (ICU).

Measurement of the inferior vena cava (IVC) diameter by ultrasonography is a rapid and effective non-invasive method to assess intravascular volume as well as response to fluid therapy in critical patients. This technique has the advantage of having minimal risk of complications compared to invasive methods such as pulmonary artery catheterization and can be performed directly at the patient's bedside, making it a practical tool in hemodynamic evaluation.[4,5] Previous studies have identified that variability in IVC diameter is comparable to variation in pulse pressure in predicting response to fluid therapy.[6,7]

Although IVC measurements have advantages, their accuracy can be affected by technical factors, individual anatomical variations, and operator dependency. The use of ultrasonography for IVC measurement can also be expensive, require specialized skills, and have limited availability, especially in remote areas with limited resources. In addition, special skills and training are required to maximize the results of these measurements.

This study aims to determine and analyze the comparison of IVC diameter and PPV as a Predictor of Fluid Responsiveness in Sepsis Patients in the ICU.

METHOD

This study used an experimental design with a total sample of 36 sepsis patients. The research samples were taken from ICU patients at Dr. Kariadi Hospital who met the inclusion and exclusion criteria in September 2023. Inclusion criteria: (1) aged 18 - 60 years; (2) body mass index 18.5 - 24.9; (3) patients diagnosed with sepsis according to the International

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Consensus Definitions for Sepsis criteria; (4) patients using a mechanical ventilator in ICU; (5) regular sinus heart rhythm with heart rate ≥50x/min. Exclusion criteria: (1) the patient's family refused the study; (2) patients have a history of hepatic disorders; (3) patients have a history of heart failure or heart valve disorders; (4) patients have a history of thoracic or abdominal surgery with incisions as high as the processus xiphoideus; (5) patients with increased intra-abdominal pressure.

Samples were taken by the consecutive sampling method based on patient arrival at Dr. Kariadi Hospital, Semarang. Patients who met the research criteria were used as research subjects.

The families of the study participants were informed about the background of the study, the purpose of the study, and the entire series of research that would be undergone. Then, the consent of the research participants to participate in the study was sought. All research samples that meet the criteria will be set up in full control mode ventilator using lung protective strategy with a target tidal volume of 6 ml/kg (predicted body weight), then an artery line is installed in the radial artery, and PPV monitoring is carried out IVC-DI examination using non-invasive ultrasound, and echo hemodynamic examination is carried out to measure SV.

The patient was then given 500 cc of fluid loading for 15 minutes. After fluid administration, SV was monitored using non-invasive ultrasound; if there was an increase of >15%, it was classified as fluid responsive. Recording via non-invasive ultrasound was done alternately with the same steps by 2 operators to reduce bias. Data were recorded and then written in a report format.

RESULTS

This study was an experimental study conducted on 36 sepsis patients admitted to the ICU who met the inclusion criteria.

Characteristics of the study subjects, including age, weight, and height variables, with statistics such as minimum, maximum, mean, and standard deviation values (Table 1). The minimum age was 20 years, the maximum was 59 years, with a mean of 46.11 years, and the standard deviation was 11.32 years. Subject weight ranged from 40.11 kg to 94 kg, with a mean of 51.22 kg and a standard deviation of 23.33 kg. The subject's height ranged from 146 cm - 176 cm, with an average of 160 cm and a standard deviation of 31.80 cm, positive end-expiratory pressure (PEEP) used in the ventilator had a maximum value of 12 and a minimum value of 5, with an average of 7.31 and a standard deviation of 2.41 from the normality test, it was found that the overall distribution was normal.

The characteristics of the study subjects are presented in the form of numerical data. First, in terms of gender, there were 27 female subjects (75%) and 9 male subjects (25%). Then, in terms of the type of disease suffered by the research subjects, the data were divided into several categories. Intracranial tumors were the most common type of disease among the subjects, with 10 subjects (28%) suffering from this condition. Next, gastrointestinal diseases and cardiovascular diseases were each found in 5 subjects (14%), while respiratory and postoperative diseases were each found in 4 subjects (11%). Infectious diseases were the least common, found in only 2 subjects (5%). From the normality test, it was found that the overall distribution was normal. (Table 2)

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The PPV had a sensitivity of 93%, meaning it was able to identify 93% of patients who would respond with an increase in cardiac output or stroke volume (SV) > 15% after fluid administration. In addition, PPV had a specificity of 90%, indicating a strong ability to identify patients who would not respond with an increase in SV > 15%.

Of the 36 patients studied, 15 had an increase in SV > 15%, and PPV correctly detected 14 of these patients as fluid responsive (true positives). There was only 1 patient who had an increase in SV > 15% but was not detected by PPV (false negative). On the other hand, of the patients who did not have an increase in SV > 15%, all of them were correctly identified by PPV as fluid non-responsive (true negatives), with only 2 patients erroneously identified as responsive (false positives). PPV and SV < 15% showed a very strong correlation ($r = .832$, $p < .001$). This very close relationship between PPV and SV < 15% indicates that they may be measuring very similar aspects of fluid responsiveness in sepsis patients. (Table 3)

IVC-DI had a sensitivity of 80%, meaning it was able to identify 80% of patients who would respond with an increase in cardiac output or SV > 15% after fluid administration, and a specificity of 71%, indicating a strong ability to identify patients who would not respond with an increase in SV > 15%. The positive predictive value (PPV) was 87.5%, calculated from 14 true positive results out of a total of 16 positive results (14 true positives and 2 false positives). Furthermore, the negative predictive value (NPV) reached 95%, resulting from 19 correct negative results out of a total of 20 negative results (19 correct negatives and 1 false negative). The overall accuracy of the test was 91.6%, which was obtained from the sum of both positive and negative correct results (15 true positives and 7 true negatives) divided by the total number of cases tested, which was 27. These metrics demonstrate the effectiveness of the test in identifying SV conditions that are elevated above 15%. Of the 36 patients studied, 15 had SV elevation > 15%, and PPV correctly detected 12 of these patients as fluid-responsive (true positives). Only 3 patients had an increase in SV > 15%, but were not detected by PPV (false negatives). On the other hand, of the 21 patients who did not have an increase in SV > 15%, 15 of them were correctly identified by IVC-DI as fluid non-responsive (true negatives), with only 6 patients erroneously identified as responsive (false positives). IVC-DI and SV < 15% also showed a moderate correlation ($r = .507$, $p = .002$), meaning that the two have a correlation, but not as strong as the relationship between PPV and SV < 15%. (Table 4)

The calculated Kappa value is 1.00, which indicates perfect agreement. This is an indication that the assessment method used by both observers is highly consistent and reliable. (Table 5)

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Table 1. Numerical data of research subject characteristics

Variable	Minimum	Maximum	Mean	Std Deviation	Normality Test
Age (year)	20.00	59.00	46.11	11.32	0.13
Weight (kg)	40.11	94.00	51.22	23.33	0.22
Height (cm)	146.00	176.00	160.00	31.80	0.28
PEEP	5.00	12.00	7.31	2.14	0.07

P>0.05 using the Saphiro-Wilk test

Table 2. Categorical data of research subject characteristics

Variable (n=36)		n	%	Normality Test
Gender	Man	9	25%	0.31
	Woman	27	75%	
Type of Disease	Intracranial Tumor	10	28%	0.18
	Gastrointestinal	5	14%	
	Cardiovascular	4	11%	
	Respiratory	5	14%	
	Postoperative	4	11%	
	Infection	2	5%	
PPV	Positive	16		0.11*
	Negative	20		
IVC-DI	Positive	18		0.089*
	Negative	18		
SV > 15% Improvement	Positive	15		0.31*
	Negative	21		

P>0.05 using the Shapiro-Wilk test

Table 3. PPV data against increased SV > 15%

PPV	SV > 15% Improvement +	SV > 15% Improvement -	Total	P*	Pearson Correlation (r)
+	14	2	16	0.01*	0.83
-	1	19	20		

*Significant with Pearson correlation test, p<0.05

Table 4. IVC-DI data against SV > 15% improvement

IVC-DI	SV > 15% Improvement +	SV > 15% Improvement -	Total	P*	Pearson Correlation (r)
+	12	6	18	0.02*	0.507
-	3	15	18		

*Significant with Pearson correlation test, p<0.05

Table 5. Kappa analysis of 2 observers on IVC-DI

IVC-DI		Observer 1 Positive	Observer 1 Negative	Value Kappa
Observer 2	Positive	18	0	1.00
	Negative	0	18	

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DISCUSSION

Based on the results of an experimental study conducted on 36 sepsis patients admitted to the ICU, it was found that PPV and IVC-DI are highly accurate predictors for assessing fluid response in patients with sepsis. The findings showed sensitivity and specificity values in line with previous studies and confirmed the validity of both parameters in a clinical context. In particular, PPV and IVC-DI show significant potential as hemodynamic assessment tools, providing critical insight into fluid therapy decision-making in this complex patient population.

PPV showed a sensitivity of 93% and specificity of 90%, with a very strong correlation to SV improvement >15% ($r = 0.832$, $p < 0.001$). This suggests that PPV is a highly effective tool to evaluate fluid responsiveness in mechanically ventilated patients. The high sensitivity means that PPV rarely gives false negative results, making it reliable for identifying patients who will respond to fluid administration. From 2006 to 2013, studies have shown that PPV is effective as a predictive tool for fluid management in patients. This is in line with a meta-analysis study conducted by Yang et al, which showed the relationship between predicted PPV measurements and fluid response showed significant variation in sensitivity and specificity based on the methods and tools used.[8] Charron and Monnet (2006) found high sensitivity (89% and 88%) and moderate specificity (83% and 93%) with waveform analysis using computer software.[9] This improvement was continued with the Feissel study in 2007, which achieved 100% sensitivity and 94% specificity.[10] The accuracy of PPV is supported by dynamic monitoring of pulse pressure during the breathing cycle, which provides a real-time evaluation of the patient's volemic status. This is particularly relevant in critical situations, where quick and precise decisions are required.[6,7]

As for the effectiveness of IVC-DI, the results showed 80% sensitivity and 71% specificity, with a moderate correlation to SV improvement ($r = 0.507$, $p = 0.002$). Despite its benefits, IVC-DI has lower accuracy than PPV. Factors such as variations in patient anatomy and operator dependency may affect the results of IVC-DI measurements.

Barbier et al. (2004) found that IVC-DI with a threshold of 18% could differentiate fluid responsiveness with 90% sensitivity and specificity, as well as a strong correlation ($r=0.9$) to improved cardiac index after volume expansion.[11] Studies by Zhang et al. and Feissel et al. (2004) support these findings, with up to 93% sensitivity and 92% specificity, especially in mechanically ventilated patients.[6,12] However, a review by Cardozo et al. in spontaneously breathing patients showed moderate accuracy with 63% sensitivity and 83% specificity, as well as a high risk of bias across studies. This suggests that IVC-DI is effective in certain situations, but has limitations when used in isolation.[13]

PPV is more accurate than IVC-DI as a predictor of fluid responsiveness in sepsis patients receiving mechanical ventilation. PPV reflects both pulmonary blood volume changes and right ventricular SV, providing a more comprehensive picture of total cardiac volume changes during the respiratory cycle.[14] In contrast, IVC-DI is more limited as it only reflects right ventricular volume changes related to its preload reserve, which is influenced by

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factors such as intra-abdominal pressure and pulmonary vascular resistance. The accuracy of IVC-DI also depends on the skill of the operator and the condition of the patient. For example, increased intra-abdominal pressure in patients with severe sepsis may reduce the accuracy of IVC-DI measurements as the pressure around the IVC reduces the volume of blood filling during the inspiratory phase of mechanical ventilation. This results in a decrease in the maximum IVC value (IVDmax) and a lower-than-actual IVC-DI values that are lower than actual. Nonetheless, these two parameters remain useful and can be used complementarily to improve the accuracy of fluid response prediction under complex hemodynamic conditions.[14,15]

As a developmental step, this study can be expanded by involving more diverse subjects and larger numbers to increase the validity of the findings. In addition, further research can utilize more sophisticated cardiac output monitoring technology, such as pulse indicator continuous cardiac output (PiCCO) or pediatric respiratory assessment measure (PRAM), to obtain more accurate and continuous measurements. In-depth research on extravascular fluid status in sepsis patients also needs to be conducted to understand fluid requirements more comprehensively and provide more optimal fluid management guidelines in sepsis patients.

CONCLUSION

This study shows that PPV has higher accuracy than the inferior vena cava distensibility index (IVC-DI) in predicting fluid responsiveness in sepsis patients receiving mechanical ventilation. PPV is more representative as it reflects the dynamics of pulmonary blood volume and right ventricular SV during the respiratory cycle, whereas IVC-DI only reflects changes in right ventricular volume. Although IVC-DI is useful, the accuracy of its measurement is more influenced by the patient's condition and the skill of the operator. Overall, these two parameters can be used complementarily to improve the accuracy of fluid response prediction, aiding better clinical decision-making in fluid management in sepsis patients with complex hemodynamic conditions.

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