ORIGINAL ARTICLE

Determining the Merit of Inferior Vena Cava Distensibility Index in The Estimation of Fluid Responsiveness in Ventilated Septic Patient in Intensive Care Unit

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ABSTRACT

Introduction: There is no single haemodynamic parameters either static central venous pressure (CVP) or dynamic stroke volume variation, inferior vena cava distensibility index (SVV,IVCd) that can be used precisely to assess fluid responsiveness. It must be performed concurrently with clinical assessment. Therefore, this study was conducted to determine the correlation between these 3 parameters. **Methods:** This was a cross sectional non-interventional study conducted in intensive care unit. Each patient who fulfilled the criteria will have their CVP, SVV and IVCd measured instantaneously. Analysis of correlation was done using bivariate (Pearson) correlation, while agreement between SVV and IVCd was assessed using Cohen's Kappa analysis. **Results:** A total of 37 patients were enrolled in this study. 70.3% were males and 29.7% were females. Mean age was 59.7 ± 13.3. Mean APACHE score was 24.1 ± 6.1. IVCd had significant positive correlation with SVV (r = 0.391, p = 0.017). Agreement between IVCd and SVV was 0.329 (0.95 CI = 0.0174 – 0.6412; p = 0.033). There was non-significant negative correlation between IVCd with CVP and SVV with CVP with r = -0.155 (p=0.359) and r = -0.068 (p= 0.691) respectively. **Conclusion:** There is only fair correlation between IVCd and SVV in determining fluid responsiveness. However, CVP does not correlate to both SVV and IVCd. Neither one of them is a good method in assessing fluid responsiveness during standard care in our centre. Therefore, the usage of above methods needs to combine with clinical parameters to yield better result.

Keywords: Inferior vena cava, Inferior vena cava distensibility index, Stroke volume variation, Central venous pressure, Fluid responsiveness

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INTRODUCTION

Fluid resuscitation and fluid challenge remains the first line modality in the management of circulatory shock, including septic shock. Even the latest sepsis guideline recommended fluid resuscitation with at least 30ml/kg of IV crystalloid within the first 3 hours (1). Fluid challenge is intended mainly to increase cardiac output (CO) and consequently to improve tissue perfusion and oxygen delivery. However, in most critically ill patients where there is an increase in capillary permeability, there is a narrow therapeutic window for fluid resuscitation, beyond which, it might cause more harm than good. Excessive fluid challenge may result in tissue oedema, which will further hinder tissue perfusion. It can also lead to volume overload, pulmonary oedema, bowel oedema, other organ impairment, and even mortality. Clinical studies showed that only 50% of critically ill patients responded to fluid challenge i.e. is fluid responsive (2–3). Thus, it is imperative for clinicians to identify fluid responsive patient to avoid unnecessary fluid challenge. Classically, static parameters such as pulmonary artery occlusion pressure (PAOP) and central venous pressure (CVP) had been the common practice in assessing fluid responsiveness (4–5). However, a lot of recent studies have disputed its reliability (5–8).

Thermodilution method using pulmonary artery catheter (PAC) is still considered as the gold standard method in cardiac output monitoring (9). Nevertheless, several dynamic indices which were minimally invasive had shown significant accuracy in assessing fluid responsiveness and gaining more popularity (7–10). Dynamic indices are based on heart-lung interaction during respiration (11–12.) Examples of these parameters include systolic pressure variation (SPV),

pulse pressure variation, stroke volume variation (SVV), IVC distensibility index (IVCd), IVC variability index, plethyhsmography variation index (PVI), passive leg raising (PLR) test, and respiratory changes in aortic blood flow velocity (13–14). They range from non-invasive to minimally invasive, as opposed to PAC insertion which can lead to complications such as infection, pulmonary artery rupture, arythmia during insertion and thrombosis, especially if performed by untrained clinicians (15–17).

Measurement of SVV by using minimally invasive cardiac output monitoring, eg PiCCO (Pulse Medical System, Munich Germany), LiDCO (LiDCO Group PLC, London, England) and Flotrac sensor (Edwards Lifesciences, Irvine, Ca, USA) has gain wide recognition. Many studies have validated the sensitivity and specificity of these modalities in assessing fluid responsiveness (10,18–20). The latest flotrac system automatically updates the parameters every 20 seconds and allows for contiuous monitoring of cardiac output and SVV and the results are comparable to other modalities (21–23). However, Flotrac sensors are disposable and each sensor is quite costly,(24) hence the need for another option which is more easily accessible and cost effective.

IVC distensibility index has good predictive value of fluid responsiveness with sensitivity and specificity of >90% (25–26). It is non-invasive as it utilizes transthoracic echocardiography or abdominal ultrasound and hence is a valuable tool in patient with coagulopathy in whom invasive technique may risk bleeding and other complication. It can also be performed by the bedside and does not require extra adjuncts apart from portable ultrasound and a suitable ultrasound probe.

Even though there are numerous studies that validated the use of SVV and respiratory variation of IVC in assessing fluid responsiveness, studies comparing IVC and SVV is somewhat lacking. The aim of this study is to determine the correlation between of IVCd and SVV in the assessment of fluid responsiveness in mechanically ventilated septic patient and to study the relevance of CVP compared to these two dynamic indices.

MATERIALS AND METHODS

Study design and respondents
This was a non-interventional cross-sectional study conducted in the Intensive Care Unit (ICU) of Hospital Universiti Sains Malaysia (HUSM) between June 2016 to May 2018. It was approved by the Research Ethics Committee (Human) (JEPeM) of Universiti Sains Malaysia (JEPeM Code: USM/JEPeM/16040154). Patients were enrolled after written consent was obtained from their next of kin.

A total of 37 patients who are more than 18 years old, in sepsis, sedated and mechanically ventilated with intra-arterial line and central venous line in situ were recruited for this study. An exclusion criteria includes presence of arrhythmia, heart failure or valvular heart disease as evidenced by echocardiography, unacceptable ultrasound finding, intraabdominal abnormality, pregnant lady and obesity.

Measurement
After enrolment, patient's demographic data such as vital signs, body weight, estimated height, age and sex were recorded. The diagnosis upon ICU admission, indication for ventilation, ventilator parameters such as peak airway pressure and positive end expiratory pressure (PEEP), tidal volume and fraction of inspired oxygen (FiO2) were taken and their APACHE score were calculated.

Prior to measurement of the parameters, it was ensured that patients were synchronized to ventilator with no spontaneous breathing present. Measurement of IVC was done first to ensure no bias in the reading, followed by CVP and SVV. A total of 3 readings were taken and the mean were taken as the final value. Apart from that, cardiac output (CO), systemic vascular resistant and systemic vascular resistant index were recorded as well.

IVC Measurement
IVC was assessed with the patient in semi recumbent position, subcostally, in a longitudinal axis. The portable bedside ultrasound from Samsung (model HM70A) with phase array probe was used with its probe put in longitudinal view with 16 cm depth. IVC diameter was measured 2cm from hepatic vein and 4 cm away from right atrium. The three values of inferior vena cava maximum (on inspiration) and minimum (on expiration) diameter were taken using M mode tracing. IVC distensibility index were calculated by subtracting maximum IVC diameter and minimum IVC diameter divided by minimum IVC diameter and expressed as percentage. IVCd of >18% is considered as fluid responsive based on study done by Barbier et al (25). The operator has had more than a year of experience in measuring the IVC and the reading was cross checked with the attending anaesthetist to ensure accuracy of the reading.

Stroke Volume Variation (SVV) Measurement
Stroke volume variation was measured by using FloTrac™ sensor connected to Vigileo™ monitor and the value was expressed as percentage. SVV was calculated automatically by the monitor and displayed on the screen as a continuous monitoring. Prior to the measurement, good waveform of the arterial line, absence of arrhythmia, sedation score of -3 to -4 and tidal volume were checked to ensure the accuracy and validity of the reading. SVV of >13% is taken as fluid responsive (27).

Central Venous Pressure (CVP) Measurement
Central venous pressure was measured with patient in

semi recumbent position, and transducer at phlebostaxis axis (fourth intercostals space intersects with midway between xiphoid and back).

CVP transduscer was zeroed (close to patient but open to air) before reading and the pressure used was 300mmHg (1cmH20=0.74mmHg). Three measurements of central venous pressure were taken at the end of expiration on each subject and the average calculated for the final value.

Statistical Analysis.
Using StatsToDo: Sample Size for Pearson's Correlation Coefficient Program,(28) with the expected correlation coefficient of 0.4, power 0.8 and probability of Type 1 error of 0.05 a sample size of 37 was calculated. Data entry and analysis were done using Statistical Package of Social Science (SPSS) version 24.0. Continuous variables were tested for normality of distribution. Descriptive analysis of categorical variable was expressed as frequency and percentage, while mean and standard deviation were used for numerical variables. The correlations between the IVCd, SVV and CVP were tested with Pearson correlation. Agreement between the IVCd and SVV was tested with Cohen's Kappa analysis.

RESULTS

Patient characteristic
In total, 37 mechanically ventilated septic patients were recruited in this study. The demographic data and clinical variables were reported in Table I.

Patient's mean age was 59.7 ± 13.3 with majority are male patients [26/37 (70.3%)], as opposed to 11/37

Table I: Patient Demographic and Clinical Variables

Variable	Value [N (%) or mean ± SD] N=37
Age (years)	59.7 ± 13.3
Gender	
Male	26 (70.3)
Female	11 (29.7)
Weight (kg)	71.5 ± 12.0
Height (cm)	165.7 ± 7.9
Diagnosis	
Hospital acquired pneumonia	14 (37.8)
Community acquired pneumonia	7 (18.9)
Soft tissue infection	8 (21.6)
Intraabdominal infection	5 (13.5)
Leptospirosis	1 (2.7)
Genitourinary infection	2 (5.4)
APACHE score	24.1 ± 6.1
PEEP	8.24 ±2.5
Tidal volume	
6 (ml/kg)	16 (43.2)
7 (ml/kg)	13 (35.1)
8 (ml/kg)	6 (16.2)
9 (ml/kg)	1 (2.7)
10 (ml/kg)	1 (2.7)

APACHE = acute physiology and chronic health evaluation, PEEP = positive end expiratory pressure

(9.7%) female patients. Average estimated weight and height was 71.5kg and 165.7cm respectively. Majority patients had hospital acquired pneumonia [14 (37.8%)], followed by community acquired pneumonia [7 (18.9%)], soft tissue infection [8 (21.6)], intraabdominal infection [5 (13.5)], leptospirosis [1(2.7%)] and genitourinary infection [1 (2.7%)] as diagnosis upon admitted to ICU. Mean APACHE score was 24.1 ± 6.1, and mean PEEP was 8.2 ± 2.5 mmHg. Most patient were ventilated with 6mls/kg tidal volume, 16/37 (43.2%), followed by 7ml/kg, 13/37 (35.1%), 8mls/kg, 6/37 (16.2%) and both 9 and 10 ml/kg are 1/37 (2.7%) respectively.

Patient haemodynamic variable were listed in Table II. Means for MAP, HR, C.O, SVR, SVRI and IVC was 73.6 ± 12.8, 98.5 ± 12.8, 5.9 ± 2.2, 1017.9 ± 383.8, 1800.2 ± 656.7, and 1.75 ± 4.42 respectively. Mean for IVCd was 20.0% ± 14.0, while SVV was 12.2% ± 7.2 and CVP was 7.76mmHg ± 5.372.

Table II: Patient Haemodynamic Variables

| Variable	Mean ± SD (N=37)
MAP (mmHg)	73.61 ± 12.8
HR (bpm)	98.49 ± 18.8
SVV (%)	12.209 ± 7.2
C.O (l/min)	5.876 ± 2.2
SVR (dyns/cm^5)	1017.89 ± 383.8
SVRI (dyns/cm^{5}m^2)	1800.22 ± 656.7
IVC (cm)	1.748 ± 0.4
IVCd (%)	20.011 ± 14.0
CVP (mmHg)	7.76 ± 5.4

MAP = mean arterial pressure; HR = heart rate; SVV = stroke volume variation; C.O = cardiac output; SVR = systemic vascular resistance; SVRI = systemic vascular resistance index; IVC = inferior vena cava; IVCd = inferior vena cava distensibility index; CVP = central venous pressure

### Comparison between IVCd, SVV and CVP
IVCd and SVV had significant, positive and fair correlation with r = 0.39 (p < 0.05; Figure 1). However, both SVV-CVP and IVCd- CVP showed no significant, negative and little correlation, with r = -0.068 (p = 0.69; Figure 2) and r= - 0.155 (p = 0.35; Figure 3) respectively. Summary of the results were recorded in Table III.
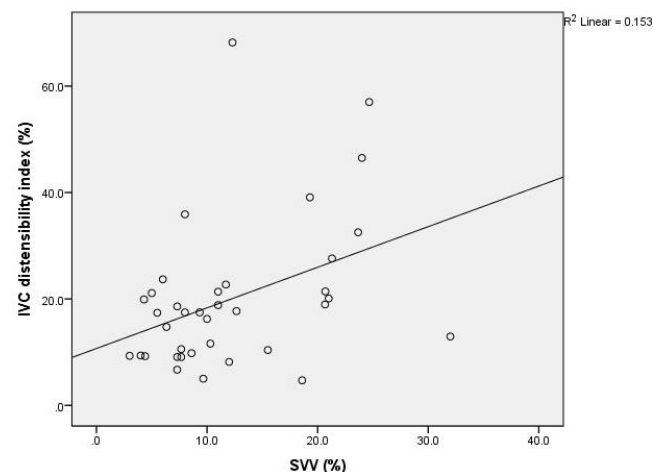
Figure 1: Relationship between inferior vena cava distensibiility (IVCd) index and stroke volume variation (SVV)
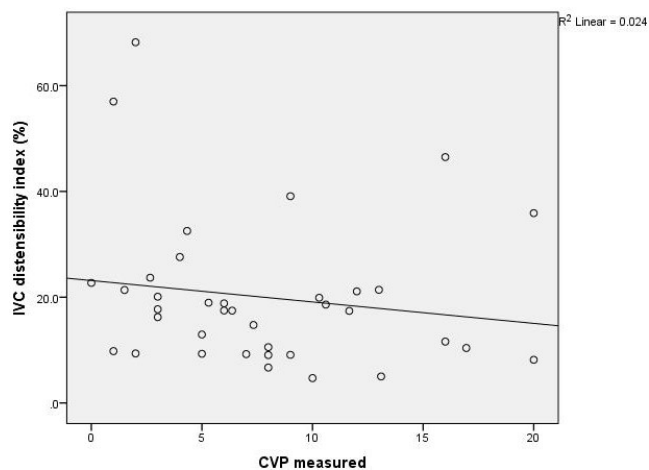
Figure 2: Relationship between inferior vena cava distensibiility (IVCd) index and central venous pressure (CVP)
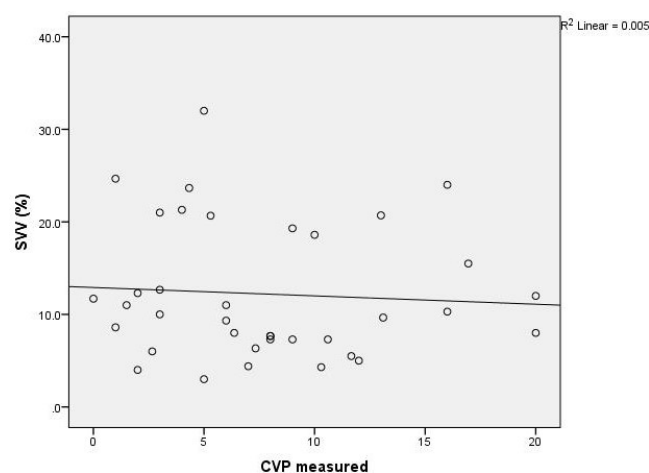
Figure 3: Relationship between stroke volume variation (SVV) and central venous pressure (CVP)

Table III: Correlation value of fluid status parameters

Variable	Pearson correlation	
	r	P
SVV vs IVCd	0.391	[a]0.017
CVP vs IVCd	-0.155	0.359
CVP vs SVV	-0.068	0.691

[a] correlation is significant at 0.05 level; SVV = stroke volume variation; IVCd = inferior vena cava distensibility index; CVP = central venous pressure.

Agreement between SVV and IVCd

The values for IVCd and SVV were further categorized into fluid responsive and non-fluid responsive with the cut-off value for IVCd and SVV was >18% (25) and >13% (29) respectively.

Degree of agreement between this categorical variable in determining fluid responsiveness was analysed using Cohen's Kappa (K) and the result were summarized in table IV. There was fair agreement between IVCd and SVV in determining fluid status, with K = 0.3293 (0.95 CI: 0.0174 – 0.6412), p<0.05.

Table IV: Degree of agreement between IVCd and SVV

		SVV (%)		Kappa (K)	P value	0.95 CI
		<13	≥13			
IVCd (%)	≤18	17	3	0.329	0.033	0.0174 – 0.6412
	>18	9	8			

[a]Unweighted Kappa was used; IVCd = Inferior Vena Cava Distensibility Index; SVV = Stroke Volume Variation; CI = confidence interval

DISCUSSION

Determining fluid responsiveness in critically ill patient remains a challenge to clinicians in intensive care setting. Though it has been determined that dynamic indices are the most reliable compared to static indices, most of the dynamic parameter are either not easily performed or not easily accessible. Furthermore, in ICU, there are a lot of factors that can influence the reading of dynamic parameters measured. Factors that can affect the IVCd are raised in intraabdominal pressure, right ventricular dysfunction and pulmonary hypertension (29). In ventilated patient, ventilator setting such as larger tidal volume more than 8ml/kg and higher PEEP may affect the intrathoracic pressure. It is believed that increased in trathoracic pressure will decrease the venous return, causing venous stasis. Venous stasis results in increasing inferior vena cava diameter during inspiration which in turn increase the IVCd. Increase in PEEP more than physiological value (3-5mmHg) may affect the CVP and IVCd. However, the PEEP is not transmitted straight to the central vein. Therefore, high PEEP value might affect the CVP and IVCd.

Inferior Vena Cava distensibility index (IVCd) is easily performed by bedside ultrasound by a trained anaesthesiologist or emergency physician. It requires short duration of training. However, its correlation with CVP parameters in our study is not great. This result was consistent with other study which reported (r = -0.315, p = 0.023) (29). The possible explanation is that a few parameters that might affect the CVP and IVCd reading unable to controlled and standardised to all the patient. This is because of our methodology which not going to intervene the patient management. The results are more accurate if all the patient can be paralysed with muscle relaxant prior to data collection. This can eliminate the variation in intrathoracic pressure. In this study, the mean of PEEP is 8 mmHg, average tidal of tidal volume is 6-7 ml/kg and the average level of sedation is RASS score -3. These values are in acceptable range which will not interfere with CVP and IVCd measurement.

Accuracy of SVV in determining fluid responsiveness has been well established, and numerous studies had confirmed the reliability of SVV measured with Flotrac transducer (Edwards Lifescience). It is minimally

invasive, only requiring presence of intra-arterial catheter which is then connected to the transducer. However, the transducers are quite costly and are only meant for single use, hence the need for a more cost effective and accessible alternative.

Our study showed fair correlation between IVCd and SVV (R= 0.391, p<0.05) in mechanically ventilated septic patient. Although there was no previous studies that directly measures the correlation between IVCd with SVV, the correlation between these parameters and other dynamic indices has been well established (5,22,31–33). A study by Delgado et al that compared IVC variation index and SVV (measured with Flotrac) in mechanically ventilated septic patient showed that IVC variation can be useful to assess fluid responsiveness (R^2 = 0.51 with receiver operating characteristic (ROC) curve of 0.81), however, he found that SVV failed to predict fluid responsiveness (R^2 = 0.12 with an ROC curve of 0.57) (34). However, this might be due to the fact that the previous study used the earlier version (Version 1.07) of Vigileo monitor while our current study used the latest version of flow trac transducer system (Version 4).

As per expected, there were no significant correlation between IVCd with CVP and SVV with CVP. This correlates well with other studies that shows poor predictive value of CVP (6,18,27,35). CVP is meant for pressure measurement of the right atrium. Fluid status was determined from how high or low the pressure is. Since it is a static measurement, CVP can be affected by a lot of factors eg PEEP, patient's cardiac status, pulmonary disease, and poor placement of the tip, to name a few. It is also an invasive procedure and might be relatively contraindicated in patients with coagulopathy, which is commonly seen in septic patient.

With regards to agreement between IVCd and SVV in determining fluid responsiveness, there was a fair degree of agreement for fluid responsiveness with IVCd and SVV cut-off point of >18% and ≥ 13% respectively. There were other cut-off points suggested by other studies, but IVCd of >18% was shown to have 90% sensitivity and specificity (25) and hence accepted as the reference point in this study. SVV ≥13% was taken as the reference point for this study based on the manufacturer's recommendation (30). There is a possibility that the degree of agreement might differ if other reference value is taken. Further studies should be done to determine the agreement between these parameters with other cut-off values.

This study shows that IVCd is not a good dynamic parameter of assessing fluid responsiveness in our standard care since it only gives a fair correlation. However, it can be added to other clinical and other dynamic indices to get a better assessment. It can be performed by the bedside, is non-invasive and does not require extra equipment apart from an ultrasound machine and a suitable probe. It can also be performed in patients with arrhythmia as opposed to SVV and PPV, and in patients with no lower limbs as opposed to passive leg rising. As it is non-invasive, it is also useful in coagulopathy patients, in which invasive procedures are relative contraindication.

However, it has several weaknesses as well. IVC assessment in patients with distended abdomen or presence of abnormality intraabdominally might be difficult and inaccurate. It is also affected by an increase in right atrial pressure and hence not applicable in patient with right heart failure or pulmonary hypertension. Since the IVCd is only validated in mechanically ventilated patients with no spontaneous breathing,(26) its practicality in ventilated patients with spontaneous breathing is questionable. Further studies need to be done to find the best IVC variable for this group of patients. Furthermore, it is operator dependent and one must learn the technique of performing ultrasound scan before they can utilize IVCd in daily practise.

There were a few limitations in this study. Firstly, this was a cross sectional observational study, with no intervention. The parameters were taken at one single point of time, and no fluid challenge was done to prove fluid responsiveness. As patient's selection was via convenience sampling, the ventilator settings were variable, with PEEP ranging from 6-11mmHg and tidal volume of 6-10mls/kg. Furthermore, majority of the patients (43.2%) had tidal volume of 6ml/kg as opposed to the optimal tidal volume of 8ml/kg (36). These tidal volumes were calculated from patient's estimated weight, which might not be accurate. These greatly can affect the result of this study.

CONCLUSION

In conclusion, IVCd alone is not a good alternative dynamic parameters in predicting fluid responsiveness. Multiples dynamic parameters in combination with clinical signs can be useful in predicting fluid responsiveness.

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