Ultrasound evaluation of the respiratory changes of the inferior vena cava and axillary vein diameter at rest and during positive pressure ventilation in healthy volunteers

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ABSTRACT

Introduction: Ultrasound assessment of the inferior vena cava (IVC), a large compliant capacitance vein, has gained favour in aiding fluid management of critically ill patients. The respiro-phasic changes in IVC diameter have given clinicians a tool for assessing patient volume status. There are however, limitations as to when and under what circumstances this tool can be reliably used. The aim of this study was to assess IVC and axillary vein (Axv) diameter size and respiratory variation in spontaneously breathing participants at rest and with the application of increasing positive end-expiratory pressure (PEEP) via non-invasive ventilation (NIV). The Axv was studied as an alternative vein to the IVC because it is accessible for ultrasound visualisation and independent of intra-abdominal pressure.

Methods: The IVC and Axv diameters of 28 healthy adult volunteers were measured using ultrasound, at rest and during positive pressure ventilation via NIV. The collapsibility index (CI) and distensibility index (DI) of these vessels were calculated and compared. The correlation between increasing PEEP levels and DI was evaluated.

Results: Positive pressure ventilation delivered via NIV produced equivalent respiro-phasic diameter changes in the IVC and Axv. Both vessel diameter variations at baseline (collapsibility index) and with increasing levels of PEEP (distensibility index) were non-uniform and unpredictable in this study population. The respiro-phasic diameter changes of the IVC and Axv showed no correlation with the level of PEEP.

Conclusion: These findings confirm the current clinical limitations of determining volume responsiveness using the IVC in spontaneously breathing patients with and without PEEP. The Axv cannot be used as an alternative vessel to the IVC as it also displays similar unpredictability.

INTRODUCTION

Critically ill and injured patients are seen daily in the Emergency Department (ED).Volume assessment and volume responsiveness in these patients has become a particular topic of interest in critical care and emergency medicine literature. The implications of incorrect volume management in critically ill patients can be devastating [1]. Clinicians therefore need a reliable tool to determine when to administer fluids without causing harm. Static indices such as central venous pressure (CVP) lack good evidence for accuracy in determining volume responsiveness [2]. Dynamic indices such as vena cavae measurements have provided good evidence for predicting volume responsiveness in controlled, mechanically ventilated patients [3, 4].

Most intensive care units (ICU) are moving away from the practice of rigorous patient sedation and controlled mechanical ventilation as this has produced poor patient outcomes and prolonged ICU stays [1,5].This move has created a knowledge gap in the clinical determination of volume responsiveness in spontaneously breathing, non-sedated patients receiving ventilator support.

The passive leg raise (PLR), combined with stroke volume indices, is currently the most reliable dynamic index that can be used to predict volume responsiveness in this patient population [6]. This method of determining volume responsiveness with echocardiography requires determination of stroke volume or cardiac output in real-time which can be cumbersome especially if measurements have to be repeated. PLR is also not advisable in critically ill trauma patients with pelvic, spinal or lower limb long bone injuries.

Collapsibility Index (CI)

The IVC CI is used to assess volume status in the non-ventilated spontaneously breathing patient [7].The IVC CI is a dynamic index and is expressed as a percentage. The IVC CI is the difference between the maximum IVC diameter and the minimum IVC diameter divided by the maximum IVC diameter.

IVC CI = (IVCmax-IVCmin)/ IVCmax X 100 [7].

The IVCmax in the non-ventilated patient is measured during expiration and the IVCmin during inspiration. The opposite is true during mechanical ventilation.

Distensibility Index (DI)

Cavallaro organised dynamic indices into three groups wherein the IVC distensibility index (dIVC) can be found. Group A are stroke volume-related indices e.g. pulse pressure variation and stroke volume variation. Group B are non-stroke volume indices e.g. IVC and superior vena cava measurements. Group C are preload redistribution techniques e.g. PLR. Both group A and B are utilised in the setting of mechanical ventilation [8].

Group A and B indices are based on the premise of heart-lung dependency in a closed chest cavity which results in blood volume shifts with increased intra-thoracic pressure. In group B, the dIVC has been successfully tested to predict volume responsiveness with good sensitivity (90%) and specificity (90%) in ventilated patients [3, 4].

dIVC = IVCmax-IVCmin/IVCmin X 100 [8]

Increased intra-thoracic pressure occurs during positive pressure lung insufflation via mechanical ventilation. Positive pressure ventilation can be delivered via invasive or non-invasive methods. Non-invasive ventilation (NIV) can be delivered via face mask, nasal prongs or head masks. Similar dynamic changes in blood volume shifts secondary to invasive mechanical ventilation should therefore be expected with NIV [3, 4].

The IVC and positive end-expiratory pressure

Lambert et al studied the effect of increasing levels of positive end-expiratory pressure (PEEP) on stroke volume in healthy pigs [9]. The authors observed that at a PEEP of 10cmH_2O in hypovolaemic and normovolaemic pigs the stroke volume, cardiac output and mean arterial pressure all significantly decreased while the stroke volume variation and heart rate increased. Most importantly, all these changes induced by increasing levels of PEEP, were reversed after fluid loading. Even with its limitations, this study was able to conclude that increasing PEEP levels alone could be used to create a heart-lung dynamic environment which could influence the dynamic indices of stroke volume variation and dIVC.

Alternate vessel to the IVC

Viellard-Baron et al produced one of the few studies to date to evaluate the diameter changes of a central vein other than the IVC for volume responsiveness: The superior vena cava (SVC) [10]. The advantage of the SVC over the IVC is that it resides wholly in the chest cavity and is not exposed to intra-abdominal pressures which may produce confounding results when measuring the IVC. As described by Viellard-Baron, the SVC obeys an “all or nothing law”, that is, once the intravascular opening pressure is overcome it will definitely collapse. The most accurate way to visualise SVC is via transoesophageal echocardiography (TOE). However, TOE is an invasive and uncomfortable procedure in the conscious patient. Additionally, TOE is generally not accessible in the ED. These limitations present an opportunity for researchers to seek an alternative central vein to the vena cavae that can be used to determine volume responsiveness.

The Axv is a central vein easily accessible for ultrasound visualisation and independent of intra-abdominal pressure. The internal jugular vein was excluded as an option as it tends to overestimate collapsibility whilst the femoral vein tends to under-estimate collapsibility [11]. Sonographic access to the subclavian vein is commonly impeded by its position relative to the clavicle [12]. The right axillary vein was therefore the most feasible alternative central vein to the vena cavae by way of proximity to the right side of the heart.

The primary aim of this study was therefore to evaluate the respiratory variation of the IVC and Axv diameter sizes using ultrasound, at rest and during positive pressure ventilation with increasing levels of PEEP via NIV.

METHODS AND MATERIALS

This prospective cross-sectional study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Witwatersrand. Healthy adult (>18years old) volunteers were invited to participate in the study.

Participants known with cardiac disease, chronic obstructive lung disease, pregnant women and claustrophobic volunteers were excluded from the study. The final study sample included 28 participants.

Equipment

-Participants' vital signs were measured using the Mindray VS-800 multi-parameter

vital signs monitor.

-The Draeger Savina 300 ventilator was used to provide NIV.

-The Mindray DP-50 Ultrasound machine was used for sonographic measurements.

Data Collection

1) Each participant lay on a stretcher at a 45º semi-recumbent position
2) Baseline vital signs were recorded (at rest): Blood pressure/ heart rate/ respiratory rate / oxygen saturation
3) A Curvilinear 3.5MHz probe was used to visualise and measure the IVC in the subcostal view; longitudinal section
4) The IVC diameter was measured 2cm from its entrance into the right atrium
5) IVC maximum and minimum diameters were measured during a single respiratory cycle
6) The Axv was located in the right delto-pectoral groove
7) The Axv was visualised and measured using a 7.5MHz linear probe
8) The Axv maximum and minimum diameters were measured during a single respiratory cycle
9) Each participant was then attached to the ventilator via an NIV mask.
10) PEEP was set to 5cmH_2O then 10cmH_2O
11) A five minute participant acclimatisation period to the positive pressure ventilation at PEEP of 5cmH_2O and again at 10cmH_2O was allowed prior to taking measurements.

12) Vital signs, IVC and Axv diameters were re-measured at PEEP of 5cmH_2O and again at PEEP of 10cmH_2O as per point 3) 5) 6) and 8)

13) The IVC and Axv diameters were measured three times and the average taken for final analysis. All measurements were taken by the same investigator.

DATA ANALYSIS

For each outcome, the differences between the PEEP levels were analysed by a repeated measures model. This model allowed for the comparison of the outcomes within and between subjects.

A linear regression analysis studied whether a correlation between vessel variability and PEEP level existed.

The 5% significance level was used. The data analysis was carried out using SAS software, version 9.3 for Windows, Cary, NC, USA: SAS Institute. (2002-2010).

RESULTS

Thirty five participants were enrolled into the study. Eight participants were excluded because of inadequate image visualisation on sonography.

Sixty eight percent of the participants were female. The median age of the group was 29 years (IQR 27-31).

Table 1. Baseline and dynamic results

	Baseline	**Dynamic**		
PEEP	**0cmH_2O**	**5cmH_2O**	**10cmH_2O**	**p value for between group difference**
RR (breaths per minute)	19 (14-25)	15 (5-23)	15 (9-23)	0.0002
HR (beats per minute)	75 (57-104)	72 (53-91)	70 (55-89)	0.01
SBP (mmHg)	128 (107-176)	125 (100-186)	123 (96-176)	0.02
DBP (mmHg)	82 (45-119)	81 (67-124)	80 (64-120)	0.56
Oxygen saturation (%)	97 (95-100)	97 (94-100)	98 (95-100)	0.02

PEEP	**0 cmH_2O**	**5cmH_2O**	**10cmH_2O**	**p value**
Tidal Volume (L)	0.504 (0.468-0.544)	0.667 (0.589-0.885)	0.768 (0.640-0.990)	0.0001
IVC max (cm)	1.45 (1.25-1.78)	1.56 (1.36-1.72)	1.72 (1.52-1.86)	0.0009
IVC min (cm)	1.20 (0.96-1.52)	1.12 (0.92-1.42)	1.38 (1.06-1.54)	0.02
Axvmax (cm)	0.63 (0.48-0.77)	0.58 (0.48-0.67)	0.66 (0.52-0.86)	0.04
Axvmin (cm)	0.53 (0.41-0.64)	0.46 (0.34-0.56)	0.54 (0.37-0.68)	0.06

Table 2. IVC Collapsibility index (IVC CI) and Axv Collapsibility Index (Axv CI)

PEEP cmH_2O = 0	**IVC CI (%)**	**Axv CI (%)**	**P value**
	17.5	15.3	0.21

Table 3. IVC distensibilty index (dIVC) and Axv distensibility Index (dAxv)

PEEP	**5cmH_2O**	**10cmH_2O**	**p value**
dIVC (%)	22.1(14.9-53)	23.2(15.3-37.6)	0.61
dAxv (%)	22.2(14.1-34.2)	21.7(9.3-33.7)	0.37

The mean respiratory rate (RR) at PEEP =0cmH_2O was significantly higher than that at PEEP 5cmH_2O and PEEP 10cmH_2O (p=0.0002).

The mean heart rate (HR) at PEEP 0cmH_2O was significantly higher than that at PEEP 10cmH_2O (p=0.01).

The mean systolic blood pressure (SBP) at PEEP 0cmH_2O was significantly higher than that at PEEP 10cmH_2O (p=0.02). Increase in PEEP had no significant effect on mean diastolic blood pressure (DBP) (p=0.56).

The mean oxygen saturation at PEEP 0cmH_2O was significantly lower than that at PEEP 10cmH_2O (p=0.02). The difference is small but statistically significant. The difference is not clinically significant.

Median tidal volume increased with each increase in PEEP level (p= 0.0001).

The median IVCmax at PEEP 10cmH_2O was higher than that at PEEP 0 cmH_2O and PEEP 5cmH_2O (p=0.0009). Although the analysis for median IVCmin was also significant (p=0.02), post hoc comparisons showed no significant inbetween-group differences.

The median Axvmax at PEEP 10cmH_2O was higher than that at PEEP 5cmH_2O (p=0.04).

The median Axvmin experienced no significant change with increase in PEEP (p=0.06).

The median IVC CI and Axv CI at baseline were 17.5% and 15.2% respectively. There was no significant difference between the two values (p=0.21).

Increasing PEEP had no significant effect on median dIVC (p=0.61) or dAxv (p=0.37).

At PEEP 5cmH_2O there was no significant difference between dIVC and dAxv (p=0.47). Similarly at PEEP 10cmH_2O there was no significant difference between dIVC and dAxv (p=0.17).

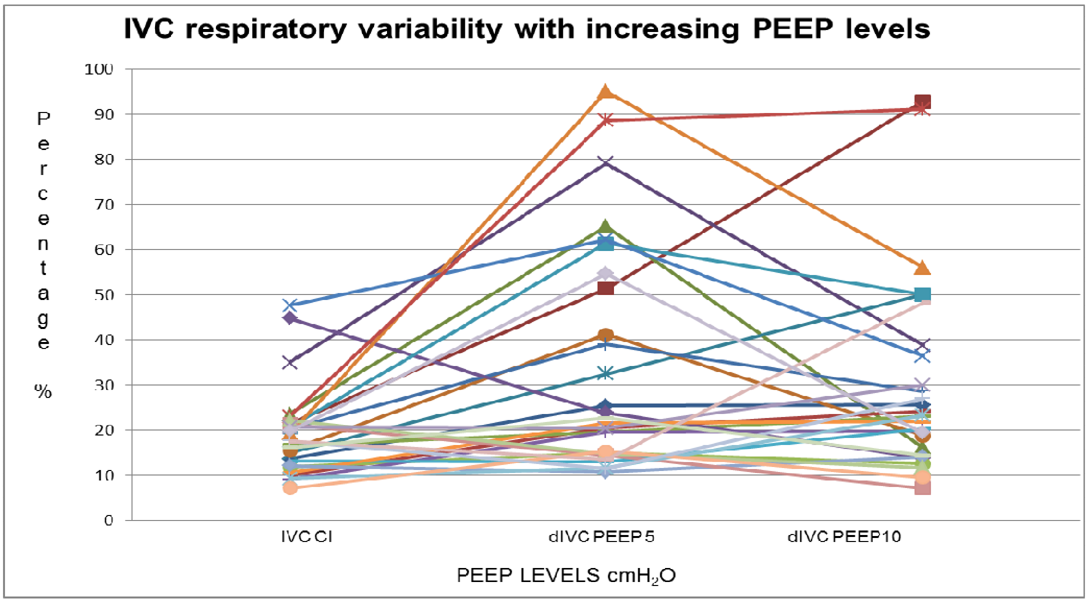

Figure 1: Respiratory diameter variation of IVC with increasing PEEP levels

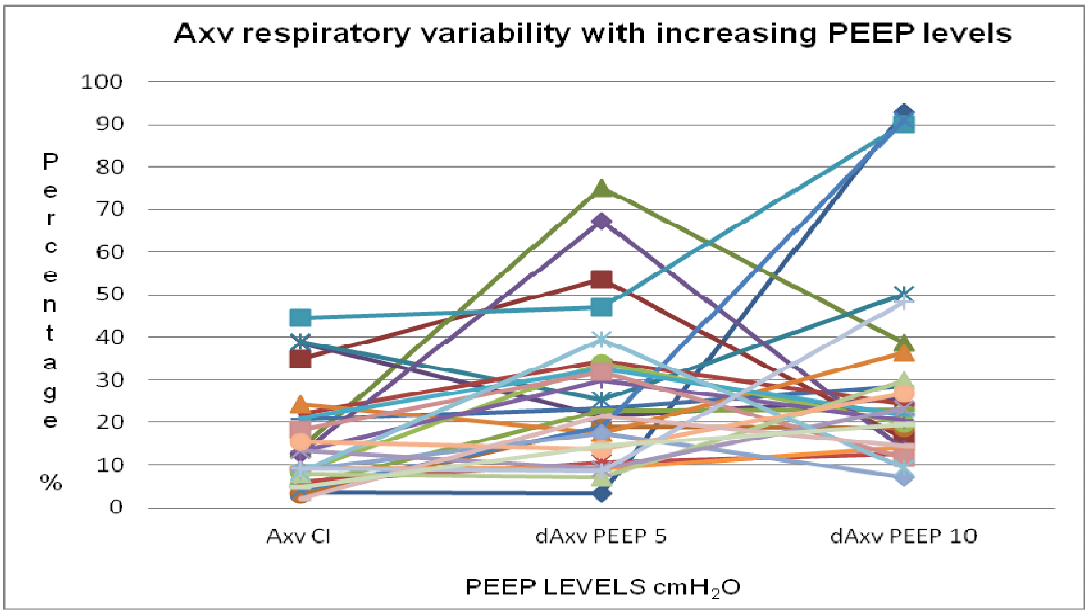

Figure 2: Respiratory diameter variation of Axv with increasing PEEP levels

The IVC and Axv diameter variability at PEEP 0cmH_2O (baseline) was less than 50% for all participants; the majority observed to be less than 30% (see figure 1)

Once positive pressure ventilation was introduced (PEEP 5cmH_2O), the diameter variability for both the IVC and the Axv were random without any discernible trend. The unpredictable variability was also observed at PEEP 10cmH_2O for both vessels. (see figure 2)

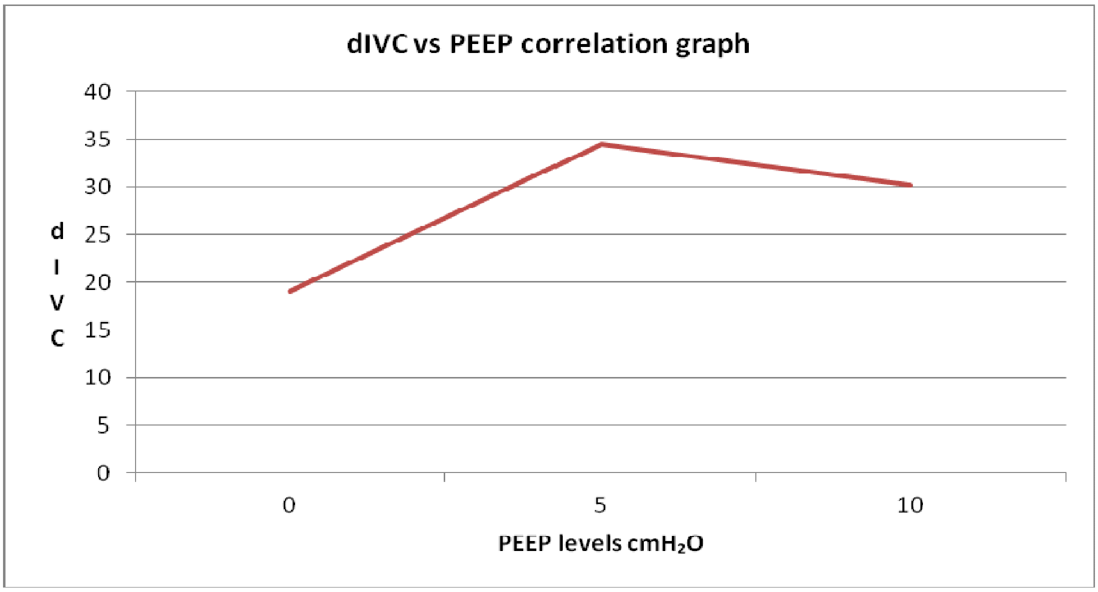

Figure 3: Correlation graph dIVC vs PEEP

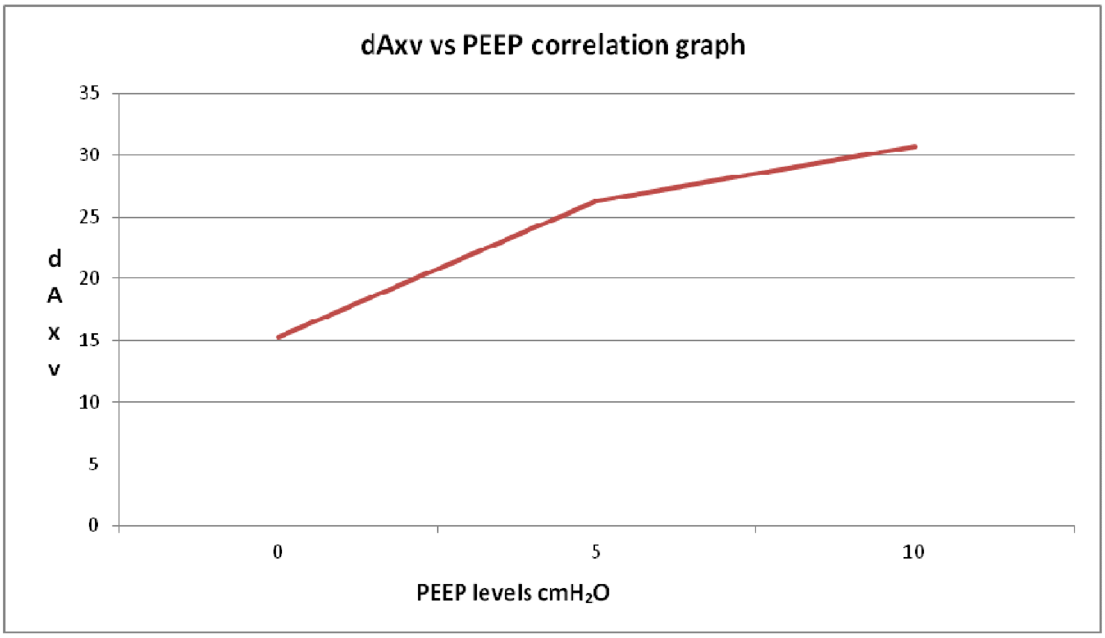

Figure 4: Correlation graph dAxv vs PEEP

Figure 3 and 4 demonstrates the lack of correlation between IVC and Axv variation with increasing PEEP. Each graph represents the median DI for all 28 participants at PEEP 0, 5 and 10cmH_2O. Studying the graph in isolation (figure 3), the dIVC showed a marked increase from PEEP 0cmH_2O to PEEP 5cmH_2O. This may be explained by the expected physiological decrease in venous return with increase in PEEP. This is effect is lost however when PEEP is increased to 10cmH_2O.

Figure 4 initially suggested a linear increasing trend of dAxv with increasing PEEP but on closer inspection the amount of change of dAxv from PEEP 0cmH_2O to 5cmH_2O versus from PEEP 5cmH_2O to 10cmH_2O is not equal.

These correlation graphs further confirm the unpredictable behaviour of these two vessels with increasing levels of PEEP.

DISCUSSION

The respiratory variability of the IVC diameter has never been investigated in patients receiving NIV. A patient receiving NIV experiences the physiological changes of positive pressure ventilation whilst breathing spontaneously. This study sought to observe the respiratory variation of the IVC and Axv diameters during positive pressure ventilation via NIV and considered the clinical implications thereof.

This study demonstrated that positive pressure ventilation delivered via NIV significantly increased intra-thoracic pressure and subsequently significantly influenced IVCmax and Axvmax diameter variability. Increase in PEEP did not significantly affect IVCmin or Axvmin diameters. The final results also showed that positive pressure ventilation produced equivalent respiro-phasic diameter changes in the IVC and the Axv.

A dIVC and dAxv greater than 18% was observed in this study. A median dIVC of 22.1% and 23.2% was observed at PEEP of 5cmH_2O and 10cmH_2O respectively. Median dAxv was 22.2% and 21.7% at PEEP of 5cmH_2O and 10cmH_2O.

"For a given plasma volume in a given patient, the increase in tidal volume and the application of PEEP can alter IVC diameter"- Barbier [3]

Barbier et al found a strong positive correlation between increase in dIVC and subsequent increase in cardiac output. A dIVC of greater than 18% allowed prediction of volume responsiveness in septic, ventilated patients with a sensitivity and specificity of 90% [3]. Another study found a dIVC greater than 12%, using a different equation, to be significant [4]. Yet another study showed a dIVC greater than 16% to be significant for volume responsiveness [13]. Although these studies highlight the significant effect of ventilation on IVC diameter variability, a standard approach to the interpretation of central vein diameter variation is distinctly lacking in the current literature and this study may highlight some of the reasons.

This study also revealed that the response from negative pressure ventilation to positive pressure ventilation was different for each participant. The results (see figure 1) showed a non-uniform change in IVC diameter variability for each participant from PEEP 0cmH_2O to 5cmH_2O and from PEEP 5cmH_2O to 10cmH_2O. The median dIVC at PEEP 5cmH_2O was 22.1% but ranged from 14.9%- 53%. The median dIVC at

PEEP 10cmH_2O was 23.2% IQR 15.3%-37.6%. dAxv was similarly unpredictable and non-uniform for each participant (see figure 2). Subsequent correlation graphs (figure 3 and 4) confirm above-mentioned findings. Perhaps a standard interpretation to IVC diameter variation is lacking because it is non-existent.

Factors affecting use of sonography

Twenty three percent of enrolled participants were excluded because of poor visualisation of the IVC. The IVC can be obscured by bowel gas and may also not be visualised in obese patients. Bowel gas is a well described limitation for abdominal ultrasound [14]. This is especially relevant to the non-fasted patient presenting acutely to the ED.

Global population figures for obesity are rising and challenging ED physician's management of patients as seen in the airway management of the obese patient [15]. The use of ultrasound in the face of these very real obstacles may limit its utility.

Factors affecting IVC variation

THE INVESTIGATOR

The entire data collection process was performed by a single investigator with level 1 ultrasound accreditation. A single investigator reduced the possibility of investigator bias.

BREATHING PATTERNS

The IVC and Axv diameter changes observed in this study were in spontaneously breathing participants without instruction or additional breathing manoeuvres. The investigator allowed for a five minute participant acclimatisation period to the positive pressure ventilation at PEEP of 5cmH_2O and again at 10cmH_2O prior to taking measurements [16]. Acclimatisation was monitored by stabilisation of vital signs and constant communication and positive feedback from the participant in the form of head or hand gestures.

The commonly stated reason why IVC diameter measurements are unreliable in spontaneously breathing patients is due to variable patient breathing patterns and variable tidal volumes with each breath. Median tidal volumes in this study were 0.667L at PEEP 5cmH_2O and 0.768L at PEEP 10cmH_2O. IVCmax increased significantly with increased tidal volume demonstrating the effect of increasing levels of PEEP. The IVC was however randomly affected; increasing PEEP levels had no significant effect on IVCmin.

NON-UNIFORM IVC MEASUREMENTS

Keith Corl et al also speculated over the non-uniform collapsibility of the IVC as another contributory factor [17]. In this study, this argument was mitigated by measuring the IVC at the same place each time (2 cm from the entrance to the right atrium) and measuring the IVC in B-mode. Pasquero et al highlighted the fact that currently there is no standard site to measure the IVC. Their study compared IVC measurements at the hepatic long axis versus the hepatic short axis versus the renal short axis positions [18]. Hepatic long axis performed the best as it consistently allowed better views. There were no significant differences between IVC diameter and collapsibility in all three views.

AGE

A majority of the studies looking at IVC diameter size and variability were conducted in patients of average age sixty and above [2,3,4,14]. This study was conducted in patients with a median age of 29 years. All possible factors affecting the IVC need to be described including the influence of age. A weak correlation between older age and decreased IVC diameter and increased IVC collapsibility was found by Masugata et al and begs the question of how many other physiological factors may affect the IVC diameter and its variation besides intra-thoracic pressures [19].

THE AXILLARY VEIN

The twin aim of this study was to observe the respiro-phasic diameter changes of an alternate blood vessel to the IVC and to compare the changes of the new vessel to those of the IVC. The hypothesized advantage of the Axv was that it lacked all the limitations involved in measuring the IVC, i.e. exposure to intra-abdominal pressure and IVC diaphragmatic excursion measurement challenges.

PARTICIPANT POSITION

In this study the Axv was visualised in the right delto-pectoral groove with the patient in a 45º semi-recumbent position. Participant position was unchanged for IVC and Axv measurements. The IVC metrics do not change significantly based on patient position [20]. This knowledge is especially important as in real life clinical scenarios patients may not always be able to lie supine.

Of note is that the Axv can be visualised on sonar in various arm positions for intravenous catheter placement [21]. It is however unlikely that a different arm position would have dramatically altered the results observed in this study.

IVC VERSUS AXV

The collapsibility index for the Axv was calculated as per IVC CI. The median IVC CI was 17.5% and the median Axv CI 15.3%. There was no significant difference between the two values (p=0.21).

There were no significant differences between dIVC and dAxv at PEEP 5cmH_2O (p=0.47) or at PEEP 10cmH_2O (p=0.17). The dAxv findings were interesting because the Axv, where it was measured, was not exposed to any direct intra-thoracic pressure. The effect of increasing PEEP was therefore as a result of the backward pressure from the SVC all the way to reach the Axv.

The findings from this study showed Axv respiro-phasic diameter changes comparable to those of the IVC. At individual participant level the dAxv showed the same unpredictable nature as seen with the dIVC with increasing levels of PEEP (see figure 2).

PASSIVE LEG RAISE

There are studies, even with the above-mentioned limitations, which showed volume responsiveness could be predicted in the spontaneously breathing patient with a sensitivity of 77% and specificity 100% [19]. This is feasible with stroke volume indices (Cavallaro group A) combined with PLR. This technique is however limited in certain patient populations where PLR would be not be advisable.

IVC and Axv diameter variation are unreliable in the spontaneously breathing participant receiving positive pressure ventilation. It is difficult to foresee any progress in IVC literature in the near future until the IVC is paid absolute scrutiny regarding its anatomical and physiological influences. Also, consensus regarding technique of IVC measurement is desperately needed.

Conclusion

This study showed that the IVC and Axv diameters behaved in a similar fashion when exposed to positive pressure ventilation via NIV. Both vessels had distensibility indices of greater than 18% at PEEP levels of 5cmH_2O and 10cmH_2O. The unpredictable nature of both vessels diameter variability and unexplained inter-individual differences limits use and interpretation of dIVC and dAxv in the fluid status management of spontaneously breathing patients on ventilator support.

Limitations

The small study population limits the wider application of the findings to other populations. This study may have been affected by participant volunteer bias and by the significant number of participants excluded because of inadequate image visualisation on sonography.

Recommendations

The authors would recommend a larger study to support the outcomes of this study and standardization of IVC measurement techniques.

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