ULTRASOUND OF THE INFERIOR VENA CAVA DOES NOT PREDICT HEMODYNAMIC RESPONSE TO EARLY HEMORRHAGE

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Abstract—Background: Ultrasonographic evaluation of the inferior vena cava (IVC) provides information on central hemodynamics and predicts fluid responsiveness during positive pressure ventilation. In spontaneously breathing patients, the correlations between IVC dynamics and the hemodynamic response to volume shifts remain to be described. Objectives: We aimed to describe the correlation between IVC dynamics and the changes in cardiac output (CO) caused by controlled hemorrhage. Methods: Healthy donors from the blood bank were eligible for inclusion. Measurements of the IVC and CO were performed before and immediately after blood donation using ultrasound methods. A control group served to evaluate the effect of resting. Results: Thirty-seven participants completed the study. IVC collapsibility index (IVC-CI) and IVC end expiratory diameter (IVCe) both changed significantly after blood donation (p < 0.001). The baseline IVC-CI and IVCe did not correlate with the change in CO (p-values ≥ 0.40). The alterations in IVC-CI and IVCe induced by blood donation also did not correlate with the change in CO (p ≥ 0.71). The sensitivities of IVC-CI or IVCe, defined as an increase in IVC-CI and a decrease in IVCe, for picking up any decrease in CO were 81.3% and 84.4%, respectively. In the control group, no effect was seen between measurements. Conclusion: IVC-CI and IVCe did not correlate with the magnitude of hemodynamic response to early hemorrhage. The sensitivity of serial IVC measurements was approximately 80% for detecting early blood loss. © 2013 Elsevier Inc.

Keywords—ultrasound; echocardiography; hemorrhage; trauma; inferior vena cava; phlebotomy

INTRODUCTION

Evaluation of volume status remains a difficult challenge in critically ill patients. Ultrasound evaluation of the inferior vena cava (IVC) dimensions provides information on central hemodynamics that is non-invasive, repeatable, and easily obtainable by operators with little echocardiographic experience (1). The expiratory diameter of the IVC (IVCe) and its change during the respiratory cycle, and the IVC collapsibility index (IVC-CI) reflect volume status in shock, sepsis, and hemodialysis patients (1–3). Further, the IVCe correlates reasonably well with central venous pressure (4–6). In regard to treatment response, the IVC distensibility facilitated by positive pressure ventilation is predictive of volume responsiveness. This has been shown in patients with sepsis and subarachnoid hemorrhage, where an IVC distensibility exceeding 12–18% was predictive of an increase in cardiac output (CO) > 15% (7–9).

Conflict of Interest: Erik Sloth has received fees for lectures from BK Medical and General Electrics. The other authors have no competing interests.
However, in spontaneously breathing patients, the correlations between IVC measures and the changes in CO induced by volume shifts remain to be described. This includes the effects of volume loss. In the trauma or perioperative settings, this would help to identify the patients most vulnerable to the effects of hemorrhage and guide volume therapy.

We therefore hypothesized that 1) the IVC-CI and IVCe, as viewed before volume reduction, would correlate with changes in CO caused by controlled hemorrhage, and 2) that changes in IVC-CI and IVCe induced by hemorrhage would correlate with the change in CO.

METHODS

The study was approved by the Central Region Ethical Committee of Denmark (journal no. M-20110110), and enrollment was conditional upon written consent. The study was conducted in accordance with the Helsinki Declaration. All donors from the blood bank were eligible for inclusion (participants). Standard exclusion criteria for blood donation included any disease that may affect the cardiovascular system, including hypertension, diabetes mellitus, any cardiac or renal disease, previous cerebral stroke, and pregnancy. Additional criteria were blood pressure above 180/100 mm Hg or below 100/50 mm Hg, heart rate outside the range of 50–110 min⁻¹, and body weight below 50 kg.

In addition, a control group of 10 volunteers (controls) with identical exclusion criteria was recruited for evaluation of the effects of an identical resting protocol on IVC dynamics and CO.

Ultrasound Data Collection

Upon arrival at the blood bank, participants rested in the supine position for at least 15 min before examination. Participants were subject to ultrasonographic measurement of the IVC and CO before blood donation and immediately after needle withdrawal, thereby minimizing volume re-distribution. The IVC was visualized from the transhepatic, subcostal view during quiet breathing. Longitudinal 2-dimensional (2D) cine loops spanning at least one respiratory cycle were stored for off-line analysis (Figure 1). Participants were then placed in the left lateral position for imaging of the left ventricular outflow tract (LVOT) in the cardiac apical five-chamber view. The velocity time integral (VTI) of the LVOT was acquired, employing pulsed wave Doppler (Figure 1). All examinations were performed by one of two sonographers experienced in echocardiography using a vivid E9 echocardiography system fitted with an M5S phased array transducer (1.5–4.5 MHz) (GE Healthcare, Horten, Norway).

An identical scanning protocol, in terms of resting periods and timing of imaging, was applied to the controls.

Data Analysis

Images and cine loops were analyzed off-line by an observer blinded to the time of examination in relation to blood donation. Analyses were reanalyzed by a second observer, similarly blinded, for calculation of interobserver variation. Commercially available software (Echopac, GE Healthcare) was used. The IVC was calibrated with tracings perpendicular to the vessel walls approximately 2 cm caudal to the inflow of the hepatic veins. The maximal expiratory (IVCe) and inspiratory (IVCi) diameters of the IVC were meticulously found by frame-by-frame analysis. The inner-edge to inner-edge technique was used.

The collapsibility index of the IVC was calculated as IVC-CI = (IVCe−IVCi)/IVCe. The VTI was averaged from triplicates, and the CO was found by the equation CO = VTI*cross-sectional area of the LVOT*heart rate (10).

Statistical Analysis

Measurements before and after blood donation were compared with a paired-samples Student’s t-test. Correlations were analyzed with Spearman’s rank correlation

Figure 1. Left: Sagittal image of the inferior vena cava with calibration of the diameter during expiration (IVCe). Right: Measurement of the velocity time interval of the left ventricular outflow tract (LVOT), enabling calculation of stroke volume and cardiac output.
coefficient, as the IVC-CI and the relative difference in CO were not normally distributed. Interobserver variation was calculated as the mean difference in readings divided by the mean, expressed as a percentage and presented as mean variation with its corresponding 95% limits of agreement (LoA) and 95% confidence interval (CI). Statistical significance was set at \( p < 0.05 \). Calculations were performed with STATA software (StataCorp LP, College Station, TX).

**RESULTS**

Forty participants were enrolled, and of these, 3 were later excluded due to a vasovagal reaction (n = 1), inadequate image quality (n = 1), and left bundle branch block (n = 1). Demographics for the remaining 37 participants were: men 27 (73.0%), mean age 32.6 years (range 19–60 years), and mean body mass index (BMI) 25.3 (range 20.4–45.8). Volume reduction was exactly 480 mL for all participants except one (413 mL), due to slow bleeding. Demographics for the controls were: men 6 (60%), mean age 32.4 years (range 25–54 years), and mean BMI 22.6 (range 18.9–27.2).

The effects of blood donation on IVC measures and CO are displayed in Table 1. Neither the baseline IVC-CI nor IVCe correlated with the CO changes induced (Figures 2, 3). In addition, alterations in IVC-CI and IVCe facilitated by blood donation did not correlate with changes in CO. This was found for the absolute increase in IVC-CI \( (p = 0.71, \ r = 0.07) \). In regard to IVCe, the corresponding values for the absolute and relative changes were \( p = 0.87, \ r = 0.03 \) and \( p = 0.77, \ r = −0.05 \), respectively.

For controls, all parameters remained unchanged between measurements (Table 1). Mean inter-observer variation was 2.97% (LoA: −15.95–21.88%; 95% CI −1.36–4.57%) for IVC diameters and 5.24% (LoA: 6.80–17.27%; 95% CI 3.81–6.66%) for VTIs.

**DISCUSSION**

This study shows that the IVC-CI and IVCe did not correlate with the hemodynamic response generated by early hemorrhage. With respect to the alterations generated by blood donation, values of IVC-CI and IVC diameters in both respiratory phases changed significantly (Table 1). To the best of our knowledge, this study is the first to correlate measures of IVC with the hemodynamic response to volume reduction during spontaneous respiration. As no significant correlations were found, however, our results cannot substantiate the use of IVC-CI or IVCe to identify individuals who are particularly vulnerable to further volume depletion. Likewise, the degree of change in IVC-CI or IVCe caused by blood loss did not reflect the individual hemodynamic response.

A contributing factor for this finding may have been spontaneous breathing itself. The fluctuation in the IVC diameter generated by inspiration reflects the pressure difference over the IVC vessel wall. This gradient is a complex product of pre-inspiratory IVC blood content, venous blood mobilization due to increased abdominal pressure, and the abdominal pressure itself (11). Although
participants were studied during quiet breathing, inspiratory effort and the resulting intra-thoracic and abdominal pressures may have varied. This random variation may cancel out any systematic correlation, but rather reflects patient-related variation that cannot be corrected for. This is in keeping with a previous study focusing on participant-triggered positive pressure ventilation (12).

The use of a control group showing no change on all end points effectively rules out that IVC measures or cardiac output were altered merely due to the prolonged resting period. Therefore, resting itself was not a confounder with the potential for blurring of potential correlations.

We found that blood donation caused a significant increase in IVC-CI and decrease in IVC diameters in both inspiration and expiration. Despite statistical significance, IVC-CI decreased or was unaffected in 8 (21.6%) of our participants and the IVCe increased or stayed the same in 7 (18.9%). A post hoc analysis showed that the sensitivity for detecting any decrease in CO as a hemodynamic response to hemorrhage was 81.3% (95% CI 63.0–92.1%) for IVC-CI (defined as any increase in IVC-CI) and 84.4% (95% CI 66.4–94.1%) for IVCe (defined as any decrease in IVCe). Hence, IVC-CI and IVCe detected early blood loss in approximately four out of five cases, with a similar probability of detection if the blood loss actually caused a drop in CO.

Previous studies addressing the effects of blood donation on IVC measures have yielded different results. Lyon et al. found that both IVCe and IVCi decreased after donation and therefore recommended the use of ultrasound (13). Conversely, Resnick et al. concluded that both IVCe and IVCi decreased statistically with blood loss, but showed considerable variation (14). Likewise, IVC-CI remained unchanged and the authors discouraged the use of IVC measurements for tracking blood loss. The differences between Resnick et al. and our results are likely explained by different measurement techniques. Resnick et al. used M-mode for calibrating the IVC, whereas we used frame-to-frame analysis of 2D cine loops. M-mode does not compensate for translation of organs during respiration and introduces significant bias, as previously described (12).

Clinical Implications

IVC values did not reflect the magnitude of the hemodynamic response to hemorrhage, and the results of this study discourage the use of quantitative IVC dynamics as a means of identifying individuals in whom subsequent bleeding will cause a pronounced decrease in cardiac output. However, the sensitivity for detecting minor bleeding (480 mL), viewed as purely a dichotomous outcome (bleeding or not bleeding), was moderate at 80%. This supports the use of serial measurements of the IVC in individuals with potential hemorrhage, as even minor blood loss affected dynamic IVC measures in approximately 80% of cases. The potential clinical utility of this is underscored by previous observations that blood donation, as a surrogate for early bleeding, does not influence common clinical parameters such as blood pressure and heart rate. This has been established not only in healthy young individuals, but also in the elderly and in patients with significant heart and lung disease (15,16).

Limitations

The volume reduction was relatively small and, in the clinical context, only representative of early hemorrhage. Despite this, the median decrease in CO was 9.9%. The effects of a greater volume reduction may have yielded
a more pronounced effect on CO and IVC diameters, and revealed a systematic correlation.

Five participants actually had increased CO upon blood donation. We speculate that this was caused by an altered sympathetic tone in individual participants or the inherent measurement error of the method used for CO quantification. The effects of an increased sympathetic tone on CO are well known, whereas its effect on the IVC remains to be established. Conditions for ultrasonic imaging were optimal, with a relatively lean study population free from surgical dressings and drains, etc. This kept the random variation of both IVC and CO measurement to an absolute minimum, thus reducing the chance of type II error.

CONCLUSION

Baseline IVC-CI and IVCe did not correlate with the relative decrease in CO induced by blood donation. Therefore, baseline measurements did not reflect the following hemodynamic response. A lack of correlation with the decrease in CO was also found for the changes in IVC-CI and IVCe caused by blood loss. The sensitivity of dynamic IVC measures for detecting early blood loss was around 80%. Although IVC measures did not correlate with hemodynamic response, the moderate sensitivity supports the use of ultrasonography for assessment of patients with suspected hemorrhage.

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ARTICLE SUMMARY

1. Why is this topic important?
   Ultrasound of the inferior vena cava (IVC) provides information on volume status and is increasingly used in emergency settings.

2. What does this study attempt to show?
   This study describes the correlation between dynamics of the inferior vena cava and the hemodynamic response to early hemorrhage in healthy volunteers.

3. What are the key findings?
   The study showed no significant correlation between IVC dynamics and hemodynamic response, but proved moderately sensitive in detecting individuals with minor bleeding.

4. How is patient care impacted?
   Ultrasound of the IVC may be used for serial assessment of individuals suspected of hemorrhage.