ultrasound does not detect early blood loss in healthy volunteers donating blood

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Abstract—Background: Ultrasound has been suggested as a useful non-invasive tool for the detection of early blood loss. Two possible sonographic markers for hypovolemia are the diameter of the inferior vena cava (IVC) and the thickness of the left ventricle (LV). Study Objectives: The goal of the study was to evaluate the utility of ultrasound to detect signs of early hemorrhagic shock in healthy volunteers, compared with changes in vital signs. Methods: In the current study, healthy volunteers from blood donation drives were used as models for early hemorrhage. Changes in vital signs, IVC diameter, and LV wall thickness were recorded after approximately 500 cc of blood loss. Results: Thirty-eight subjects were enrolled and completed the study. After blood donation, there was a 7-mm Hg (8%) decrease in mean arterial pressure without a significant change in heart rate. There was a decrease in maximum IVC diameter (IVCmax) (12% decrease [95% confidence interval (CI) −6 to −19] in short axis and 20% decrease [95% CI −12 to −27] in long axis), but no change was seen in the respiratory caval index ((IVCmax − IVCmin)/IVCmax) × 100). There was no change in LV wall thickness. Conclusion: In this study, serial changes in vital signs, IVC diameter, and LV wall thickness were clinically insignificant after approximately 500 cc of blood loss in healthy volunteers. © 2011 Elsevier Inc.

Keywords—ultrasound; IVC diameter; blood loss

INTRODUCTION

Bedside ultrasound is being increasingly utilized in emergency and critical care medicine to non-invasively aid diagnosis and guide resuscitation of patients. Ultrasound in the trauma patient has focused on detecting hemoperitoneum and hemopericardium and, more recently, in evaluating for pneumothorax and hemothorax. The role of ultrasound in diagnosing early hemorrhagic shock and ongoing blood loss in the trauma patient has been introduced but has not gained widespread use. Currently available non-invasive measures, such as heart rate and blood pressure monitoring, may not coincide with significant blood loss, as neurohormonal influences during stress in critically injured patients can mask depressed cardiac output and impending severe hypotension (1).

Clinicians would benefit from a non-invasive tool that is independent of neurohormonal influences to measure early hemorrhagic shock. Two possible markers for hypovolemia are the diameter of the inferior vena cava (IVC) and the thickness of the left ventricle (2–7). These measurements could be utilized not only in the hospital setting but also in the pre-hospital and military settings to better triage patients and direct resuscitations in austere environments.

The goal of the study was to evaluate the utility of ultrasound to detect signs of early hemorrhagic shock in
healthy volunteers compared with changes in vital signs. The primary outcomes of the current study were changes in IVC diameter and left ventricle thickness after blood donation compared with changes in heart rate and mean arterial pressure.

**MATERIALS AND METHODS**

The hospital’s Institutional Review Board approved the study. Healthy volunteers from blood donation drives were used as models for early hemorrhage. The utility of ultrasound to evaluate changes predictive of early hemorrhagic shock was evaluated. Subjects were enrolled after volunteering to donate blood through Lifeshare Blood Donation drives at various non-hospital sites in Ohio. Standard blood donation screening protocols were followed, which included obtaining weight, measuring vital signs in the upright-seated position, and completing a brief questionnaire. Criteria for exclusion from blood donation were hemoglobin < 12.5 g/dL, weight < 110 lbs, blood pressure over 180/100 mm Hg, heart rate over 100 beats/min, temperature over 37.5°C (99.5°F), or increased risk of blood transmissible diseases.

After Lifeshare staff screened volunteers, the principal investigator (JR) or co-investigator (EP) approached patients to enroll them in the ultrasound study. Volunteers who agreed to participate signed informed consent and moved to a separate area with privacy screens to complete the pre-donation cardiac and IVC measurements. The volunteer was positioned in a recumbent position for all ultrasound measurements as well as during the blood donation. Ultrasound measurements were taken immediately before blood donation and immediately after the completion of blood donation.

Before blood donation began, a Sonosite® Micro-maxx (Sonosite, Bothell, WA) phased-array probe (P21) was used to image the IVC and the heart. The anteroposterior diameter of the IVC 2 cm from the right atrial-caval junction was measured in both short and long axis using M-mode. Maximum and minimum diameters were taken over one complete respiratory cycle during resting breathing (Figure 1). The thickness of the posterior wall of the left ventricle and the interventricular septum were measured in the parasternal long-axis window at the mitral valve insertion at end diastole. End diastole was identified by visualization of the mitral valve leaflets starting to close (Figure 2). This procedure was repeated immediately after completion of blood donation, along with measurement of blood pressure and heart rate. All measurements were taken by either the principal investigator (JR) or the co-investigator (EP).

Adverse symptoms were recorded. After subtracting the tare weight of the bag and the anticoagulant (98.4 g), adequate samples weighed between 531.6 and 584.6 g. Given the density of whole blood averages of 1.06 g/mL, an adequate sample had a volume between 501.5 and 551.5 mL. Lifeshare does not record the exact weights of the samples.

**Calculations**

After IVC and cardiac measurements were taken, the following calculations were made: 1) respiratory caval index = [(IVCmax − IVCmin)/IVCmax] × 100 (in which IVCmax = maximum IVC diameter and IVCmin = minimum IVC diameter); 2) mean wall thickness = [(septal wall thickness + left ventricle posterior wall thickness)/2] (7,8).
Statistical Analysis

Analyses were performed using STATA SE 10.2 (StataCorp, College Station, TX). Each donor was used as his or her own control. Data were analyzed using the paired t test and presented as means with 95% confidence intervals. Associations between continuous variables were analyzed with Pearson correlation coefficient. Based on an average IVC diameter of 17.4 mm before blood donation and 14.8 mm after blood donation with a standard deviation of 3.4, the study required 16 patients to detect a 15% difference with 80% power (3).

RESULTS

Forty-one volunteers were enrolled. Two subjects did not complete blood donation, one because the blood stopped flowing and another for unknown reasons. One subject felt lightheaded after completed donation. One subject with low-volume donation was excluded from the study. Three IVC measurements and three cardiac measurements were uninterpretable due to bowel gas (n = 3), large breasts (n = 1), or barrel chest (n = 2).

Table 1. Demographics of Subjects (Men n = 20, Women n = 19)

<table>
<thead>
<tr>
<th>Study Subjects</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>34</td>
<td>27 to 40</td>
</tr>
<tr>
<td>Women</td>
<td>29</td>
<td>21 to 35</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>85.7</td>
<td>78.9 to 92</td>
</tr>
<tr>
<td>Women</td>
<td>66.9</td>
<td>61.5 to 72.3</td>
</tr>
<tr>
<td>Height (inches)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>71.2</td>
<td>69.7 to 72.8</td>
</tr>
<tr>
<td>Women</td>
<td>64.8</td>
<td>63.8 to 65.9</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>26.1</td>
<td>24.4 to 27.8</td>
</tr>
<tr>
<td>Women</td>
<td>24.5</td>
<td>22.9 to 26.3</td>
</tr>
</tbody>
</table>

CI = confidence interval; BMI = body mass index.

Steady subjects’ demographics are listed in Table 1. Sample size did not permit separate analysis of men and women. No subject had a history of significant heart or lung disease. After blood donation, there was no clinically significant change in mean arterial pressure or heart rate (Table 2). IVCmax measurements in short axis and long axis were not statistically different. There was a small decrease in IVCmax and IVCmin diameter after blood donation in both short and long axis, but no change was seen in the respiratory caval index (Table 2).

There was no change in left ventricle wall thickness, septal wall thickness, or mean wall thickness before and after donation. There was no correlation between change in IVCmax and change in heart rate or mean arterial pressure. There was no correlation between change in IVCmax or change in mean ventricular wall thickness and body mass index (BMI).

DISCUSSION

Changes in the IVC diameter after 500 cc of blood donation were not clinically significant. The small decreases in IVC diameter, combined with measurement errors, made ultrasound an imperfect tool for detecting early hemorrhage in this model. Similar to other studies on vital signs after mild to moderate blood loss, IVC diameter measured by ultrasound is not sensitive to detect early hemorrhage (9,10).

Lyon et al. reported a 5-mm decrease in the diameter of the IVC after 450 cc of blood loss in healthy blood donors (3). No data on changes in heart rate or blood pressure were reported. The difference in this study’s baseline IVC diameter measurements from Lyon’s study can be explained by the difference in technique in measuring the IVC diameter. Lyon recorded a clip of the long axis of the IVC and then cine-looped back to measure the maximum and minimum anteroposterior diameter with calipers perpendicular to the long axis of the IVC. In our study, M-mode measurements sometimes

Table 2. Pre- and Post-donation Measurements

<table>
<thead>
<tr>
<th>Study Variables</th>
<th>n</th>
<th>Pre Mean</th>
<th>95% CI</th>
<th>Post Mean</th>
<th>95% CI</th>
<th>Absolute Change</th>
<th>95% CI</th>
<th>Percent Change</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>39</td>
<td>74</td>
<td>71 to 77</td>
<td>73</td>
<td>68 to 77</td>
<td>-1</td>
<td>-3 to -5</td>
<td>0</td>
<td>-6 to -4</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>39</td>
<td>94</td>
<td>90 to 98</td>
<td>87</td>
<td>82.6 to 90.9</td>
<td>-7.61</td>
<td>-5 to -11</td>
<td>-8</td>
<td>-11 to -5</td>
</tr>
<tr>
<td>IVCsamax (cm)</td>
<td>38</td>
<td>2.17</td>
<td>1.99 to 2.34</td>
<td>1.87</td>
<td>1.72 to 2.02</td>
<td>-0.31</td>
<td>-0.17 to -0.44</td>
<td>-12.2</td>
<td>-6.0 to -19.0</td>
</tr>
<tr>
<td>IVCclamax (cm)</td>
<td>38</td>
<td>2.23</td>
<td>2.04 to 2.41</td>
<td>1.73</td>
<td>1.55 to 1.92</td>
<td>-0.5</td>
<td>-0.32 to -0.6</td>
<td>-19.9</td>
<td>-12.4 to -27.4</td>
</tr>
<tr>
<td>IVCsamin (cm)</td>
<td>36</td>
<td>1.54</td>
<td>1.36 to 1.72</td>
<td>1.37</td>
<td>1.24 to 1.51</td>
<td>-0.16</td>
<td>0.00 to -0.33</td>
<td>-2.08</td>
<td>-84 to 58</td>
</tr>
<tr>
<td>IVCamin (cm)</td>
<td>36</td>
<td>1.54</td>
<td>1.30 to 1.79</td>
<td>1.25</td>
<td>1.09 to 1.42</td>
<td>-0.29</td>
<td>-0.11 to -0.47</td>
<td>11.2</td>
<td>36 to 58.6</td>
</tr>
<tr>
<td>RCI (percentage)</td>
<td>38</td>
<td>29</td>
<td>22.9 to 34.8</td>
<td>25.6</td>
<td>20.2 to 30.9</td>
<td>-3.3</td>
<td>3.18 to 9.79</td>
<td>-16</td>
<td>46 to 14</td>
</tr>
</tbody>
</table>

CI = confidence interval; HR = heart rate; MAP = mean arterial pressure; IVC = inferior vena cava; IVCsamax = maximum diameter of the IVC measured in short axis; IVCclamax = maximum diameter of the IVC measured in long axis; IVCsamin = minimum diameter of the IVC measured in short axis; IVCamin = minimum diameter of the IVC measured in long axis; RCI= respiratory caval index.
overestimated the diameter of the IVC when the IVC and M-mode line were not orthogonal (Figure 3). We used M-mode because we could easily visualize and record the respiratory phasicity in the IVC and choose the maximum and minimum diameters. Techniques available for measuring the IVC diameter will depend on the machine settings. As long as the measurements are taken consistently and the serial changes are the desired measurement, the method of calculation should produce the same result with similar potentials for measurement error.

In 1998, Jeffrey et al. reported that a flat vena cava seen on abdominal computed tomography scan in blunt abdominal trauma patients was predictive of the need for emergency surgery to control hemorrhage (2). In 2005, Yanagawa et al. noted a correlation between IVC diameter < 9 mm and the need for blood transfusion in traumatically injured patients (4). Sefidbakht et al. found a statistically significant difference in the IVC diameter of patients in traumatic shock compared with normotensive patients (6). A more recent study showed that serial changes in IVC diameter were more reliable in predicting ongoing hemorrhagic shock than blood pressure or heart rate (5). Wo et al. found that non-survivors maintained blood pressure during concomitant decreased cardiac output until a precipitous drop in blood pressure occurred (1). These studies suggest that catecholamine and neurohormonal influences on maintaining heart rate and blood pressure may mask ongoing hemorrhage. Although the current model did not detect clinically significant changes in IVC diameter after blood donation, ultrasound may still be useful to detect stage-one hemorrhagic shock in the trauma patient with ongoing blood loss by using serial measurements and response to intravenous fluids. For example, if IVCmax decreases by 25% after 1-L fluid bolus, ongoing blood loss may be suspected. In addition to IVC diameter measurements being completely non-invasive, if IVC diameter can be shown to be independent of catecholamine output, the utility of this non-invasive measurement will be even greater.

Pseudohypertrophy of the left ventricle has been reported as another possible non-invasive marker for early hemorrhagic shock. Di Segni et al. measured an increase in the thickness of the left ventricle in pigs that were bled of 30% of their circulatory volume (7). The current study was not able to reproduce these results using human models after a smaller percentage circulatory volume loss. Measurement error may have obscured any small change in the ventricular thickness or there may not have been enough blood volume lost to produce a significant change in the ventricular thickness. Although these measurements did not produce meaningful results in the current study, other cardiac measurements, such as hyperdynamic cardiac function or end-systolic left ventricular collapse have been useful in other human studies of predicting volume status non-invasively (11).

Limitations

The main limitations in this study are the potential for measurement error in IVC diameter measurements and the imperfect model of blood donation for early hemorrhagic shock. Measurements were obtained with resting respiratory phasicity, which varies depending on how deeply a patient breathes at rest. In analyzing pre- and post-measurements of IVCmax and IVCmin, we expected to find only decreases in numbers; however, IVCmax measurements increased in seven cases in short axis and five cases in long axis. IVCmin measurements increased in 15 cases in short axis and seven cases in long axis. Whereas IVCmin increases are likely the result of variability in breathing, IVCmax increases are more likely a measurement error. The contribution of neurohormonal influences in IVC changes during blood loss is unclear. Risk factors for IVCmax measurement errors were higher BMIs (8 of 12 had higher BMI than mean BMI) and smaller starting IVC diameter (11 of 12 had a smaller starting diameter than the mean).

Using blood donors to mimic early hemorrhagic shock is convenient but imperfect. The study may have produced different results if we had allowed the subjects’ blood volume to equilibrate. The changes in IVC diameter are so small in this model that minor errors due to body habitus or respiratory variability have a greater impact on the results. In a trauma patient with ongoing blood loss exceeding 500 cc, serial changes in the IVC may be more impressive. Other limitations to the study are the small sample size and the non-blinding of the sonographers.

Figure 3. Note that the M-mode line is < 90 degrees to the long axis of the inferior vena cava (IVC) and therefore overestimates the anteroposterior measurement of the IVC diameter in this patient.
CONCLUSION

Serial changes of IVC diameter after 500 cc of blood loss were clinically insignificant. Sonographic measurement errors were more frequent in short-axis measurements than long-axis measurements, and subjects with higher BMIs and smaller starting IVC diameters. The response of the IVC to catecholamine output should be further investigated.

Acknowledgment—The authors wish to thank Lifeshare Community Blood Services for participating in this study.

REFERENCES


ARTICLE SUMMARY

1. Why is this topic important?
   Finding a tool to non-invasively detect early blood loss is important.

2. What does this study attempt to show?
   Ultrasound does not detect early blood loss.

3. What are the key findings?
   After approximately 500 cc of blood loss, healthy blood donors had no clinically significant changes in inferior vena cava diameter, left ventricular wall thickness, or vital signs.

4. How is patient care impacted?
   Ultrasound is not reliable to detect early hemorrhage.