Atrial Structure and Function

New Method for Noninvasive Quantification of Central Venous Pressure by Ultrasound

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Background—The central venous pressure (CVP) is essential for assessing the cardiac preload and circulating blood volume in clinic. The invasive CVP measurement by central venous catheter has been reported with various complications. The aim of this study was to develop a new noninvasive method for quantification of CVP by ultrasound.

Methods and Results—Seventy-six patients who had their CVP monitored for intraoperative or postoperative management were recruited. By accurate location of the collapse point of the internal jugular vein and the center of the right atrium using ultrasound imaging, the height of the fluid column between those 2 points was measured as the noninvasive CVP (CVPn). A total of 118 measurements were performed and compared with the invasive CVP (CVPi). Linear correlation analysis revealed a significant correlation between CVPi and CVPn (preoperative measurements, r=0.90; P<0.01 and postoperative measurements, r=0.93; P<0.01). Bland–Altman plots showed a good agreement between CVPi and CVPn with the mean difference of 0.22 mm Hg (preoperative measurements) and −0.09 mm Hg (postoperative measurements), respectively.

Conclusions—The new noninvasive CVP quantification method based on the location of both the collapse point of internal jugular vein and the center of right atrium by ultrasound could be used as a reliable approach for monitoring the hemodynamic status in clinic. (Circ Cardiovasc Imaging. 2015;8:e003085. DOI: 10.1161/CIRCIMAGING.114.003085.)

Key Words: central venous pressure ■ ultrasonography

Central venous pressure (CVP) is frequently used in clinical practice for the assessment of volume status and cardiac preload.1 Accurate determination of CVP is essential for the management of a variety of critical illnesses and monitoring hemodynamics during the surgery.2,3 CVP can be measured directly via central venous catheterization, but it is invasive with potential complications.4,5

See Clinical Perspective

Since first proposed by Sir Thomas Lewis in 1930, the noninvasive determination of CVP using the physical examination has not been widely used all along.6 This is mainly because it is hard to accurately locate the 2 end points of the fluid column whose height represents CVP.7,8 Even though some investigators proposed that ultrasound could be used to identify the highest point of oscillation of the jugular vein,9 however, the other end point, that is, the center of the right atrium (RA), still could not be identified precisely. Obviously, the key factor for the disagreement and inaccuracy between studies of CVP measurement is the failure to locate the external reference point of RA in patients with various positions.1,11

We thus sought to explore a new echocardiographic method to locate the center of RA precisely based on solid geometry, and to develop a noninvasive method of quantification of CVP by combination with the location of the collapse point of the jugular vein by ultrasound.

Methods

Preliminary Validation of the Echocardiographic Location of RA Center by Comparison With Computed Tomography

Patients and Data Collection

This study was performed at our institution, a tertiary medical center. Patients who were candidates for multi-slice three-dimensional computed tomography (3D-CT) of the chest were recruited. Age, sex, height, body mass index, and clinical diagnosis were recorded for all patients. Informed consent was obtained from all patients and the study was approved by the ethics committee of Fourth Military Medical University.

CT Examination

Chest 3D-CT were performed on the patients with the use of a General Electric Light-Speed VCT scanner (General Electric, Milwaukee, WI). The data were further reconstructed into 3D images with the General Electric Advantage Windows 3D workstation (General Electric, version 4.5). These reconstructed images were then processed at the workstation into color-shade surface display and shaded volume render images. With the 3D volume rendering images and the...
corresponding 2D images, the center of RA was located by the scanner technician. When necessary, we rotated the 3D volume rendering image to display the standard coronal view. After locating the center of RA in the corresponding 2D images, we acquired the same point in the 3D image by autoprocessing at the workstation. The accurate position of that point in the coronal plane was recorded as shown in Figure I in the Data Supplement.

**Echocardiography**

Patients were kept in the same supine position as done during the previous CT examination. A commercially available echocardiography system equipped with a 3.5 MHz transducer (Vivid E9; General Electric Healthcare, Milwaukee, WI) was used to scan the heart. First, an adjusted apical 4-chamber view in which the RA was placed in the middle of the sector image was acquired. The distance from the top of image to the center of RA was measured and recorded. Then the probe was fixed at the image acquired direction and position by the operator. The assistant put a pencil next to the probe and made it perpendicular to the coronal plane. After that, a ruler with its direction parallel with the long-axis of the probe was used to locate the surface projection of the center of RA. The ruler was made intersected with both the pencil and the anterior chest wall, and distance between the 2 intersections was kept the same distance as previously recorded. The intersection of the ruler and the anterior chest wall was the surface projection of the center of RA on the anterior chest wall. The distance between the probe contact point and the surface projection of the center of RA (Figure 1). The time needed for the locating process was recorded.

**Comparison and Analysis**

After the surface projection of the center of RA located by echocardiography was marked, the surface projection point acquired with CT was also marked in the anterior chest wall. Then the absolute distance (Da) and vertical distance (Dv) between the 2 points in the direction of coronal plane were measured. As the point marked according to CT location was the standard point, if the echo-location point was superior to it, Dv was defined as +, otherwise − (Figure S2).

To evaluate the accuracy of the echo-location method, mean value and 95% confidence interval (CI) of Da, Dv were calculated. To evaluate the feasibility, data in both men and women were obtained and compared using Student unpaired t test, and the time spent on the ultrasound location was also recorded.

Fifteen patients were randomly selected to assess the inter- and intraobserver reproducibility. For the interobserver reproducibility assessment, location point marked by 1 of the 2 investigators was identified as the standard point, if the other point was superior to it, Dv was defined as +, otherwise −. For the intraobserver reproducibility assessment, the first-time location point was identified as the standard point. Mean value and 95% CI of Da, Dv were calculated.

**Comparison of the Noninvasive and Invasive Measurements of CVP**

**Patients and Data Collection**

Patients who would have their CVP monitored for intraoperative or postoperative management were eligible for enrollment. Exclusion criteria were neck injury at the measurement site, mass of neck that could compress the internal jugular vein (IJV), thrombosis or altered blood flow in the IJV, uncontrollable exaggerated or irregular respiration, incapability of semireclining position, significant tricuspid regurgitation, and poor echocardiographic windows. Informed consent was obtained from all patients before the measurement. The study was approved by the ethics committee of our university.

**Noninvasive Measurement of CVP by Ultrasound**

The noninvasive measurements of CVP were performed before or after the surgical operation.

**Location of the Center of RA.** Patients were kept in a supine position. A commercially available portable ultrasound machine (M-Turbo; SonoSite Inc, Bothell, Washington, DC) equipped with a 3.5 MHz transducer (P21x/5-1 MHz) was used. The location procedures were the same as described in the preliminary validation study above. After the surface projection of the center of RA on the anterior chest wall was located, the transverse plane that contained the RA center point was also obtained. The intersections of the bilateral midaxillary lines and that plane were marked.

**Location of the Collapse Point of IJV.** A broadband linear array transducer (L38xi/10-5 MHz) was used to visualize the IJV. The probe was moved gently on the neck rotating between longitudinal and transverse views to locate the region of vein collapse. The bed angle was

![Figure 1. Location of the center of right atrium.](image1)

**Figure 1. Location of the center of right atrium.** A, Adjusted apical 4-chamber view. This view is acquired by adjusting the standard apical 4-chamber to make the right atrium in the middle of the sector image. The length of line segment AB represents the distance between the probe contact point and the center of the right atrium. B, Location procedure. The probe is fixed after acquiring the image shown in A. A pencil is put next to the probe and make it perpendicular to the anterior chest wall. The ruler is made to be in parallel with the long-axis central line of the probe and to intersect with both the stick and the anterior chest wall. The distance between the 2 intersections is equal to segment AB in A. The intersection of the ruler and the anterior chest wall is the surface projection of the center of the right atrium.

![Figure 2. Collapse region of the internal jugular vein.](image2)

**Figure 2. Collapse region of the internal jugular vein.** A, Longitudinal view of internal jugular vein (IJV). The skin surface is at the top of the figure and the total depth of the image is 2.5 cm. The left side is cephalad. The arrow shows the highest point of oscillation of the IJV. This is where the jugular pulsations are present in real-time. B, Corresponding transverse view of IJV. ICA indicates internal carotid artery.
adjusted to yield the best view. The highest point of oscillation of IJV was marked on the neck using the longitudinal view (Figure 2).

Measurement of CVP. Without changing the bed angle, the height between the collapse point of IJV and the previous marked point in the midaxillary line was measured, and the value was recorded as noninvasive CVP (CVPn, cm H2O) and converted to millimeters of mercury (1 mm Hg=1.36 cm H2O). The measurements were made at the right IJV before the surgical operation and at the left IJV after the operation. The time for noninvasive measurement was recorded.

Invasive Measurement of CVP by Central Venous Catheter
The central venous catheterization measurement of CVP was done within 15 minutes after the noninvasive measurement by ultrasound. The central venous catheters were inserted into the right IJV or subclavian vein by an experienced anesthesiologist after the standard procedures. Then the catheters were connected to the multimodular monitor (S/5; GE Datax-Ohmeda, Helsinki, Finland) via a pressure transducer. After the transducer had been zeroed to the level of the heart, the mean value of CVP (cm Hg) over time was displayed real time on the monitor and recorded as invasive CVP (CVPi). The CVPi was continuously monitored after operation. The ultrasound investigator was blinded to the CVPi results and vice versa.

Statistical Analysis
Statistical analysis was performed using SPSS 20.0 (SPSS, Inc, Chicago, IL). Normality distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Data were presented as mean±SD. Student paired t test was used to compare CVPi versus CVPn for the preoperative and postoperative measurements separately. Correlations between CVPi and CVPn were estimated using Pearson correlation. Bland–Altman analysis was performed to quantify the agreement between CVPi and CVPn. The data from patients who underwent both the preoperative and postoperative measurements were used to verify the ability of the noninvasive method in tracking changes in CVP. Where appropriate, 95% CIs were reported. For all analysis, a 2-sided P<0.05 was considered significant.

Results
Preliminary Validation of the Echocardiographic Location of RA Center
A total of 40 patients were recruited into this study. Patient characteristics were given in Table 1 in the Data Supplement. By 3D-CT location, levels of the mid-RA varied from the third intercostal space at the sternum to the upper limb of the sixth costal cartilage.

Accuracy and Feasibility of Echo-Location
Mean Da and Dv of the whole subjects were 0.77 cm, 0.04 cm, and the mean time spending on the locating process was 42.52 s, with no significant difference between the men and women groups (Table S2). The points located by CT and echocardiography were almost at the same level in the vertical direction of the coronal plane with the 95% CI of Dv (−0.13 to 0.21 cm).

Reproducibility
Inter- and intraobserver reproducibility for echocardiographic method were summarized in Table S3. With respect to the degree of accuracy for location of RA, the echocardiographic method was found to be highly reproducible in terms of both inter- and intraobserver variability.

Comparison of the Noninvasive and Invasive Measurements of CVP
Seventy-six patients were recruited into this study. Patient characteristics were given in Table 1. Details of clinical diagnoses were given in Table S4. A total of 118 noninvasive measurements by ultrasound were performed (74 preoperative measurements and 44 postoperative measurements). The mean time for noninvasive measurement was ~3 minutes (182±47 s).

The values of CVPI and CVPn were compared in Table 2. No statistically significant difference was found for both preoperative and postoperative measurements. The correlation and Bland–Altman plots between CVPi and CVPn were shown in Figure 3. Linear correlation analysis revealed a significantly positive correlation between CVPi and CVPn (preoperative measurements, r=0.90; P<0.01 and postoperative measurements, r=0.93; P<0.01). Bland–Altman plots showed that the mean bias between CVPi and CVPn was 0.22 mm Hg with the limits of agreement being −2.16 to 2.59 mm Hg (preoperative measurements) and −0.09 mm Hg with the limits of agreement being −2.12 to 1.94 mm Hg (postoperative measurements). There was no systematic bias between CVPi and CVPn. The bias in preoperative measurements was slightly larger than postoperative measurements (0.22 mm Hg; 95% CI, −0.06 to 0.50 mm Hg versus −0.09 mm Hg; 95% CI, −0.41 to 0.22 mm Hg).

There were 42 patients who had 2 sets of measurements. The mean bias between changes in CVPI and CVPn was −0.08 mm Hg (95% CI, −0.43 to 0.26 mm Hg) with the limits of agreement being −2.25 to 2.08 mm Hg. Correlation analysis showed a high degree of correlation between changes in CVPI and CVPn (r=0.91; P<0.01).

Discussion
In this study, a new noninvasive method for CVP quantification was developed by location of both the collapse point of IJV and the center of RA using ultrasound. CVPn determined using our new method has been proven to have a strong correlation and high agreement with the CVPi measured by the central venous catheterization.

CVP is essential for monitoring hemodynamics in critically ill patients and estimating the cardiac preload and circulating...
blood volume in surgery.\textsuperscript{1-3} The current standard technique for measurement of CVP is invasive, requiring insertion of a catheter into the subclavian or IJV, and has potential complications.\textsuperscript{4,5,14} Therefore, a noninvasive, simple and accurate method of CVP quantification is greatly needed, especially in cases of hemodynamic emergencies.
The noninvasive estimation of CVP by physical examination has been described by Sir Thomas Lewis, and refined by a lot of investigators.\textsuperscript{6,11,15,16} However, because this method is difficult to master and lack of accuracy, it has not been widely used all along. In recent years, some investigators tried to improve the accuracy of this noninvasive method by identifying the collapse point using ultrasound, but the improvement was limited for their significant bias after comparing with the invasive measurement.\textsuperscript{9,10} Indeed, the height of the blood column in the jugular veins that represents CVP could not be precisely quantified only if both the collapse point of IJV and the center of RA are accurately located. Thus, the key obstacle to the noninvasive CVP measurement is the failure to accurately locate the external reference point of RA in patients with different positions. There are a few methods that have been proposed for locating the center of RA (or mid-RA). The most widely used method is to assume that the distance from the sternal angle to the upper limb of the sixth costal cartilage verified by 3D-CT examination. Seth et al\textsuperscript{17} had proven that the vertical distance from sternal angle to the level of mid-RA varies considerably between individuals and with patient’s different positions. Another method to mark the mid-RA is to find the intersection of the midaxillary line and a perpendicular extended to the fourth intercostal space at the sternum.\textsuperscript{11} However, the levels of mid-RA varied from the third intercostal space at the sternum to the upper limb of the sixth costal cartilage verified by 3D-CT examination. Obviously, both of these 2 methods ignored the differences of patient’s clinical status and position, and thus neither of them could serve as a reliable method for locating the center of RA, and accordingly, for the assessment of CVP.

Ultrasound has been widely used as an optimal tool of localization and guidance in clinic.\textsuperscript{18,19} However, the main part of RA is sheltered by the sternum, making it difficult to directly locate the RA center by echocardiography. To solve this problem, we proposed this geometric method to locate the surface projection of the center of RA under the guidance of echocardiography. Figure 4 illustrates the spatial relationship in the RA location procedure. The line segment between points A and B is in the same direction with the probe long-axis, and the 2 end points represent the center of RA and the contact point between the probe and the anterior chest wall, respectively. Line segment CD that represents the ruler parallels and has equal length with segment AB. Thus, quadrilateral ABCD is a parallelogram. Because segment BC is perpendicular to the coronal plane that contains the contact point B, segment CD is also perpendicular to the coronal plane. Finally, point D is the surface projection of point A, that is, the center of RA.

Thus, the precise measurement of CVP was realized by accurately locating the collapse point of IJV and the center of RA by ultrasound using our new method, and the results were confirmed by comparison with the central venous catheterization. The Bland–Altman plot revealed no tendency for a systematic bias and the linear correlation analysis showed a high degree of correlation between CVPi and CVPn. With respect to the ability of the noninvasive method in tracking changes in CVP, Bland–Altman analysis revealed a good agreement between changes of CVPi and CVPn (mean bias, −0.08 mm Hg), which indicated that the new method could track changes in CVP reliably. The slight discrepancy in bias between the preoperative and postoperative measurements (0.22 versus −0.09 mm Hg) might be caused by several factors, such as the observation point of the noninvasive measurements and the time interval between the invasive and noninvasive measurements.

Even though there were some other noninvasive methods of CVP measurement, such as controlled compression sonography on the peripheral vein,\textsuperscript{20,21} forearm volume plethysmography,\textsuperscript{22,23} and neck inductive plethysmography,\textsuperscript{24} they relied on additional instruments that are not readily available in routine clinical practice. By contrast, the instruments that we use in the new method of quantification of CVP are just a ruler and a pencil besides a portable ultrasound machine, which is widely available. Thus, this method is applicable for bedside measurement.

Furthermore, because CVP is equal to the right atrial pressure as long as there is no obstruction of the vena cava, the noninvasive measurement of CVP could be useful in noninvasive estimation of the pulmonary arterial pressure. In comparison with currently used semiquantitative Doppler echocardiographic methods for estimation of the right atrial pressure,\textsuperscript{3} our new quantitative method might be a better choice.

Limitations

There are several limitations to this new method that may limit its clinical application. First, the presence of any mass that
compresses the IJV, thrombosis, or altered blood flow in the central vein that impedes venous return will cause a false measurement. Previous neck injury, IJV cannulation will interfere the measurement. Second, uncontrollable exaggerated or irregular respiration and significant tricuspid regurgitation will disturb the measurement of CVP. Third, this new method for noninvasive measurement of CVP may not be practical to monitor the CVP continuously, but could be repeatedly performed if needed with no harm to the patient.

Conclusions
The new method for noninvasive quantification of CVP based on the ultrasound location of the collapse point of the IJV and the center of RA might be an alternative approach for monitoring the volume status and cardiac preload in clinic.

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Disclosures
None.

References

CLINICAL PERSPECTIVE
Knowledge of central venous pressure (CVP) is essential for monitoring hemodynamics in critically ill patients and estimating cardiac preload and circulating blood volume in surgery. The current standard technique for measuring CVP is invasive, requiring insertion of a catheter into the subclavian or internal jugular vein, and has potential complications. The noninvasive estimation of CVP by physical examination has been described by Sir Thomas Lewis, and refined by subsequent investigators. However, because of the challenges of mastering the technique and its lack of accuracy, this approach is not used quantitatively. In this study, precise and noninvasive measurement of CVP was achieved by accurately locating the collapse point of the internal jugular vein and the center of the right atrium by ultrasound using our new method, with the results confirmed by comparison with invasively measured CVP. The instruments used in this new method are widely available and portable, making it applicable for bedside measurement in critically ill and emergency room patients. Furthermore, because CVP is equal to the right atrial pressure as long as there is no obstruction of the vena cava, this new noninvasive and quantitative measurement of CVP is also a crucial step toward an accurate noninvasive determination of the pulmonary arterial pressure based on the right ventricle–right atrium gradient calculated by echocardiography.
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SUPPLEMENTAL MATERIAL

Supplemental Tables

Table S1. Characteristics of 40 patients in the preliminary validation of the echo-location method

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>46.1 ± 11.1</td>
</tr>
<tr>
<td>Male (Female)</td>
<td>21 (19)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.4 ± 6.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59.7 ± 9.6</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>21.5 ± 2.7</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
<td>72 ± 11</td>
</tr>
</tbody>
</table>

Data are given as mean ± SD.

Table S2. Accuracy and feasibility of the echo-location method

<table>
<thead>
<tr>
<th></th>
<th>All (n=40)</th>
<th>Male (n=21)</th>
<th>Female (n=19)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Da, cm</td>
<td>0.77±0.25 (0.69, 0.85)</td>
<td>0.74±0.24 (0.63, 0.85)</td>
<td>0.81±0.26 (0.68, 0.94)</td>
<td>&gt; 0.10</td>
</tr>
<tr>
<td>Dv, cm</td>
<td>0.04±0.55 (-0.13, 0.21)</td>
<td>-0.07±0.54 (-0.31, 0.17)</td>
<td>0.16±0.53 (-0.09, 0.43)</td>
<td>&gt; 0.10</td>
</tr>
<tr>
<td>Time, sec</td>
<td>42.52±9.65 (39.4, 45.6)</td>
<td>43.71±9.34 (39.46, 47.97)</td>
<td>41.21 ± 10.06 (36.35, 46.06)</td>
<td>&gt; 0.10</td>
</tr>
</tbody>
</table>

Data are given as mean ± SD and 95% CI (Lower bound, Upper bound). Values obtained in males and females were compared using Student’s unpaired t-tests. Da, distance between points located by CT and echocardiography in the direction of coronal plane. Dv, vertical distance between the two points.
Table S3. Inter-observer and intra-observer reproducibility for the echo-location method
(n=15)

<table>
<thead>
<tr>
<th></th>
<th>Da, cm</th>
<th>Dv, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inter-observer</td>
<td>0.45 ± 0.27 (0.29, 0.59)</td>
<td>0.05 ± 0.41 (-0.18,0.27)</td>
</tr>
<tr>
<td>intra-observer</td>
<td>0.34 ± 0.22 (0.22, 0.46)</td>
<td>-0.03 ± 0.30 (-0.20, 0.13)</td>
</tr>
</tbody>
</table>

Data are given as mean ± SD and 95% CI (Lower bound, Upper bound). Da, distance between the two points located either by two observers (inter-observer) or by one observer before and after (intra-observer). Dv, vertical distance between the two points.

Table S4. Details of clinical diagnoses of the patients for the central venous pressure measurements

<table>
<thead>
<tr>
<th>Clinical diagnosis for surgery</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic cirrhosis</td>
<td>22</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td>10</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>8</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>8</td>
</tr>
<tr>
<td>Carcinoma of pancreas</td>
<td>7</td>
</tr>
<tr>
<td>Gastroenteric tumor</td>
<td>6</td>
</tr>
<tr>
<td>Carcinoma of gallbladder</td>
<td>6</td>
</tr>
<tr>
<td>Liver cancer</td>
<td>3</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage</td>
<td>2</td>
</tr>
<tr>
<td>Common duct stones</td>
<td>2</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
</tr>
</tbody>
</table>

“Others” referred to intestinal obstruction and choledochoctasia.
Supplemental Figures with Figure Legends

Figure S1. RA location by CT

After locating the center of the right atrium (RA) in coronal plane and transverse plane through two-dimensional (2D) images (red dot), we got the same point (red dot) in the three-dimensional (3D) image by auto-processing at the workstation. Images in the top panel and the bottom panel were separately obtained from patients undergoing chest multislice 3D-CT with and without angiography.
Figure S2. Illustration of the definition of the vertical distance and absolute distance.

Point A represents the center of the right atrium located by CT, i.e. the standard point. Point B and D represent different positions of echo-location points related to the CT-location point. Segment BC and CD represent the corresponding vertical distance (Dv) between the points marked by the echocardiography and CT. If the echo-location point is superior (Point B), Dv is defined as “+”, otherwise “-” (Point D). Segment AD represents the absolute distance (Da).