Measurement of Central Blood Volume by External Monitoring

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With extensive application of the Hamilton-Stewart dye-dilution technique for measurement of central blood volume (CBV), it has become apparent that the method may be insensitive to small but significant changes in volume. Reasons for this, presumably, rest with the rather large volume measured and the inherent errors of the technique. Using a peripheral vein injection, the volume measured may be as high as 60 per cent of the total blood volume. Only by using pulmonary-artery injection can it be reduced to 20 per cent of total blood volume. It would appear that, with these large volumes, small but significant changes (on the order of 100 to 200 cc.) could occur in various disease states or acute situations without being detected.

Use of radioactive materials and external monitoring appears to offer a method for measuring just the blood in the heart and lungs without the need for cardiac catheterization. By the use of a sensitive counter over the precordium and a gamma-emitting isotope, separate peaks for right and left ventricular filling can be measured. The difference in time between the two peaks multiplied by the cardiac output gives a measure of pulmonary blood volume (PBV). Although the initial work with this technique was done by Prinzmetal in 1949, the central blood volume has not been studied in a large series of normal subjects. This investigation was undertaken to evaluate the technique in such a series.

Methods

Hospitalized ambulatory patients without evidence of cardiovascular disease were used in the study, the majority coming from the general medical wards of a Veterans Administration Hospital. A total of 39 patients is reported.

The external counter used was a DS 5-1 Nuclear Chicago probe, with a one-inch thallium-activated sodium iodide crystal. This was used with three different combinations of collimation and counter placement. In all cases, the counter was placed over the precordium under fluoroscopic control. The output from the counter was fed into a radiation analyzer using a five-volt window. This output, in turn, was fed into a binary sealer which had been modified to record four counts, or multiples thereof, as a deflection ("blip") on an oscillographic tracing. Both an electrocardiogram and an injection marker were recorded simultaneously on the tracing. The results were discarded when obvious variation in the heart rate during this measurement indicated an unsteady state. The oscillographic tracings of precordial activity were read as "blip" intervals per second and plotted on semi-log paper.

All patients were studied when fasting and supine. Under local anesthesia, an 18 Cournand needle was placed in the left brachial artery and, through a 14-gauge thin-walled needle in the right antecubital vein, a polyethylene catheter (length 30 cm., I.D. 1 mm.) was passed into the axillary vein and kept open with a drip of 5 per cent glucose and water. After the needles were placed, the patient was fluoroscoped and the counter positioned. The patient rested 10 minutes, and the first determination was then done, using 40 µc of radioactive iodinated human serum albumin (RISA) and a 20-ml saline rinse. To achieve as sharp a bolus of indicator in the right atrium as possible, a 3-ml capacity polyethylene tube was attached to the catheter. This was filled with RISA through one limb of a three-way stopcock, the limb was changed, and 20 ml of saline was rinsed in as rapidly as possible by syringe. With this rinse system, the indicator appeared in the right atrium within two seconds. After an additional 10 minutes' rest, a repeat determination was then done, using 40 µc of radioactive iodinated human serum albumin (RISA) and a 20-ml saline rinse. To achieve as sharp a bolus of indicator in the right atrium as possible, a 3-ml capacity polyethylene tube was attached to the catheter. This was filled with RISA through one limb of a three-way stopcock, the limb was changed, and 20 ml of saline was rinsed in as rapidly as possible by syringe. With this rinse system, the indicator appeared in the right atrium within two seconds. After an additional 10 minutes' rest, a repeat determination was then done, using 40 µc. Simultaneously with the external monitoring, cardiac output was determined using the interrupted-sample technique with samples taken from the brachial artery. Starting with the injection, samples were collected at two-second intervals in heparinized tubes for 48 sec-

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### Table 1*

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Cardiac index (L/min./M²)</th>
<th>Mean circulation time</th>
<th>Central blood volume (L./M²)</th>
<th>External monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td><strong>Series I:</strong> Single counter without added collimation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3.89</td>
<td>3.70</td>
<td>21.3</td>
<td>21.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.89</td>
<td>0.84</td>
<td>1.78</td>
<td>1.78</td>
</tr>
<tr>
<td><strong>Series II:</strong> Dual counters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3.54</td>
<td>3.52</td>
<td>21.2</td>
<td>21.3</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.28</td>
<td>0.39</td>
<td>4.09</td>
<td>4.24</td>
</tr>
<tr>
<td><strong>Series III:</strong> Single counter with added collimation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3.53</td>
<td>3.63</td>
<td>22.0</td>
<td>22.1</td>
</tr>
<tr>
<td>S.D.</td>
<td>0.83</td>
<td>1.07</td>
<td>5.4</td>
<td>5.6</td>
</tr>
<tr>
<td><strong>Series IV:</strong> Single counter with added collimation—run II done after tilting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>4.67</td>
<td>3.76</td>
<td>17.9</td>
<td>20.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>1.55</td>
<td>1.40</td>
<td>5.5</td>
<td>7.9</td>
</tr>
</tbody>
</table>

*Four detailed tables have been deposited with the ADI Auxiliary Publications Project as Document number 6557. A copy may be obtained by citing the Document number and by remitting $1.25 for photoprints, or $1.25 for 35 mm. microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress (address: Washington 25, D. C.).

Mean circulation time (MCT).

To calculate the output, the standard interrupted-sample dye-dilution technique was used, taking two second samples over a 48-second period. The samples were pipeted into distilled water and counted in a well counter. The results were plotted on semi-log paper, then replotted on linear graph paper. Cardiac output (COP) was calculated from the formula:

\[
\text{COP (L/min.)} = \frac{I \times 60}{c \times t}
\]

in which (I) equals the amount injected in counts/min., (c) equals the mean concentration for the curve in counts/min./L., and (t) equals the duration of single circulation in seconds. Central blood volume was calculated from the formula: CBV (L.) = MCT times COP in L/see. MCT is the mean circulation time (seconds) and is calculated used with this counter extended the 3.5-cm. shielding out to 10 cm. from the crystal, with an I.D. of 2.8 cm. The field seen was approximately straight for 10 cm. from the front. Series III consisted of nine patients studied with the single right ventricular counter of series II centered over the precordium. In series IV, which consisted of eight patients, the same counter was used, but for the second determination the patient was tilted 60 degrees toward the upright position. As soon as the counter could be repositioned, the determination was repeated.

The patients were divided into four groups, depending on counter placement and collimation. In series I, 12 patients were studied using only the basic shielding, with the counter centered over the precordium and aimed directly anteroposterior. The shielding consisted of 3.5 cm. of lead, with a 3.5-cm. diameter aperture, and the crystal was recessed 3.5 cm. from the front. In air, a field 6 cm. in diameter was seen 3 cm. from the front of the shield. This field increased to 9 cm. at 6 cm. from the front. In series II, 10 patients were studied using a dual-counter setup. One counter was centered over the right ventricle anteroposteriorly, and the aperture was then pointed 10 degrees to the left in order to avoid the superior vena cava. With this counter, the crystal was 3.5 cm. from the front of the shielding, and additional collimation was used so that the aperture diameter narrowed to 1.5 cm. at the front, gradually increasing to 2.5 cm. adjacent to the crystal. Using this additional shielding, the field was narrowed to approximately one-fifth that with the standard shielding used in series I. The second counter was aimed directly at the left ventricular apex and pointed 45 degrees to the right from the anteroposterior. The collimation rounds. To limit the amount of radioactivity to 100 µc, only two determinations were done in any one patient.
from the formula $MCT = \frac{\sum (C \cdot T)}{\sum C}$, in which

$(C)$ is the concentration at each one-second interval from the time of injection, and $(T)$ is the time from injection. Total blood volume was obtained by using the concentration from a sample taken 10 minutes after injection. The formula used was total blood volume (L.) $= \frac{\text{counts/min.}}{\text{concentration L.}}$ of the 10-minute sample. The volume so measured is not identical with total blood volume, but is considered accurate enough for use.5

For external counting using a single counter (series I, III, and IV), a peak time for each ventricle was obtained from the semi-log plot of the original oscillographic tracing. The right ventricular curve downslope was extrapolated and the extrapolated values subtracted from the left ventricular curve. Thus, the left side was corrected for the right-sided counts. The time between the right ventricular peak and the corrected left was used as the corrected pulmonary circulation time, and is similar to that described by Shipley et al.6 This time multiplied by the cardiac output in cc/sec, as determined from the arterial curve measured by the interrupted samples, was used as the pulmonary blood volume (PBV). This volume includes blood contained in both the right and the left ventricles, as well as that in the pulmonary vascular bed. With the dual-counter setup, a complete curve could be obtained for each ventricle, and thus a mean circulation time determined for each. The difference between the two times was used as the pulmonary circulation time, and the volume measured again includes blood in both the right and left ventricles and the pulmonary circulation.6

For the dual counters, a slope was calculated for each ventricle using the formula:

$$\text{slope} = \frac{\log e \cdot \text{cone. 1} - \log e \cdot \text{cone. 2}}{\text{time 2} - \text{time 1}}$$

A slope was calculated for the arterial curves by using the same formula.

Results

In figures 1 through 3, typical replotted curves obtained with the various counter positions and collimation are shown. As seen in figures 1 and 3, with the single counter only the corrected peak-to-peak time could be obtained. With the heavier collimation, the curve obtained showed a sharper peak for the right ventricle and a less sharp one for the left ventricle (fig. 3). Typical curves obtained with the dual counters are shown in figure 2. The left ventricular slope is drawn in. In general, this was done by eye, but when the slope was obtained by the method of least squares, the agreement was satisfactory.
The overall data obtained for each series are shown in Table 1. For the 33 patients taken as a group, excluding the tilting series, who were not considered to be in a steady state, the cardiac output obtained by arterial sampling gave a mean cardiac index of 3.74 L./min./M.² (S.D. ± 0.77) and a mean central blood volume of 1.27 L./M.² (S.D. ± 0.22). For this total group, the time components of the curve, as used by Wood, were: appearance time, 13.5 sec. ± 2.9; build-up time, 6.4 sec. ± 1.4; and disappearance time, 17.2 sec. ± 4.7. The mean percentage change in the cardiac index after 10 minutes was a decrease of 2 per cent with a S.D. of 12 per cent for the group as a whole. In analyzing the reproducibility of the central-blood-volume measurement at a 10-minute interval, the results are given separately for each series, depending on the collimation and counter positioning used. For series I (single counter without additional collimation), the second determination showed a mean fall of 7 ± 26 per cent for the arterial CBV, and a mean decrease of 5 ± 24 per cent for the external PBV.

In series II, with the dual-counter setup, the mean arterial CBV was 42 per cent of total blood volume. While the external counting PBV was 15 per cent of total blood volume, the mean change in 10 minutes was small, being zero for the arterial method and −2 per cent for the external method. However, the standard deviation of the change was ± 15 per cent for the arterial and only ± 8.7 per cent for the external method.

In series III, using a single heavily collimated counter centered over the precordium, the mean CBV by the arterial method was again 42 per cent of the total blood volume, compared with 14 per cent by external counting. The reproducibility of this series for arterial CBV was a mean increase of 3 ± 21 per cent; for the external PBV, 13 ± 37 per cent.

In series IV, done before and after tilting for comparison of external monitoring and arterial CBV in following acute changes, both the PBV and the arterial CBV changed in the same direction in all except two subjects. In all series, the correlation between output and CBV or PBV was 0.5 to 0.6.

Using the dual counters, a slope was calculated for the right and left ventricles and for the arterial curves. The mean slope for the right ventricle was 0.54 ± 0.20; for the left, 0.27 ± 0.07; and for the arterial curves, 0.21 ± 0.03.

**Discussion**

Application of external monitoring techniques to measurement of "central blood volume" is exceedingly attractive in theory, offering, as it does, a method of measuring just the blood in the heart and lungs without the need for elaborate catheterization procedures. In this study, use of a single counter centered over the precordium permitted measurement of a volume which, although somewhat vague in its boundaries, was limited to the blood in the heart and lungs and was only one-third of the conventional "needle-to-needle" volume from the catheter to the brachial artery. However, using the single counter with or without high collimation, the upslope for the left ventricular curve was obscured, and only a peak-to-peak time could be obtained. There are both theoretical and practical objections to
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use of this time, even if the left side is corrected for the right.

First, in theory, in any measurement of volume by the Stewart formula, which uses the product of time and flow, the time should be a mean circulation time.\(^6\)\(^7\) This represents the average time of passage for a series of small and hypothetically isolated units of blood which move at different rates because of chance variation. Second, the mean circulation time is most advantageous on a practical basis, as it offers a method of mathematically smoothing the curve. The curves obtained by monitoring are at best somewhat irregular, as can be seen in figures 1 through 3, and a peak-to-peak time can vary by one to two seconds for this reason. This source of error can be reduced by the use of a mean circulation time. In this study, it was found necessary to use a separate counter aimed at the left ventricle to obtain the mean circulation time for the left side. The superiority of the mean circulation time over the peak-to-peak time can be seen in the reproducibility studies; only in series II, where the mean times were used, is the reproducibility of the pulmonary blood volume better than that of the conventional ‘‘needle-to-needle’’ volume.

Using either the single or dual counters, the pulmonary blood volume measured is approximately one-third of the ‘‘needle-to-needle’’ volume, and 15 per cent of the total blood volume. While this is somewhat at variance with the results of Pritchard et al. and Lammerant, who found 25 per cent,\(^6\)\(^9\) the mean circulation times are similar to those found by Shipley et al. with this technique,\(^6\) and assuming a normal cardiac output, the volume would be the same. There is, at present, no method for accurately measuring central blood volume in normal subjects, so proof of the validity of the 15 per cent figure is lacking. This volume, however, is reproducible and would appear to be small enough to be sensitive to rather small changes.

Summary

Central blood volume was measured in 39 normal subjects, using external monitoring and interrupted arterial samples. The volume obtained by external counting was 15 per cent of the total blood volume, compared with 42 per cent obtained with the arterial curve. The importance of collimation and counter position was evaluated, and only with a dual-counter setup could a mean circulation time (MCT) for each ventricle be obtained. An MCT was necessary for satisfactory reproducibility of externally measured central blood volume. While the method has limitations, it does appear to offer a technique for measuring just the amount of blood in the heart and lungs with a satisfactory reproducibility, and would appear to be worth further application in problems involving measurement of central blood volume.

References

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