Influence of Attenuation on Radionuclide Stroke Volume Determinations

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Using a method for determination of absolute volumes, including correcting for attenuation, we have explored the ability of the method to determine stroke volume in humans by radionuclide techniques. Thermodilution cardiac output determinations and multigated equilibrium blood-pool scintigraphy in the LAO view were performed simultaneously in twenty patients in which no evidence of intracardiac shunts or valvular disease was present. The correlation was good between the attenuated radionuclide and thermodilution stroke volume ($r = 0.80$, s.e.e. of estimate = 12 ml; $SV_{td} = 2.31 \times SV_r + 18$ ml). When correction for attenuation was made, the correlation improved ($r = 0.96$, s.e.e. = 6 ml) and approached the line of identity ($SV_{td} = 0.99 \times SV_r + 1.2$ ml). The correlation was also good between radionuclide cardiac output, corrected for attenuation, and the thermodilution cardiac output ($r = 0.89$, s.e.e. = 0.36 l/min; $CO_{td} = 0.86 \times CO_r + 0.67$ l/min). Thus our method of correction for attenuation in the determination of absolute left-ventricular volumes has been shown to provide a reliable, noninvasive means of calculating stroke volume and cardiac output in humans, without the use of geometric assumptions or regression equations.

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Multigated equilibrium blood-pool scintigraphy has provided a noninvasive means of assessing cardiac function (*1*,*2*). Methods to calculate left-ventricular ejection fraction accurately (*3*,*4*) and to assess left-ventricular wall motion qualitatively (*5*) and quantitatively (*6*) using ECG-synchronized blood-pool images have been developed. More recently, techniques have been developed to calculate left-ventricular volume indices from gated blood-pool scintigraphy (*7–9*). The geometrical analysis of spatial measurements obtained from contrast ventriculography, using a prolate-ellipsoid model, have also shown good correlations between actual and calculated volumes (*10–12*). However, the calculation of volumes from the left-ventricular silhouette using geometric models requires assumptions that may not be valid, especially during systole (*13*,*14*). The use of a regression equation to correct the volume index derived from scintigraphy to the volume that would be obtained using the geometric model for contrast ventriculography is the essence of the most recently developed techniques.

The effects of attenuation are not accounted for in the most recently presented techniques. Of the 140-keV photons of Tc-99m, less than a third can penetrate 10 cm of water, although 85% can penetrate 2 cm. It seems, therefore, that correction for at least the self-attenuating effects of the left ventricle should be made. Links et al. have described a technique for calculating absolute left-ventricular volumes using a count attenuation method (*18*).

The purpose of this study was to assess the utility of nongeometric methods, both with and without correction for attenuation, for the determination of stroke volume and cardiac output.

METHODS

Twenty patients were studied, each within the hour following routine cardiac catheterization. None of them had clinical or angiographic evidence of valvular disease or a cardiac shunt. Simultaneous measurements of car-

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diac output with the thermodilution technique (*15,16*) and ECG-synchronized equilibrium blood-pool scintigraphy were made on each patient.

Under fluoroscopic monitoring, the tip of a catheter* was advanced to the proximal portion of the right or left pulmonary artery. At approximately one-minute intervals, bolus injections of sterile saline solution (10 ml at 0°C) were introduced into the right atrium through the proximal lumen, and the resultant change in temperature at the thermistor was recorded. Cardiac output was calculated with an analog cardiac-output computer.† Four or five thermodilution determinations of cardiac output were recorded throughout the acquisition of the scintigraphic data. Stroke volume was calculated by dividing the cardiac output by the heart rate. For the thermodilution values, the heart rate during the dilution process was used. For the radionuclide values, the average heart rate over the 5-min acquisition was used. The average of the thermodilution cardiac output values was used for the correlation with the cardiac output derived from the radionuclide data.

Following in vivo RBC labeling with 20–25 mCi of Tc-99m (*17*), patients were imaged supine in the left anterior oblique view that gave the best separation of the left ventricle from other chambers of the heart. Twenty-four ECG-synchronized images were acquired in 64- by 64-byte mode (zoom factor = 1.3) for five minutes using a mobile gamma camera equipped with a low-energy all-purpose parallel-hole collimator, interfaced with a commercial system for computer-controlled acquisition, processing, and display. A 20% window centered on the photopeak of the Tc-99m spectrum was used for all images. Halfway through the data acquisition, a 12–14 ml sample of blood was withdrawn from a peripheral vein. After completion of this view and without moving the patient or the camera, a small ("point") source of Co-57 was placed on the patient's chest in the middle of the left ventricle as perceived on the persistence scope of the camera. The camera was then placed in the anterior position and a 200,000-count image was stored in 128- and 128-byte mode (no zoom); the Co-57 marker was then removed and the imaging continued until 800,000 counts were acquired. Following acquisition of the anterior static view, two 5-ml aliquots were pipetted from the blood sample to petri dishes and imaged on the camera system for 10 min at a distance of 5 cm from the collimator.

For each frame in the cardiac cycle, activity within the region of the left ventricle was determined using a second-derivative edge-detection algorithm. For background correction we used a region six pixels wide and displaced three pixels parallel to the infero-lateral edge of the end-systolic region of interest. A background-corrected left-ventricular time-activity curve was generated from these regions of interest. From the static anterior view, the distance from the center of gravity of the left ventricle to the chest-wall marker was determined using a computer program. This program calculates the center of gravity of the counts from the left ventricle within an observer-placed ellipse. The observer then moves a cursor from this point to the center of the image of the Co-57 point source. This distance is then converted from pixels to centimeters through multiplication by the calibration value determined previously (5 pixels/cm for our instrument) from an orthogonal hole phantom. The attenuating distance (d) is then calculated by dividing by the sine of the angle of the LAO view (*18*).

The count rate from the blood sample was obtained by averaging the duplicate aliquots, dividing the total counts by the acquisition time (10 min) and back-correcting for radioactive decay from the time the sample was withdrawn during the gated acquisition to the time it was counted. Left-ventricular volumes were then determined by substitution of the values from the time-activity curve into the following formula:

$$Va = \frac{\text{LV cps}}{e^{\lambda t} \times \text{aliquot cps/ml}} \qquad (1)$$

where:

LV numerator is background-corrected counts/sec from the region of the left ventricle. Aliquot is the background-corrected counts/sec from the region of the aliquot image and averaged over two aliquots. λ is the time decay constant, per hour, for Tc-99m = 0.693/6.02. t is the time in hours between imaging the left ventricle and counting the aliquots. Va is the attenuated volume (ml).

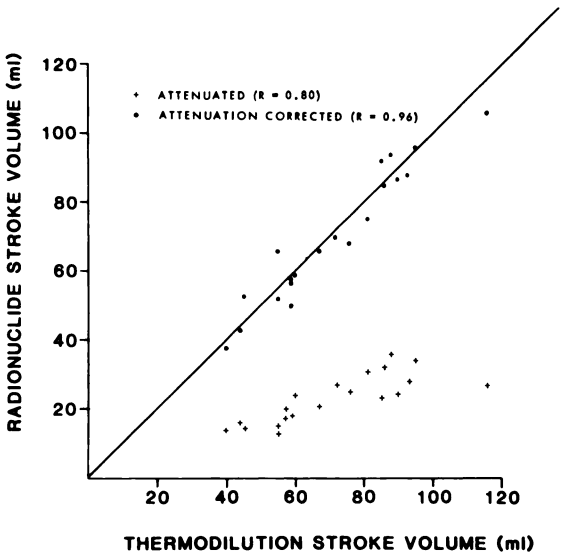

FIG. 1. Relation between thermodilution and scintigraphic stroke volumes. Attenuation-corrected values (·) closely approach identity line (s.e.e. = 6 ml) and are significantly different ($P < 0.05$) from attenuated values (+).

The attenuation-corrected volume was calculated by:

$$Vc = Va \times e^{\mu d} \quad (2)$$

where:

μ is the linear attenuation coefficient (0.15/cm), d is the attenuating distance in centimeters between the collimator face and the center of the left ventricle, Vc is the attenuation-corrected volume.

The value of 0.15/cm is the linear attenuation coefficient for Tc-99m in water and is chosen here to represent an average value for blood, bone, muscle and lung tissue (*18*).

RESULTS

The values for stroke volume (Table 1), determined by dividing the thermodilution cardiac output by the heart rate, ranged from 40 to 116 ml with a mean value of 71 ± 20 (s.d.) ml (*20*). The values of attenuated stroke volume from radionuclide techniques ranged from 13 to 36 with a mean value of 23 ± 7 ml. The values of stroke volume corrected for attenuation ranged from 38 to 106 with a mean of 70 ± 19 ml. There was a significant difference ($P < 0.05$) between the thermodilution and attenuated radionuclide stroke volume.

The correlation coefficient (Fig. 1) between the thermodilution and attenuated radionuclide stroke volume was r = 0.80 with a standard error of the estimate equal to 12 ml.

Thermal SV = 2.31 × radionuclide SV + 18.

When correction for attenuation was made, the correlation between thermodilution and radionuclide stroke volume improved to r = 0.96 with a standard error of the estimate equal to 6 ml.

Thermal SV = 0.999 × radionuclide SV + 1.2 ml.

The values for the thermodilution cardiac output (Table 1) ranged from 3.49 to 6.06 l/min (mean = 4.72 ± 0.75). The values of cardiac output determined from gated blood-pool scintigraphy using attenuated volumes ranged from 0.96 to 2.30 l/min (mean = 1.56 ± 0.41). When the left-ventricular volumes were corrected for attenuation, the values of cardiac output ranged from 3.50 to 6.10 l/min (mean = 4.70 ± 0.77). There was a significant difference ($P < 0.05$) between the thermodilution and attenuated radionuclide cardiac output.

The correlation coefficient (Fig. 2) between the attenuated cardiac output and the thermodilution cardiac output was r = 0.86 with a standard error of the estimate equal to 0.40 l/min.

Thermal CO = 1.57 × radionuclide CO + 2.30 l/min.

When correction for attenuation was made, the cor-

TABLE 1. THERMODILUTION AND RADIONUCLIDE DATA

	Thermodilution Cardiac Stroke		Radionuclide Attenuated Cardiac Stroke		Radionuclide Corrected Cardiac Stroke	
Patient	output	volume	output	volume	output	volume
	(l/min)	(ml)	(l/min)	(ml)	(l/min)	(ml)
1	5.65	81	2.17	31	5.25	75
2	6.06	95	2.16	34	6.10	96
3	4.76	59	1.46	18	4.15	50
4	5.20	85	1.42	23	5.66	92
5	5.11	76	1.69	25	4.59	68
6	4.28	40	1.50	14	4.08	38
7	5.67	86	2.11	32	5.61	85
8	3.49	55	1.01	15	3.50	52
9	3.64	59	1.05	17	3.60	57
10	4.03	59	1.43	20	4.03	57
11	4.05	55	0.96	13	4.82	66
12	5.66	88	2.30	36	6.01	94
13	5.40	72	2.03	27	5.20	70
14	5.13	93	1.65	28	5.11	88
15	4.67	67	1.47	21	4.62	66
16	4.11	45	1.37	15	4.89	53
17	4.03	44	1.47	16	3.88	43
18	4.17	60	1.63	24	4.06	59
19	4.88	90	1.27	24	4.65	87
20	4.30	116	1.08	27	4.26	106
Mean	4.72	71	1.56	23	4.70	70
s.d.	0.75	20	0.41	7	0.77	19

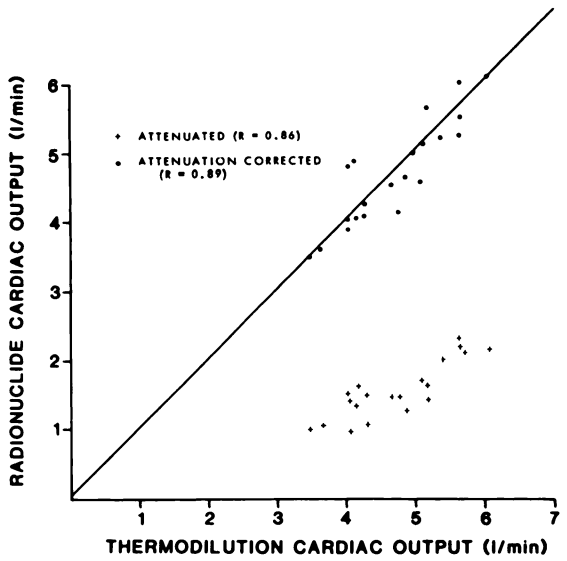

FIG. 2. Relation between thermodilution and scintigraphic cardiac outputs. Correction for attenuation effects brings these values (·) close to line of identity, and standard error of estimate is small (0.36 l/min).

relation coefficient between the thermodilution and radionuclide cardiac output was r = 0.89 with a standard error of the estimate equal to 0.36 l/min.

Thermal CO = 0.859 × radionuclide CO + 0.67 l/min.

ERROR ANALYSIS

In our study, a one pixel (2 mm) error in the measurement of the attenuating distance produces a 3% change in the calculated volume. Hence, an error of 4 to 5 pixels (~1 cm) would result in a 13 to 16% change in the calculated volume. A one-minute inaccuracy in the estimation of the time from withdrawal to counting of the blood sample results in a change of 0.2% in the calculated volume. Therefore, a 30-min error in this time interval would be necessary to change the calculated volume by 6%. The validity of this technique depends on the accuracy with which one knows the volume of the aliquot of blood. An error of 0.1 ml in the volume of the aliquot results in a 5% change in the calculated volume. In order to reduce the effect of errors in the pipetting process, we averaged determinations of counts per ml over two duplicate aliquots.

DISCUSSION

The acceptance of any new test or method in clinical medicine depends on the simplicity of its measurements and on its sensitivity compared with established methods and tests. Radionuclide techniques provide an opportunity to measure noninvasively some of the important parameters of cardiac function that are often measured through cardiac catheterization. Our present study was done in order to evaluate the noninvasive determination of absolute left-ventricular stroke volumes and cardiac output by radionuclide techniques without the use of regression equations.

Others (*7,8,18,19*) have shown that indices of left-ventricular volume, determined by radionuclide techniques that ignore or assume fixed attenuation effects, correlate well with the volumes obtained by the application of the Sandler and Dodge geometric technique to contrast ventriculography. Using this information, radionuclide volume indices are converted to geometric volumes by previously derived regression equations. In this study, we chose to compare the attenuated and attenuation-corrected stroke volumes with the thermodilution stroke volume, the last being independent of geometric assumptions. We were able to confirm a good correlation between attenuated radionuclide and thermodilution cardiac output and stroke volume. We found a somewhat better correlation with the corrected values than with the attenuated values for cardiac output and stroke volume.

The better correlation for stroke volume than for cardiac output deserves explanation. In the case of cardiac output, the heart rate used for the thermodilution cardiac output is an instantaneous one whereas the heart rate used for the radionuclide value is an average over all the beats in the five-minute study. These discrepancies tend to disappear when the cardiac output is divided by the respective heart rates to yield stroke volume.

The primary sources of error in the radionuclide technique are the determination of the attenuation distance and the assumption that a single coefficient of attenuation is necessary and sufficient. The types of tissue through which the photons must pass from the left ventricle to the collimator include: blood and soft tissue, whose densities are close to that of water; lung tissue, whose density is less than that of water; and bone, whose density is greater than that of water. On average these densities would approximate that of water, so that μ = 0.15/cm for water was chosen as a compromise value. Theoretically, the ratio of self-attenuating medium to extra-ventricular attenuating medium may be an important consideration in using a single correction for attenuation. The ability to determine the center of gravity in the left ventricle is sometimes compromised by right-ventricular activity. In our in vivo studies, the measurement of the distance from the center of gravity of left-ventricular activity to the chest-wall marker was probably the major source of error in the calculation of absolute left-ventricular volumes. In patients with hyperdynamic ventricles, it may be necessary to use different attenuating distances to correct the end-diastolic and the end-systolic volumes.

We note that thermodilution and attenuated radionuclide cardiac output are correlated well enough (r = 0.86) to permit the use of a regression equation to de-

termine cardiac output with a standard error of estimate equal to 0.40 l/min without accounting for attenuating medium. However, the patient population as well as the range of cardiac outputs should be increased substantially beyond those used in this study to provide a statistically valid estimate of true cardiac output by regression techniques. We were reluctant to use regression equations to establish a relationship between volumes derived from geometric assumptions for the contrast ventriculographic studies and volumes derived from the radionuclide studies, because changes in system sensitivity, methods of left-ventricular edge detection and background correction, changes in tracer labeling techniques, and other unanticipated factors would require the derivation of new regression equations. The technique described in this report has built-in calibrations that alleviate concern for changes in these factors.

FOOTNOTES

* Edwards Labortories #7 Swan Ganz -93A-302-7F.
† KMA Inc., Model 3500 Cardiac Output Computer.

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