

Estimation of cardiac output by first-pass transit of radiotracers

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To evaluate cardiac function with various tracers to be used for radionuclide scintigraphy, we examined the validity of a simplified method to measure cardiac output (CO) by modifying the equation of Stewart-Hamilton in the radionuclide study. After a bolus injection of I-123 or Tc-99m tracer, the total injection dose and count in the pulmonary artery during the first transit of the tracer were measured to calculate the CO Index. The CO Index was obtained from the integral of the first transit of radiotracers in the pulmonary artery divided by the total injected count. CO was estimated from the regression formula which was obtained by comparing the CO Index with CO measured by the Doppler echocardiographic method. There were close correlations between the CO Index and CO measured by Doppler echocardiography both in the study with I-123 ($n = 13$, $r = 0.85$, $p < 0.001$) and with Tc-99m ($n = 17$, $r = 0.88$, $p < 0.001$). The regression formula varied according to the radionuclide used for the study ($CO = 2.29 \times (CO \text{ Index})^{0.634}$ for I-123 and $CO = 3.18 \times (CO \text{ Index})^{0.518}$ for Tc-99m). CO measured by this method is useful for the assessment of cardiac function with various tracers in routine clinical studies, and this simple method may be utilized for assessment of organ blood flow on the basis of the microsphere model.

Key words: cardiac output, first-pass, pulmonary artery, Doppler echocardiography, time activity curve

INTRODUCTION

A RADIONUCLIDE METHOD to measure CO has been performed by the tracer dilution method with such intravascular tracers as Tc-99m labeled albumin or red blood cells.^{1,2} This method is based on the Stewart-Hamilton's equation for calculating the total injected dose from the equilibrium blood count, but the tracer is limited to blood pool agents.^{3,4} Recently, a simple method to measure CO with any radiotracer has been requested to assess regional blood flow on the basis of the microsphere model. Therefore, by modifying the original Stewart-Hamilton's equation and extending this idea to the other types of tracers which accumulate in the tissues, we evaluated the validity of the simplified method for estimating CO. The method can be applied to any tracers which pass through the right heart chamber and the pulmonary artery (PA), and it may be used in estimating organ blood flow in radionuclide

studies. This paper describes the concept and application of the method with I-123 and Tc-99m labeled tracers in comparison with Doppler echocardiography.

PRINCIPLE

In the equation of Stewart-Hamilton, the relation between the amount of indicator (Q), the cardiac output (CO) and the concentration of the indicator as a function of time (C(t)) was described,

$$CO = Q / \int C(t) dt \quad (1)$$

When this equation is applied to a radionuclide study, we substitute the total injected dose measured by the syringe count (Q_{sy}) with a gamma camera for Q, and the activity of the first transit in the region of interest ($q(t)$) for C(t). When the blood volume in the region of interest (ROI) through which the tracer passes is called V_{ROI} , the equation (1) becomes:

$$CO = k \times V_{ROI} \times Q_{sy} / \int q(t) dt \quad (2)$$

where k is a conversion factor to calibrate attenuation factors for the syringe count and the count in the ROI.

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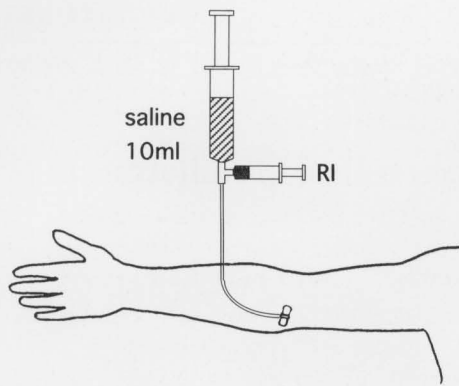


Fig. 1 Schema of the technique of bolus injection. After filling tracer in the tube, we flushed it by 10 ml of saline within 3 seconds.

Since it is difficult to obtain the k value and V_{ROI} directly, we examined the correlation between $Q_{sy}/\int q(t)dt$ and CO assuming the k value and V_{ROI} to be constant. We called the Q_{sy} value divided by $\int q(t)dt$ as the CO Index in this study.

$$\text{CO Index} = Q_{sy}/\int q(t)dt \quad (3)$$

In this study Doppler echocardiography was used at the same time to evaluate reference CO, since CO could vary on different occasions.

We assigned the ROI at the PA for the following three reasons. First, we can use any tracer even if it is trapped in the lung. Second, there is little overlap count from the pulmonary vein and the left chamber in measuring the PA count. Third, since the PA is near the surface of the thorax, there thought to be lower attenuation and PA size may vary less.

With the attained regression formula, CO was obtained from measured Q_{sy} and $\int q(t)dt$.

METHOD

We applied this method to calculate CO in 13 patients in brain SPECT studies with I-123 labeled N-isopropyl-p-iodoamphetamine (IMP) and 17 patients in a myocardial perfusion study with Tc-99m labeled 1,2-bis[bis(2-ethoxyethyl)phosphino]ethane (tetrofosmin). Patients with arrhythmia such as atrial fibrillation and valvular heart disease were excluded.

The study was performed with a dual-detector gamma camera (Optima NX; GE Medical Systems, Milwaukee) with a low energy general purpose collimator.

The total injected dose in the syringe was measured with a gamma camera at a distance of 10 cm before and after the injection to calculate the net injected dose (Q_{sy}). The bolus of 167 MBq of I-123 or 300 MBq of Tc-99m labeled tracer was injected through the right cephalic vein (Fig. 1). Serial dynamic planar images (1 frame/sec) were obtained for 60 sec from the anterior view with a 64×64

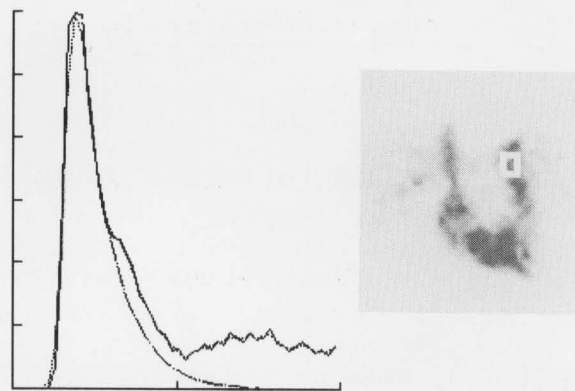


Fig. 2 Time activity curve of radioisotopes in ROI assigned at PA. PA count is the area under the curve.

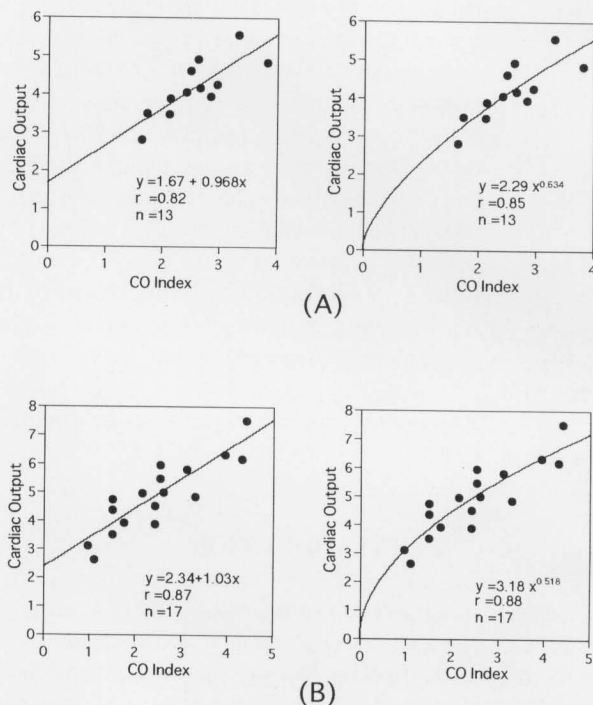


Fig. 3 Correlation between CO and CO Index of I-123 (A) and Tc-99m (B). Both linear (right) and involvement (left) regression were demonstrated.

matrix. The pixel size was 6.0 mm. The count of PA during the first transit of the tracer was measured to obtain the CO Index. To calculate the total count during the first transit of the tracer, we assigned a square ROI of 3×4 pixels (18×24 mm) at the main pulmonary artery in the anterior view (Fig. 2). After smoothing of the time activity curve, exponential curve fitting was applied to extrapolate the tail of the first curve, and the area under the time-activity curve at first passage was calculated.

Just after the data acquisition, CO was measured by the Doppler echocardiographic method in the left decubitus position on the same bed. CO was calculated by multiply-

ing the area of the left ventricular outflow by the velocity-time integral.

RESULTS

The relationship between the CO Index and the CO measured by the Doppler echocardiographic method both in the study with I-123 and with Tc-99m labeled tracer is shown in Figure 3. There was a close correlation between the CO Index and the CO, although the regression formula varies according to the radionuclide used for this study. The linear and involution regression formula and the correlation coefficient in the study with I-123 were
 $CO = 1.67 + 0.968 \times CO \text{ Index}$ $r = 0.82$ $n = 13$ $p < 0.001$
 $CO = 2.29 \times (CO \text{ Index})^{0.634}$ $r = 0.85$,
whereas the formula and correlation coefficient in the study with Tc-99m were
 $CO = 2.34 + 1.03 \times CO \text{ Index}$ $r = 0.87$ $n = 17$ $p < 0.001$
 $CO = 3.18 \times (CO \text{ Index})^{0.518}$ $r = 0.88$.

These data indicated that the involution formulae were rather suitable for the estimation of CO.

DISCUSSION

Measurement of CO by the radiotracer dilution technique has provided accurate CO based on the equation of Stewart-Hamilton, but it was necessary to use blood pool agents because the blood concentration of the tracer after complete mixing in the systemic circulation was needed to measure CO. Recently, a left ventricular volume determination method by means of electrocardiogram gated myocardial SPECT was also proposed, although radiotracers used in this method were limited to myocardial perfusion agents.

Although measurement of CO only by radiotracers does not seem to be very valuable in clinical studies, if we can obtain CO with any tracers by a simple method, the method will combine important information with the results of the original study of the radiotracer. In this study we proposed and examined the validity of the noninvasive and simplified method to measure CO with various radiotracers, and confirmed that this method can also provide a reasonable estimation of CO in routine radionuclide imaging studies.

In the tracer dilution method, the main factors in calculating CO were the total injection dose (Q) and the dilution curve of the tracer (C(t)). Therefore, by modifying the Stewart-Hamilton's equation, we substituted syringe count for the total injected dose and the time activity curve of PA for the dilution curve. Defining the CO Index as the syringe count divided by the first transit count of PA, we investigated the relationship between the CO Index and the CO and obtained the regression formulae, by which we estimate CO, since we cannot obtain CO directly without assessing the conversion factors.

The two advantages of this method are:

First, this method makes it possible to use any tracer even if it is trapped in the lung, because the ROI is placed at the PA through which all of the injected tracer passes. Second, it needs minimal extra time both for data acquisition and for data processing to obtain the CO without requiring data acquisition in the equilibrium state.

In order to measure the count of first transit we assigned ROI at the PA in the anterior planar imaging, since the size of the PA shows less individual variation and the PA count is less influenced by the count of other organs such as the left heart chamber and pulmonary vein.

In this study we applied CO measured by the Doppler echocardiographic method as the reference CO. Previous studies reported that CO measured by Doppler echocardiography correlates well with the thermodilution method.^{7,8} We measured CO by Doppler echocardiography just after the bolus injection on the bed of the gamma camera in order to minimize the change in CO.

Why the regression formulae for I-123 and Tc-99m were different from each other would be mainly due to the physical characteristics of the gamma camera on I-123 and Tc-99m, including the attenuation, scatter and dead time loss such as the collimator scattering of 529 keV photon of I-123.

There are some limitations to this study. Although we regarded blood volume in the ROI and the attenuation factors as constant values, we cannot evaluate these factors precisely. These values may be corrected by body weight or body surface area for more accurate estimation. Further, modification of the bolus injection and blood access technique will be needed to improve the accuracy of the measurements.

A simple method to measure CO is now required to measure regional blood flow with radiotracers on the basis of the microsphere model, especially in the study of cerebral blood flow.⁹ It is expected that our technique may be applied to evaluating regional blood flow in the organ in addition to information on cardiac function obtained with the same radiotracer.

CONCLUSION

Although the regression formulae for I-123 and Tc-99m are different, the CO measured by this simplified method provided reliable data and it would be useful for the assessment of cardiac function with various tracers in routine clinical studies, and this technique could be utilized to estimate regional blood flow in organs.

REFERENCES

1. MacIntyre WJ, Pritchard WH, Moir TW. The determination of cardiac output by the dilution method without arterial sampling. *Circulation* 18: 1139-1146, 1958.
2. Tarazi FMF, MacIntyre WJ. Radionuclide methods for cardiac output determination. *Eur Heart J* 11 (Suppl I): 33-40, 1990.

3. Stewart GN. Researches on the circulation time and on the influences which affect it. IV. The output of the heart. *J Physiol* 22: 159–173, 1887.
4. Hamilton WF, Moore JW, Kinsman JM, Spurling RC. Simultaneous determination of the greater and lesser circulation times, of the mean velocity of blood flow through the heart and lung, of the cardiac output and an approximation of the amount of blood actively circulation in heart and lung. *Am J Physiol* 85: 377, 1928.
5. DePuey EG, Nichols K, Dobrinsky C. Left ventricular ejection fraction assessed from gated Technetium-99m-Sestamibi SPECT. *J Nucl Med* 34: 1871–1876, 1993.
6. Germano G, Kait H, Kavanagh P, Moriel M, Mazzanti M, Su HT, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 36: 2138–2147, 1995.
7. Dubin J, Wallerson DC, Cody RJ, Devereux RB. Comparative accuracy of Doppler echocardiographic methods for clinical stroke volume determination. *Am Heart J* 120: 116–123, 1990.
8. Sun JP, Pu M, Fouad FM, Christian R, Stewart WJ, Thomas JD. Automated cardiac output measurement by spatiotemporal integration of color Doppler data. *In vitro* and clinical validation. *Circulation* 95: 932–939, 1997.
9. Yonekura Y, Iwasaki Y, Fujita T, Sasayama S, Matoba N, Sadatou N. Simple quantification of brain perfusion SPECT with IMP using a large field gamma camera. *KAKU IGAKU (Jpn J Nucl Med)* 27: 1311–1316, 1990.