Measurement of cardiac output with first-pass determination during rubidium-82 PET myocardial perfusion imaging

Eric Q. Chen[1], William J. MacIntyre[1], Fetnat M. Fouad[2], Richard C. Brunken[1], Raymundo T. Go[1], Ching-yee O. Wong[1], Gopal B. Saha[1], Khosrow Dorosti[2], Mehdi Razavi[2], Roberta Armstrong[2]

[1] Department of Nuclear Medicine, The Cleveland Clinic Foundation, Cleveland, Ohio, USA
[2] Department of Cardiology, The Cleveland Clinic Foundation, Cleveland, Ohio, USA

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Abstract. In addition to providing useful clinical information, cardiac output determined during rubidium-82 positron emission tomographic (PET) myocardial perfusion studies can be used in the measurement of absolute regional myocardial blood flow using Sapirstein's method. This investigation was conducted to compare cardiac output values obtained by post-processing data acquired in a list mode PET myocardial perfusion study with those obtained using a technetium-99m-labeled red blood cell method on the same patients. Results from 14 patients showed that cardiac output can be accurately measured simultaneously in a ^{82}Rb PET myocardial study, allowing determination of multiple perfusion and functional parameters of the heart, thus improving the cost-effectiveness of the ^{82}Rb PET study.

Key words: Cardiac output – Rubidium-82 – Positron emission tomography

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Introduction

Measurements of cardiac output are important in assessing ventricular function and in determining the myocardial contractile response to medical or surgical therapy. In myocardial infarction and in shock, measurement of cardiac output is needed to assess progress of the patient's condition. As an additional benefit, if cardiac output can be determined simultaneously with a rubidium-82 positron emission tomographic (PET) myocardial perfusion study, absolute measurements of regional myocardial blood flow at rest can be derived using Sapirstein's uptake fractionation method [1, 2]. In this paper, we present a non-invasive technique of cardiac output determination based on the indicator-dilution principle using data acquired during a ^{82}Rb PET myocardial perfusion study.

Correspondence to: E.Q. Chen, Department of Nuclear Medicine/Gb3, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH44195, USA

Materials and methods

Image data from 14 patients, aged 41–81 years (mean=61.7±20.5 years), referred for both routine ^{82}Rb PET myocardial perfusion studies and ^{99m}Tc-labeled red blood cell (^{99m}Tc-RBC) cardiac output determinations, were analyzed (Table 1). Cardiac output studies with ^{99m}Tc-RBCs were performed at rest 1–3 h prior to PET studies in nine patients, 1–3 h after PET studies in four patients, and after 24 h in one patient.

^{82}Rb PET acquisition. Data were acquired in list mode using a Posicam 6.5 positron camera (Positron Corp., Houston, Tex.). 0.5–1.3 GBg (13.5–35 mli) ^{82}Rb was provided by a ^{82}Sr/^{82}Rb generator (Bracco Diagnostics, Inc., Princeton, N.J.) and delivered to the patient by a microprocessor-controlled infusion system (CTI PET Systems, Knoxville, Tenn.). To ensure the fast delivery of ^{82}Rb in a bolus, the infusion flow rate was set at 80 ml/min, and the threshold at which activity began to be received by the patient at 92.5 MBq/ml (2.5 mCi/ml). Infusion was given through the right basilic vein whenever possible.

ECG, blood pressure, temperature, and pulse were monitored in each patient during the PET study. For attenuation correction, a germanium-68 line source transmission scan was performed, followed by a list mode emission acquisition, initiated at the onset of infusion and continued for 8 min for an average of 43 million.

Data processing. List mode data were rebinned to form 12–15 dynamic frames with durations from the initial 5 s per frame for eight frames to the final 180 s per frame. Tomographic reconstruction of 256×256 image matrices was made using filtered backprojection with a Butterworth filter of order 5 and a cutoff frequency of 0.4 cycle/cm. Twenty-one contiguous slices, each 5.125 mm thick, were generated. Correction for physical decay of ^{82}Rb and deadtime loss was done by the Posicam system. Calibration studies showed that, at the count rate during the early stage of a ^{82}Rb PET study, the effect of deadtime was less than 5%.

The tomographic data were reoriented from body axis to cardiac axis to generate short-axis and vertical and horizontal long-axis images. A midventricular section of the heart was visually selected (Fig. 1A). The short-axis midventricular image from the last dynamic frame, in which the ventricular cavity was best delineat-

Table 1. Patient data

Pt. no.	Sex	Age	Weight (kg)	Height (cm)	Diagnosis	Double product at CO_{PET}/100	Double product at CO_{Tc}/100	CO_{PET} (l/min)	CO_{Tc} (l/min)
1	M	41	140	175.5	CAD, HTN	94.7	99	8.52	8.16
2	M	47	71.6	168.5	CAD, HTN	66.2	70.4	3.87	3.66
3	M	56	97	187	Heart transplant evaluation	63.7	71.3	5.2	5.18
4	M	51	73.7	157.5	CAD	100.1	99.6	3.06	2.54
5	M	81	91.2	174	HTN, CAD	83.6	77.6	4.77	4.25
6	M	76	101	184	CAD, s/p MI	82.6	95.7	6.02	5.20
7	F	63	75.2	151	CAD, s/p CABG, HTN	132	109.8	5.01	4.87
8	F	69	47	156	CAD, HTN	85.6	88.3	3.53	3.86
9	M	78	64	171.5	CAD, s/p CABG, CHF	138.6	139.4	4.90	4.90
10	M	71	87	172	CAD, s/p CABG	93.6	94.54	5.20	6.89
11	M	67	100	175	CAD, s/p CABG	96.4	119	6.15	6.66
12	M	68	101.6	178	CAD, s/p CABG,	66.8	67.1	6.49	6.68
13	F	40	55.7	160	Hypercholesterolemia	66.2	68.8	3.33	4.05
14	F	56	89.5	159	HTN, CAD	84.4	96.5	6.42	5.86

CAD, Coronary artery disease; HTN, hypertension; MI, myocardial infarction; CABG, coronary artery bypass graft; s/p, status post; CHF, congestive heart failure

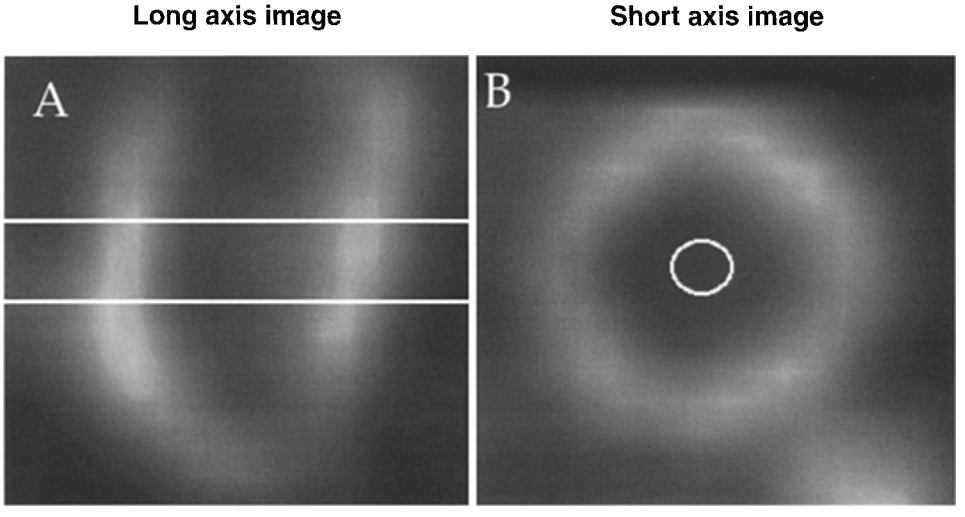

Fig. 1. A The midventricular slices of the last dynamic image (180 s) are lumped to generate a short-axis image, as shown in **B**. **B** A circular region of interest was manually drawn to sample the center of the left ventricular blood pool of all dynamic images

ed, was displayed. A circular region of interest (ROI) of approximately 1 cm^2 in area was drawn at the center of the cavity (Fig. 1B). The ROI was then duplicated in the short-axis images of all earlier dynamic frames. The size of the ROI was small enough that the spillover from the myocardium was deemed negligible. Any patient motion during the course of the scan was visually identified and interactively corrected. A time-activity curve was subsequently generated by sampling all dynamic images using the circular ROI at the ventricular cavity.

^{82}Rb PET cardiac output determination. The determination of cardiac output was accomplished by analyzing the time-activity curve obtained during the ^{82}Rb myocardial perfusion study by the Stewart-Hamilton formula [3]:

$$CO = \frac{I}{\int_0^\infty C_a(t)\,dt}, \quad (1)$$

where CO is the cardiac output, I is the amount of ^{82}Rb delivered, and $C_a(t)$ is the arterial blood activity concentration during the first passage of ^{82}Rb bolus.

The arterial blood time-activity curve was presented by the display software in terms of μCi/ml. The conversion from the pixel counts of the PET image to specific activity concentration used the conversion factor established in a cylindrical ^{68}Ga phantom calibration study.

The amount of ^{82}Rb delivered to the patient was monitored automatically by the infusion pump control system, which was calibrated daily at the infusion flow rate of 80 ml/min. The denominator in Eq. 1 was determined by integrating the left ventricular cavity time-activity curve representing the initial carculation.

Figure 2 shows a typical time-activity curve sampled at the left ventricular cavity. T represents the time when the first recirculation arrived at the ROI of the left ventricle. Separation of the dilution process due to the initial circulation from that due to recircu-

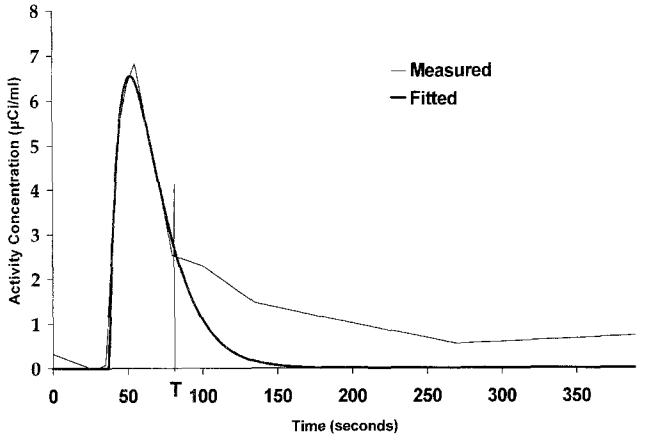

Fig. 2. A typical arterial time-activity curve sampled at the left ventricular cavity in the PET image, shown as a *thin solid line*. To separate first pass from the recirculations, the time-activity curve from 0 to T, the time when recirculation began, was fitted to a gamma variate function, shown as a *bold solid line*

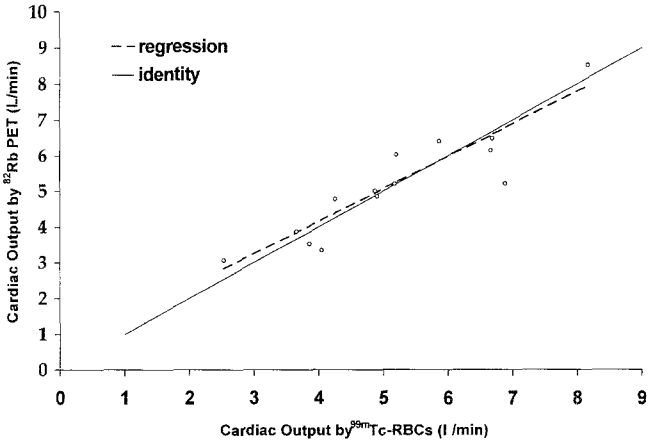

Fig. 3. Relationships between cardiac output values measured by ^{82}Rb PET study and those using a gamma camera and ^{99m}Tc-RBCs. The *solid line* is the line of identity, whereas the *dashed line* is the least square regression line (r=0.91, P<0.005)

lation was accomplished by fitting the portion of the time-activity curve prior to T to a gamma variate function [4]. The denominator in Eq. 1 can then the calculated as the area under the curve represented in Fig. 2 by the solid line.

^{99m}Tc-RBC cardiac output determination. All 14 patients involved had cardiac output determined at rest by routine measurements using ^{99m}Tc-RBCs either immediately prior to or after the resting ^{82}Rb PET study [5]. ECG, blood pressure, temperature and pulse were monitored in each patient during the determination. A portable scintillation camera with a medium-sensitivity, low-energy collimator was used for 30–45° LAO precordial recording of the tracer's passage. Data were acquired at a rate of 0.5 s/frame. A detailed description of this technique was previously reported and the results proved to be significantly correlated to the simultaneously determined results using the indocyanine green dye-dilution technique [5].

Results

In each patient, the resting double product (heart rate times blood pressure) was determined during all cardiac determinations. Paired t test indicated that, for each patient, there was no significant difference between the double product measured during the PET myocardial perfusion study and that during the first-pass cardiac output measurement (P>0.15).

There was a high correlation between cardiac output determined in the ^{82}Rb PET study (CO_{PET}) and that determined using ^{99m}Tc-RBC technique (CO_{Tc}) (Fig. 3). The correlation coefficient was 0.91 (P<0.005). The regression equation was CO_{PET}=(0.886 CO_{Tc}+0.570)± 0.652 (l/min). The mean CO_{PET} was 5.20±1.52 l/min, while the mean CO_{Tc} was 5.17±1.48 l/min.

Discussion

Although clinical measurements of arterial dilution curves have been made by PET systems using other radionuclides such as nitrogen-13 ammonia [6], or using ^{82}Rb with additional probes or other auxiliary equipment [7], the utilization of PET systems to record ^{82}Rb dilution curves in humans involves additional problems such as: (1) the short, 76-s half-life of ^{82}Rb; (2) the less than ideal high count rate performance of the PET system; and (3) the difficulty of delivering ^{82}Rb in a true bolus by the infusion system required in human studies.

In this investigation, we have demonstrated that a weight-dependent dosage, averaging 1.3 GBq (35 mCi), can be delivered to the patient in approximately 6 s, allowing easy separation of the initial circulation by fitting the tail of the dilution curve to a gamma variate function. This study has also demonstrated that the relatively low sampling rate allowed by the PET system, e.g., 5 s/frame near the peak, is adequate for recording the dilution curve.

The attempt to measure cardiac output during a routine ^{82}Rb myocardial perfusion study is part of our current effort to obtain global left ventricular perfusion and function parameters in a single PET study, in order to improve the cost-effectiveness of the ^{82}Rb PET myocardial perfusion study. We have separately reported that, with cardiac output available, regional myocardial blood flow can be obtained using Sapirstein's method [2]. Left ventricular ejection fraction and stroke volume can also be measured using ECG-gating [8]. All these measurements were obtained with no additional scan time or patient inconvenience and minimal extra effort on the part of technologists.

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