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Quantitative analysis of myocardial ischemia by technetium-99m sestamibi exercise scintigraphy: A new method for change rate mapping

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In order to quantitatively assess the extent and severity of myocardial ischemia by Tc-99m sestamibi exercise myocardial scintigraphy, we developed a new method of change rate (CR) mapping and examined its efficiency. CR was calculated to divide the counts per pixel in the stress polar map by that in the rest polar map at each corresponding pixel. The CR map showed the CR values at each pixel. To correct the differences between the stress and rest images for the dose of Tc-99m sestamibi administered, the mean counts per pixel in the stress polar map and the rest map were adjusted to the same level. Regarding the regions in which the CR value was less than 1 as ischemia, we compared the abilities of the CR map and the polar map to detect coronary artery stenosis in 5 patients with angina pectoris. The sensitivity for coronary artery stenosis was 80% in the CR map, and 40% in the polar map. The specificity for both was 75%. We concluded that the CR map was effective in assessing the extent and severity of myocardial ischemia in Tc-99m sestamibi exercise myocardial scintigraphy.

Key words: technetium-99m sestamibi, myocardial SPECT, change rate, polar map

INTRODUCTION

MYOCARDIAL EXERCISE SCINTIGRAPHY with technetium-99m hexakis 2-methoxyisobutylisonitrile (Tc-99m MIBI) needs two separate injections of radioisotope: one during exercise and a second at rest.[1] When the images were obtained on the same day,[2,3] the distribution of Tc-99m MIBI at the first imaging could affect that at the second imaging, and accurate diagnosis was sometimes difficult by visual assessment alone. Then, in order to quantitatively assess the extent and severity of myocardial ischemia by Tc-99m MIBI scintigraphy, we sought to develop a new change rate (CR) method and examine its efficiency.

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MATERIALS AND METHODS

Patients

The studies were conducted between November 4 and November 18, 1993, in 9 patients (6 males and 3 females, ages ranging from 37 to 72 years, with a mean of 60.3 years) with ischemic heart disease.

Mathematical basis of the CR

A representative diagram of blood flow and distribution of Tc-99m MIBI in the myocardium is shown in Figure 1. At the junction of the aorta and the coronary artery, the correlations between the blood flow: F (m*l*/min), the coefficient of distribution: k, and the dose of Tc-99m MIBI: D (cpm) were calculated with equations 1–5:

$$F_O = F_B + F_C. \quad \text{Eq. 1}$$

$$k_C = F_C / (F_B + F_C). \quad \text{Eq. 2}$$

$$k_B = 1 - k_C. \quad \text{Eq. 3}$$

$$D_C = k_C \times D_O. \quad \text{Eq. 4}$$

$D_B = D_O - D_C$. Eq. 5

where F_O is the cardiac output, F_B is the blood flow in the body, F_C is the blood flow in the coronary artery, k_C is the coefficient of distribution of the coronary artery, k_B is the coefficient of distribution of the body, D_O is the dose of injected Tc-99m MIBI, D_C is the dose of Tc-99m MIBI in the myocardium, and D_B is the dose of Tc-99m MIBI in the body. At the junction of the ischemic areas and normal areas of the coronary artery, the correlations of F, k, and D, were calculated with equations 6–10:

$F_C = F_I + F_N$. Eq. 6

$k_I = F_I / (F_N + F_I)$. Eq. 7

$k_N = 1 - k_I$. Eq. 8

$D_I = k_I \times D_C$. Eq. 9

$D_N = D_C - D_I$. Eq. 10

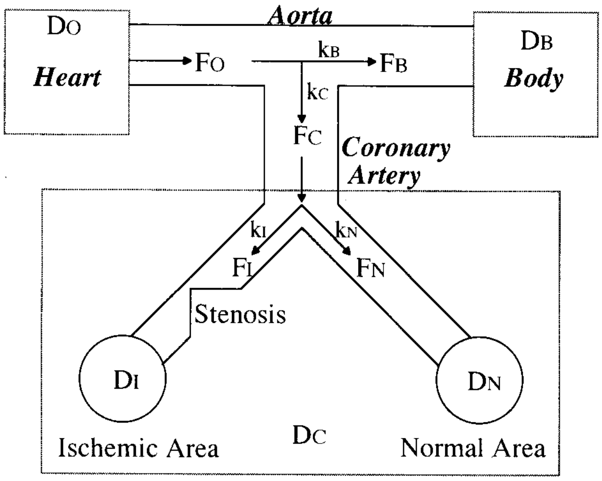

Fig. 1 Representative diagram of blood flow and distribution of Tc-99m MIBI in myocardium. The ratio of the blood flow: F (ml/min), the coefficient of distribution: k, and dose of Tc-99m MIBI: D (cpm).

where F_I is the blood flow in the ischemic areas, F_N is the blood flow in the normal areas, k_I is the coefficient of distribution of the ischemic areas, k_N is the coefficient of distribution of the normal areas, D_I is the dose of Tc-99m MIBI in the ischemic areas, and D_N is the dose of Tc-99m MIBI in the normal areas.

Assuming that D_O and k_C were fixed, D_C would be invariable but F_O might be increased (see equations 1–5). In the same way, assuming that D_O, k_C and k_I were fixed, D_I and D_N would be invariable but F_C might be increased by exercise. Therefore when D_N (D_{NR}) and D_I (D_{IR}) at rest differ from D_N (D_{NS}) and D_I (D_{IS}) at stress, the outcomes show that k_N (k_{NR}) and k_I (k_{IR}) at rest might differ from k_N (k_{NS}) and k_I (k_{IS}) at stress.

Assuming that D_C was fixed, the correlation between CR in ischemic areas (CR_I) and in normal areas (CR_N) was calculated with equations 11 and 12, i.e., the ratios of the coefficients of distribution.

$CR_I = D_{IS} / D_{IR} = (k_{IS} \times D_C) / (k_{IR} \times D_C)$

$= k_{IS} / k_{IR}$. Eq. 11

$CR_N = D_{NS} / D_{NR} = (k_{NS} \times D_C) / (k_{NR} \times D_C)$

$= k_{NS} / k_{NR}$. Eq. 12

Therefore when k_{NS} is greater than k_{NR} at stress, k_{IS} might be smaller than k_{IR}, CR in normal areas might be greater than 1.0, and CR in ischemic areas might be smaller than 1.0. Since CR_N and CR_I values were influenced by the severity of the ischemia, we standardized the CR by means of the CR_N, and the CR independent of the severity of the ischemia could be determined (Eq. 13).

$CRs = CR / CR_N$. Eq. 13

where CRs is the CR standardized with CR_N.

In this manner, CRs in normal areas was 1.0, and CRs in ischemic areas was smaller than 1.0, so that the severity of ischemia could be shown quantitatively.

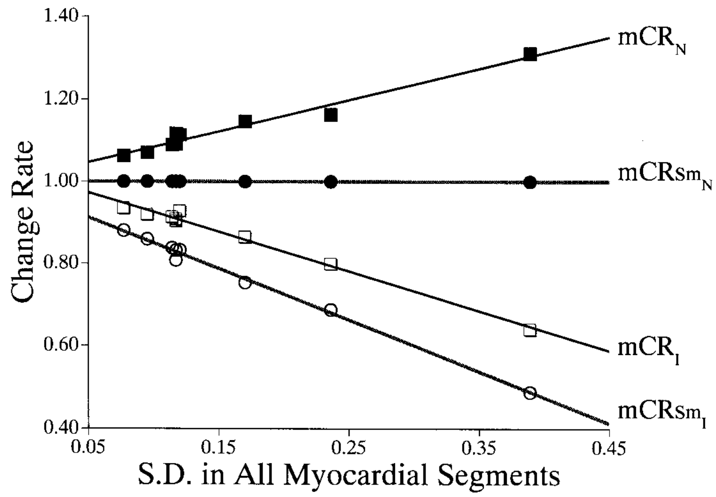

Fig. 2 The correlations between the CR and the standard deviation (SD) of the CR in all polar map segments. The mean CR where CR was greater than 1.0, mCR_N; the mean CR where CR was smaller than 1.0, mCR_I; mCR_N standardized by mCR_N, $mCRsm_N$; and mCR_I standardized by mCR_N, $mCRsm_I$.

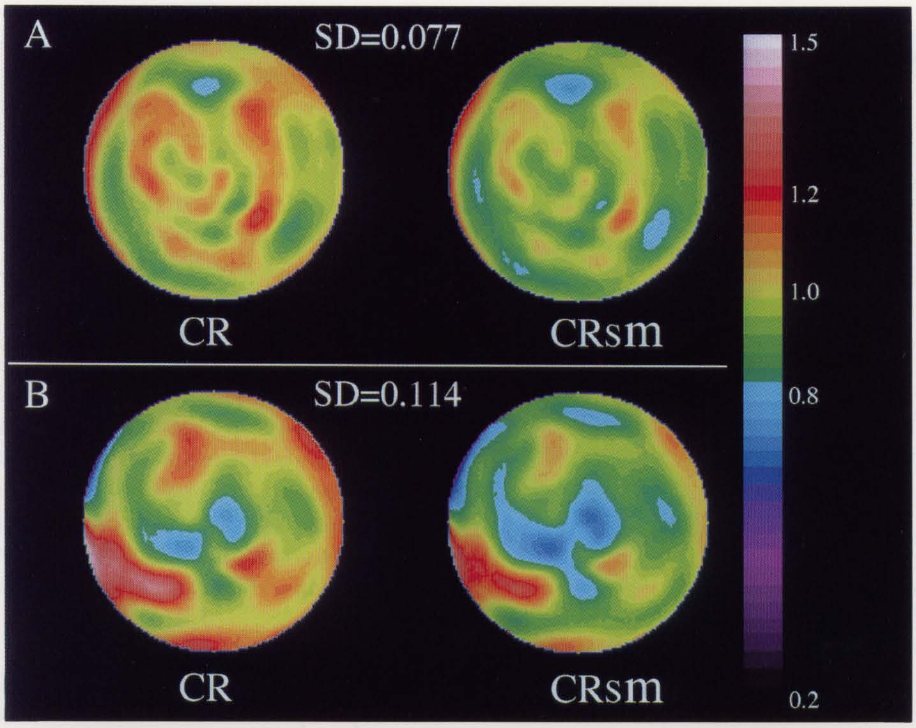

Fig. 3 Tc-99m MIBI CR and CRsm map in a case of small SD (A) and in a case of large SD (B).

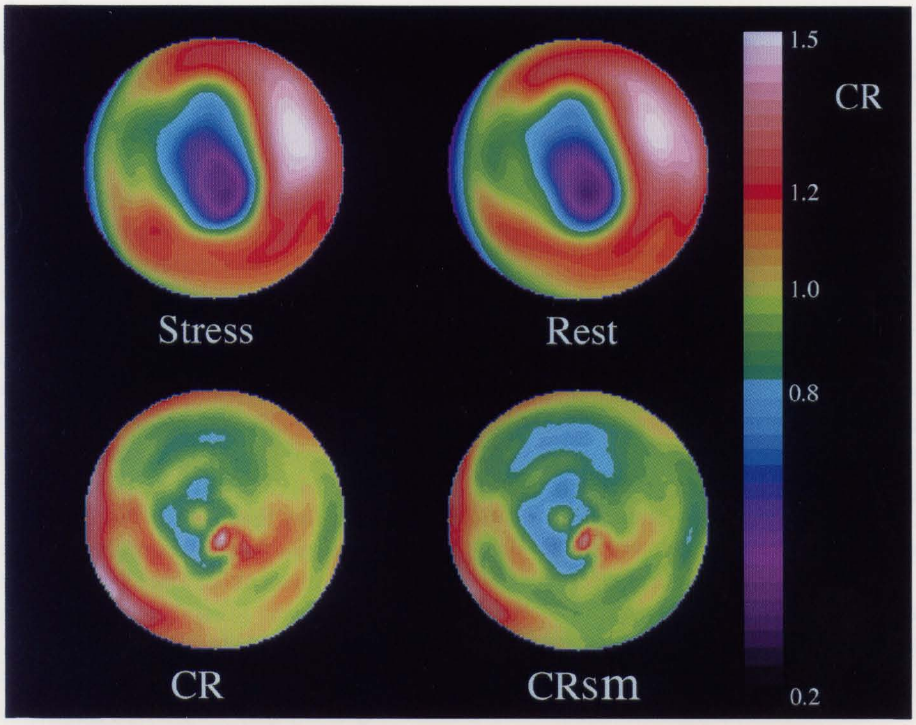

Fig. 4 Tc-99m MIBI polar map, CR map and CRsm map in a patient with postmyocardial infarction angina. The culprit lesion was segment 7, and ischemia was induced by segment 9 of 99% stenosis. The low CR was recognized in the area of segment 9.

Table 1 Findings of coronary angiography

No.	Age/Sex	Segment	Stenosis
1	67/F	#9	99%
		#3	25%
2	53/M	#6	40%
3	72/F	#7	75%
		#9	90%
		#12	70%
		#13	60%
		#4pl	50%
4	65/M	#11	50%
		#13	50%
5	66/M	#13	25%

Table 2 The detectability of ischemia by the CR map and the polar map

No.	Segment	CAG	CR map	Polar map
1	LAD	99%	+	−
	LCX	0	−	−
	RCA	25%	−	−
2	LAD	40%	+	+
	LCX	0	−	−
	RCA	0	+	+
3	LAD	75%	+	+
	LCX	70%	+	−
	RCA	50%	−	−
4	LCX	50%	+	+
	RCA	0	−	−
5	LCX	25%	−	−
	RCA	0	−	−

CAG: Coronary angiography, LAD: Left anterior descending artery, LCX: Left circumflex, RCA: Right coronary artery, +: ischemia, −: no ischemia

Calculation of CR with the polar map

CR was calculated to divide the counts per pixel in the stress polar map by that in the rest polar map at each corresponding pixel. The CR map showed the CR values at each pixel. In the same day protocol, the first image data (P_{FIRST}) must be excluded from the second image data (P_{SEC}), and the true second image data (P_{TSEC}) must be determined. These corrections were performed with mean values per pixel (M_{SEC}, M_{FIRST}) in all polar map segments as follows (Eq. 14).

$$P_{TSEC} = (P_{SEC} - P_{FIRST} \times M_{SEC} / M_{FIRST}) + P_{FIRST}. \quad \text{Eq. 14}$$

After the CR was calculated in each pixel with P_{TSEC} and P_{FIRST}, the CR was standardized by the mean CR (mCR_N) for the areas where CR was greater than 1.0, except for the basal region (Eq. 15).

$$CRsm = CR / mCR_N. \quad \text{Eq. 15}$$

where CRsm is the CR standardized with mCR_N.

Comparison of the CR map with the polar map

The detectability of ischemia with the CR map was compared with that by the stress and rest polar map in 5 patients who underwent coronary angiography (CAG). Visual evaluations were classified by two radiologists and one cardiovascular medical doctor into two classes: ischemia and no ischemia. Stenosis of the coronary arteries on CAG were measured by another cardiovascular medical doctor who had no knowledge of the patient's background.

SPECT apparatus and conditions

A three-detector gamma camera (Toshiba GCA-9300A/HG), fitted with an LEHR collimator, was used to collect SPECT data and to reconstruct the image. The image was then processed on an on-line work station (Omron Data General LUNA2001). SPECT was acquired under the following conditions: 128 × 128 matrix, 45 seconds for each 6° step and 60 steps (20 steps with each detector).

Exercise protocol

Exercise testing was performed on a bicycle ergometer in the supine position. The initial workload was 25 W and was increased by 25 W every three minutes. At the point of maximal exercise, 370 MBq of Tc-99m MIBI was administered intravenously. Sixty minutes after the injection, SPECT imaging was started, and 3 hours after the first injection, 370 MBq of Tc-99m MIBI was added. Sixty minutes later the rest images were acquired.

RESULTS

The correlations between mCR_N and mCR_I (mean CR where CR was smaller than 1.0) in 85 percent of the radius areas of polar map segments, and the standard deviation (SD) of the CR in all polar map segments are shown in Figure 2. mCR_N was greater than 1.0, and mCR_I was smaller than 1.0 as the SD was increased, and even the same CR value means different severities of myocardial ischemia in different patients. On the other hand, in the CRsm map, the mean CRsm in normal areas was 1.0 independent of SD, and the mean CRsm in ischemic areas was smaller than 1.0 as the severity of the ischemia increased, so that CRsm made it easy to understand the severity of ischemia. The CR map and the CRsm map in cases of a small SD and of a large SD are shown in Figure 3. It was possible to evaluate the extent of ischemia with the CR map and severity with the CRsm map.

Figure 4 shows the polar map, CR map and CRsm map in a patient with postmyocardial infarction angina. The culprit lesion was segment 7, and ischemia was induced by segment 9 of 99% stenosis. The low CR was recognized in the area of segment 9.

Table 1 shows the result of CAG of 5 patients, and Table 2 shows the visual evaluation and the result of CAG without the culprit lesion of myocardial infarction. The sensitivity of detecting the coronary artery stenosis ≧ 50% with the CR map and polar map were 80% and 40%, respectively and specificity with both was 75%. Moreover, degrees of sensitivity in detecting coronary artery stenosis ≧25% with the CR map and polar map were 63% and 38%, respectively.

DISCUSSION

When Tc-99m MIBI was used for myocardial SPECT at stress, imaging was often performed twice, and an image taken at stress was visually compared with an image taken at rest.[1] When images at stress and at rest were taken on the same day,[2,3] distribution at the first imaging could affect that at the second imaging. In such cases, myocardial SPECT images at stress might be assessed more accurately if visual assessment was combined with calculation of the CR that could be a more objective indicator.

The CR must be calculated after the true second image is determined and the dose of Tc-99m MIBI in myocardium at rest is equalized to that at stress in the same day protocol. By means of the correction method with the mean value per pixel in all polar map segments, a simple correction could be performed even though there were differences in the dose of Tc-99m MIBI and in the conditions at rest and at stress. Moreover, the CR was standardized by the mCR_N, and the CRsm for the normal region was about 1.0, and that for apparently ischemic regions was smaller. Therefore, it would be useful to establish a normal range of CRsm for objective evaluation of ischemic myocardial regions and for quantitatively evaluating the degree of ischemia.

The CR map was more sensitive than the polar map in detecting myocardial ischemia. The CR map may increase the accuracy of exercise Tc-99m MIBI myocardial scintigraphy, but the CR map also estimated the insignificant coronary artery stenosis, less than 50%, to be ischemia. As noted in equations 11 and 12, the CR map reflected the change in the coefficient of distribution of coronary artery during exercise, and the CR map seemed to identify the insignificant coronary artery stenosis as ischemia. Even when coronary artery stenosis was not severe, if coronary artery blood flow did not increase by the same magnitude as in the other normal vessels, the CR map identified those areas as low CR value areas. The clinical implication of these area should be elucidated in later studies.

CONCLUSION

The determination of the CR map and CRsm map seems to provide a useful means for objectively evaluating the extent and severity of ischemia in myocardial scintigraphy taken with Tc-99m MIBI at stress.

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