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Does myocardial thallium-201 SPECT combined with electron beam computed tomography improve the detectability of coronary artery disease? —Comparative study of diagnostic accuracy—

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Objective. The aim of this study is to evaluate the diagnostic accuracy of myocardial ^{201}Tl SPECT combined with EBT for detecting CAD.
Methods. The study was based on 34 patients with suspected CAD, who had EBT and myocardial ^{201}Tl SPECT. The CAD was diagnosed by the findings of coronary arteriography. Sensitivity, specificity and accuracy of EBT, myocardial ^{201}Tl SPECT and the combined diagnosis on a per vessel basis and a per-patient basis were studied.
Results. The sensitivity for detecting CAD of myocardial ^{201}Tl SPECT, EBT and the combined diagnosis was 85%, 77%, and 62%, respectively. No significant difference in the accuracy of myocardial ^{201}Tl SPECT, EBT and the combined diagnosis was observed on a patient basis and per vessel basis. In the over 70 yr age subgroup, the sensitivity and accuracy of EBT for detecting LAD lesion were significantly superior to those of myocardial ^{201}Tl SPECT. Regardless of age-based subgroups and gender, the combined diagnosis did not contribute to an improvement in diagnostic accuracy.
Conclusion. Although the sensitivity of EBT for detecting LAD lesion in patients over 70 yr of age was significantly higher than that of myocardial ^{201}Tl SPECT, in the detectability of CAD, combined use of myocardial ^{201}Tl SPECT and EBT offers no improvement.

Key words: coronary artery disease, single photon emission computed tomography, thallium-201 chloride, electron beam computed tomography

INTRODUCTION

CORONARY ARTERY DISEASE is the leading cause of morbidity and mortality in industrialized nations. Not only invasive screening tests for detecting coronary artery disease (CAD) but also noninvasive screening tests have been performed. Even though exercise SPECT with ^{201}Tl chloride (myocardial ^{201}Tl SPECT) and exercise ECG with a treadmill are useful for screening tests in detecting CAD, the results still included 10–25% false negatives.[1–10]

The recent development of electron beam computed tomography (EBT) enables us to detect CAD by assessing the degree of calcification in coronary arteries,[11–19] but some pathologic studies and studies of EBT results showed that the severity of calcification did not always indicate the degree of lumen stenosis.[15,20] Although only a few researchers compared the diagnostic accuracy of myocardial ^{201}Tl SPECT with that of EBT,[1,21] the clinical usefulness of myocardial ^{201}Tl SPECT combined with EBT is still controversial. We had a chance to compare myocardial ^{201}Tl SPECT and EBT. The aim of this study is to evaluate the clinical usefulness of myocardial ^{201}Tl SPECT combined with EBT for detecting CAD.

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MATERIALS AND METHODS

The study was based on 34 patients with suspected CAD, who received myocardial ^{201}Tl SPECT, EBT and coronary arteriography (CAG) consecutively within a week. Catheterizations were performed in all patients because of the symptoms, abnormal ECG results and heart failure.

The study group comprised 20 men and 14 women whose age ranged from 37 to 82 yr with a mean age of 63 yr. The CAD was diagnosed by significant stenotic change in coronary arteriography, defined as having more than 75% narrowing in any major coronary artery. Seventeen out of 34 patients had a myocardial infarction. Patients with cardiomyopathy or old myocardial infarction with a normal coronary arteriogram were not included in this study.

Electron beam computed tomography (EBT)

From the level of the carina to the cardiac apex, forty contiguous 3-mm thick slices were taken at a 100-ms scan time in volume mode with Imatron C-150 (Imatron company, South San Francisco, CA). Transaxial images were reconstructed by the filtered back projection method, having a 512 × 512 matrix on each tomogram. Regions of interest (an area ≥ 0.51 mm^2) were drawn over the area corresponding to three vessels (Left anterior descending artery (LAD), Left circumflex artery (LCx) and Right coronary artery (RCA)) on each slice to obtain the calcification score. The calcified lesion on the EBT image was defined as the area including a pixel with more than 130 Hounsfield units (HU) of CT density. The maximal density in each ROI was ranked from 1 to 4 as follows; 1: 130–199 HU, 2: 200–299 HU, 3: 300–399 HU and 4: 400 HU≤. A lesion score was obtained by multiplying the value for maximal density by the number of pixels of the calcified lesion in mm^2. The total calcium score for each branch and all branches was the sum of lesion scores for slices involving coronary arteries. The calcium index was the natural log (1 + calcium score) for analyzing the diagnostic accuracy of EBT.[1,14]

Single photon emission computed tomography (SPECT)

All patients fasted overnight before the myocardial ^{201}Tl SPECT. During patients' exercise with the ergometer, 111 MBq of ^{201}Tl chloride was injected intravenously when at least one of the following end points was reached; 1) ECG leads showing 0.1 mV < flat or downsloping ST segment depression; 2) Patients complaining of angina; 3) Achievement of 85% of the predicted maximal heart rate.[22,23] After patients' heart rate returned to the base line condition, early images were taken with a triple head gamma camera (Prism 3000, Picker, Ohio) attached to a low-energy general purpose collimator (spatial resolution = 14.9 mm FWHM, on the center of the reconstructed image). A 20% symmetrical energy window centered on the 80 keV photopeak was used. These gamma cameras

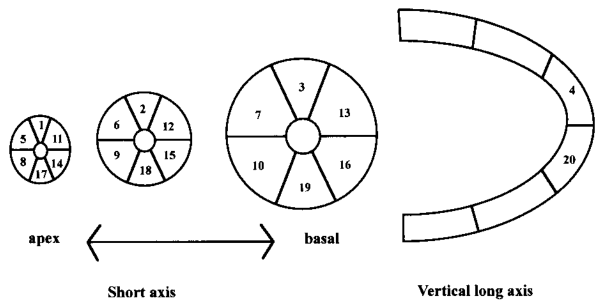


Fig. 1 Segmental analysis of myocardial ^{201}Tl SPECT. ^{201}Tl uptake on twenty segments of three short axial images and a vertical long axial image were evaluated by using a four-point scoring system.

continuously rotated at 5° intervals and took 40 sec to obtain the data for the early images and 45 sec for the delayed images. The projection data were used to reconstruct the SPECT images with filtered back projection by means of a low-pass filter. Image matrices were 64 × 64. Short axial, horizontal long axial and vertical long axial images were displayed on the film. In addition 74 MBq of ^{201}Tl was administered 10 min before the delayed imaging, 3 hours after the first ^{201}Tl injection, which was conducted in the same way as the early stress imaging.

Tomograms were divided into 20 myocardial segments (Fig. 1). Each segment was assigned to one of the three major vascular territories; LAD territory included the anterior wall (segs. 1, 2, 3, 5, 6 and 7), septum (segs. 8, 9 and 10) and apical (seg. 4) , LCx territory included lateral wall (segs. 11, 12, 13, 14, 15 and 16, RCA territory included the inferior wall (segs. 17, 18 and 19) and apex (seg. 20).

For the myocardial ^{201}Tl SPECT, regional ^{201}Tl uptake was visually analyzed and scored by means of a four-point scoring system (0 = normal tracer uptake, 1 = faint tracer uptake, 2 = moderate reduction of tracer uptake, 3 = severe reduction of tracer uptake). The maximum ^{201}Tl uptake score was used to evaluate the diagnostic accuracy of myocardial ^{201}Tl SPECT in each territory or the entire myocardium.

SPECT images were interpreted independently by two experienced nuclear physicians who had no prior information about the results of CAG, calcification scores by EBT or the patient's history. The examination was followed by a discussion until a consensus was reached.

Coronary arteriography (CAG)

Coronary arteriography was performed in multiple projections by means of standard techniques. And coronary angiograms were analyzed at weekly conferences by several experienced cardiologists who had no information about calcification scores. The lesions in each coronary vessel were visually evaluated. The degree of coronary artery stenosis was decided by multiple projections to demonstrate the maximal coronary artery luminal nar-

Table 1 Angiographic results in patients with coronary artery disease

	Number of patients		
	LAD	LCx	RCA
1VD (n = 12)	10	0	2
2VD (n = 8)	4	7	5
3VD (n = 6)	6	6	6

LAD: left anterior descending artery, LCx: left circumflex artery, RCA: right coronary artery, 1VD: one-vessel disease, 2VD: two-vessel disease, 3VD: three-vessel disease

rowing. Angiographic abnormalities were considered as significant stenosis when ≥ 75% luminal diameter stenosis was found in LAD, LCx and RCA vessels.

Data Analysis

On a patient-based diagnosis of the EBT image, a patient who had any individual coronary artery branch with a transformed calcification score of 4 or higher was diagnosed as CAD (1). And for per-vessel-based diagnosis, the territory with a transformed calcification score of 4 or higher was diagnosed as CAD.[1] The patient or the territory with a ^{201}Tl uptake score higher than 2 on the myocardial ^{201}Tl SPECT image was defined as CAD. The final diagnosis for CAD was based on the results of CAG. Sensitivity, specificity and accuracy for detecting CAD in patients and each vessel were compared for EBT, myocardial ^{201}Tl SPECT diagnosis, and the combined diagnosis by means of myocardial ^{201}Tl SPECT and EBT. The diagnostic accuracy was also compared in subgroups based on gender and age (less than 50 yr, 50–69 yr and over 70 yr).

Regarding the combined diagnosis of EBT and myocardial ^{201}Tl SPECT, patients or segments with positive results on both modalities were diagnosed as CAD. In assessment of each territory, evaluated segments with infarction defined as akinesis with echocardiograms or left ventricular graphy were excluded to assess the effect of exercise on myocardial ^{201}Tl SPECT sensitivity in detecting ischemia.

Statistical Analysis

All values showing diagnostic accuracy were reported as percentages. Data were analyzed by the McNemar-test with 1 degree of freedom for comparing categorical values.[24–26] All tests of statistical significance were defined at a probability of less than 0.05.

RESULTS

Eight of thirty-four patients (24%) showed normal coronary arteries on CAG. The CAG revealed single vessel disease in 12 patients (35%), two vessel disease in 8 patients (24%), and three vessel disease in 6 patients (18%) (Table 1). Regarding individual coronary arteries, 20 arteries of LAD (59%), 13 of LCx (38%) and 13 of

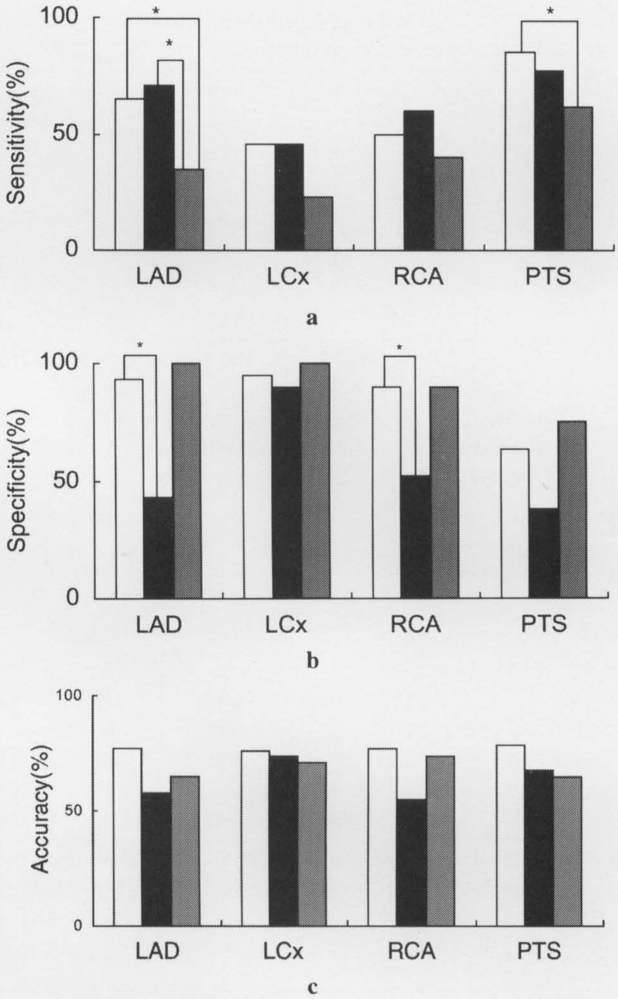


Fig. 2 Diagnostic accuracy of myocardial ^{201}Tl SPECT (□), EBT (■), combined diagnosis of myocardial ^{201}Tl SPECT and EBT (▨) for coronary artery disease on a patient-base diagnosis and on a per-vessel base diagnosis. a. Sensitivity of the combined diagnosis of myocardial ^{201}Tl SPECT and EBT was significantly lower than that of myocardial ^{201}Tl SPECT in detecting patients with CAD and significantly lower than those of myocardial ^{201}Tl SPECT and EBT in LAD lesions. b. Specificity of EBT in detecting LAD and RCA lesions was significantly lower than that of myocardial ^{201}Tl SPECT. c. The combined diagnosis did not contribute to the improvement of coronary artery disease detectability. LAD: left anterior descending artery, LCx: left circumflex artery, RCA: right coronary artery, PTS: on a patient-basis. *: $p < 0.05$.

RCA (38%) showed significant stenosis. Regarding the patients-basis diagnosis, sensitivity of myocardial ^{201}Tl SPECT and EBT for detecting CAD was 85 and 77%, respectively (Fig. 2a). The combined diagnosis of myocardial ^{201}Tl SPECT and EBT had a sensitivity of 62% which was significantly lower than that of myocardial ^{201}Tl SPECT. In sensitivity on the per-vessel basis, there was no significant difference among myocardial ^{201}Tl SPECT, EBT and their combined diagnosis, except in LAD—65%, 71% and 35% ($p < 0.05$) (Fig. 2a). The

Table 2 Comparison of sensitivity, specificity and accuracy of myocardial ^{201}Tl-SPECT and EBT

a: LAD lesion for each age subgroup

Age	Sensitivity			Specificity			Accuracy		
	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT
30 yr–49 yr (n = 3)	100[a]	50	50	100	100	100	100	67	67
	(2/2)[b]	(1/2)	(1/2)	(1/1)	(1/1)	(1/1)	(3/3)	(2/3)	(2/3)
50 yr–69 yr (n = 21)	78	78	56	92	42*	100	86	57*	81
	(7/9)	(7/9)	(5/9)	(11/12)	(5/12)	(12/12)	(18/21)	(12/21)	(17/21)
70 yr– (n = 7)	17	67*	0	0	0	100	14	57*	14
	(1/6)	(4/6)	(0/6)	(0/1)	(0/1)	(1/1)	(1/7)	(4/7)	(1/7)

Tl: myocardial ^{201}Tl-SPECT, EBT: electron beam computed tomography, Tl and EBT: Patients with positive results on both ^{201}Tl-SPECT and EBT were defined as having coronary artery disease.
[a]: Number is expressed as percentage (%), [b]: Numbers in parenthesis indicate patients number, *: Sensitivity, specificity and accuracy values were compared with those of ^{201}Tl-SPECT by McNemar-test, and significant differences were observed with $p < 0.05$

b: LCx lesion for each age subgroup

Age	Sensitivity			Specificity			Accuracy		
	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT
30 yr–49 yr (n = 4)	100[a]	100	100	100	100	100	100	100	100
	(1/1)[b]	(1/1)	(1/1)	(3/3)	(3/3)	(3/3)	(4/4)	(4/4)	(4/4)
50 yr–69 yr (n = 22)	25	38	0	93	100	100	68	77	64
	(2/8)	(3/8)	(0/8)	(13/14)	(14/14)	(14/14)	(15/22)	(17/22)	(14/22)
70 yr– (n = 8)	75	50	50	100	50	100	88	50	75
	(3/4)	(2/4)	(2/4)	(4/4)	(2/4)	(4/4)	(7/8)	(4/8)	(6/8)

[a]: Number is expressed as percentage (%), [b]: Numbers in parenthesis indicate patients number. Sensitivity, specificity and accuracy values were compared with those of ^{201}Tl-SPECT by McNemar-test, and there were no significant differences with $p < 0.05$

c: RCA lesion for each age subgroup

Age	Sensitivity			Specificity			Accuracy		
	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT
30 yr–49 yr (n = 3)	—	—	—	100[a]	100	100	100	100	100
	(0/0)[b]	(0/0)	(0/0)	(3/3)	(3/3)	(3/3)	(3/3)	(3/3)	(3/3)
50 yr–69 yr (n = 20)	50	63	36	92	50*	92	75	55	70
	(4/8)	(5/8)	(3/8)	(11/12)	(6/12)	(11/12)	(15/20)	(11/20)	(14/20)
70 yr– (n = 8)	50	50	50	83	33*	83	75	36	75
	(1/2)	(1/2)	(1/2)	(5/6)	(2/6)	(5/6)	(6/8)	(3/8)	(6/8)

[a]: Number is expressed as percentage (%), [b]: Numbers in parenthesis indicate patients number, *: Sensitivity, specificity and accuracy values were compared with those of ^{201}Tl-SPECT by McNemar-test, and significant differences were observed with $p < 0.05$

specificity of EBT for LAD and RCA lesions was significantly lower than that of myocardial ^{201}Tl SPECT (43% vs. 93% in LAD lesion and 52% vs. 90% in RCA lesion). There was no significant difference among myocardial ^{201}Tl SPECT and the combined diagnosis (63% vs. 75% on a patient-basis, 93% vs. 100% in LAD lesion, 95% vs. 100% in LCx lesion and 90% vs. 90% in RCA lesion, respectively) (Fig. 2b). No significant difference in the accuracy of myocardial ^{201}Tl SPECT, EBT and the combined diagnosis was observed on a patients-basis and a per-vessel basis (79%, 68%, 65% on a patient basis, 77%, 58%, 65% in LAD lesion, 76%, 74%, 71% in LCx lesion and 77%, 55%, 74% in RCA lesion, respectively) (Fig. 2c).

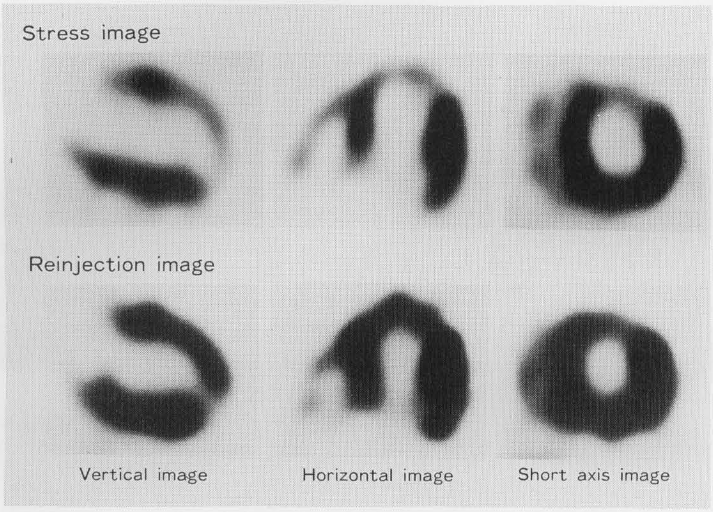
In the 50–69 yr age subgroup, the specificity and accuracy of EBT for detecting LAD lesions were significantly lower than those of myocardial ^{201}Tl SPECT, but in the over 70 yr age subgroup, the sensitivity and accuracy of EBT for detecting LAD lesion were significantly superior to those of myocardial ^{201}Tl SPECT (Table 2a). For detecting LCx lesions, there was no significant difference in the diagnostic accuracy of myocardial ^{201}Tl SPECT, EBT and the combined diagnosis, regardless of age (Table 2b). In the 50–69 yr and over 70 yr age subgroup, the

Table 3 Comparison of sensitivity, specificity and accuracy of myocardial ^{201}Tl-SPECT and EBT on a patients-basis grouped by gender

Gender	Sensitivity			Specificity			Accuracy		
	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT	Tl	EBT	Tl and EBT
Male (n = 19[a])	87[b]	73	60*	50	50	50	79	68	59
Female (n = 15)	82	82	64	75	25	100	80	67	73

Tl: myocardial ^{201}Tl-SPECT, EBT: electron beam computed tomography, Tl and EBT: Patients with positive results on both ^{201}Tl-SPECT and EBT were defined as having coronary artery disease.
[a]: Number of patients, [b]: Number is expressed as percentage (%), *: Sensitivity, specificity and accuracy values were compared with those of ^{201}Tl-SPECT by McNemar-test, and significant difference was observed with $p < 0.05$

a



b

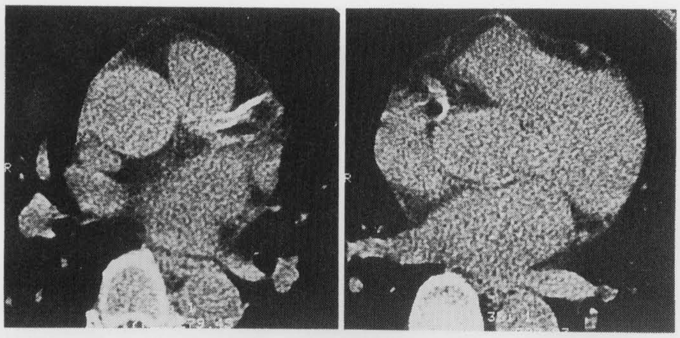


Fig. 3 a; myocardial ^{201}Tl SPECT, b; EBT. A 62 year-old female complained of chest pain, and had been medicated for hypertension. Left anterior descending artery had 99% stenotic lesion on coronary arteriograms, and normal left ventricle contraction was observed on echocardiograms. SPECT score was 3 (a) and her log transformed total calcium index was 6 (b), showing true positive results on both SPECT and EBT.

specificity of EBT for detecting RCA lesion was significantly lower than that of myocardial ^{201}Tl SPECT (Table 2c). Regardless of the subgroup, the combined diagnosis did not contribute to improving diagnostic accuracy.

In a comparison of the diagnostic accuracy of myocardial ^{201}Tl SPECT and EBT on a patient-basis grouped by gender, only sensitivity of the combined diagnosis in the male patients was significantly lower than that of myocardial ^{201}Tl SPECT (Table 3). Regardless of gender, combined diagnosis did not contribute to the improvement of diagnostic accuracy.

Illustrative cases are shown in Figs. 3 to 5.

DISCUSSION

Electrocardiographic exercise testing (ECG), exercise ^{201}Tl SPECT and stress echocardiograms are useful techniques for evaluating CAD. Overall sensitivity of ECG, myocardial ^{201}Tl SPECT and echocardiograms was reported to be about 70%, 90% and 80%, and overall specificity was about 80%, 70% and 90%, respectively.[1,4,7,8,21] When a patient with positive results on both "SPECT and exercise ECG" was defined as a patient with CAD, the sensitivity and specificity of complemental diagnosis by means of exercise ^{201}Tl SPECT and exercise ECG were reported to be 68% and 83%, respectively.[1]

Our results for sensitivity and specificity on a per-a

b

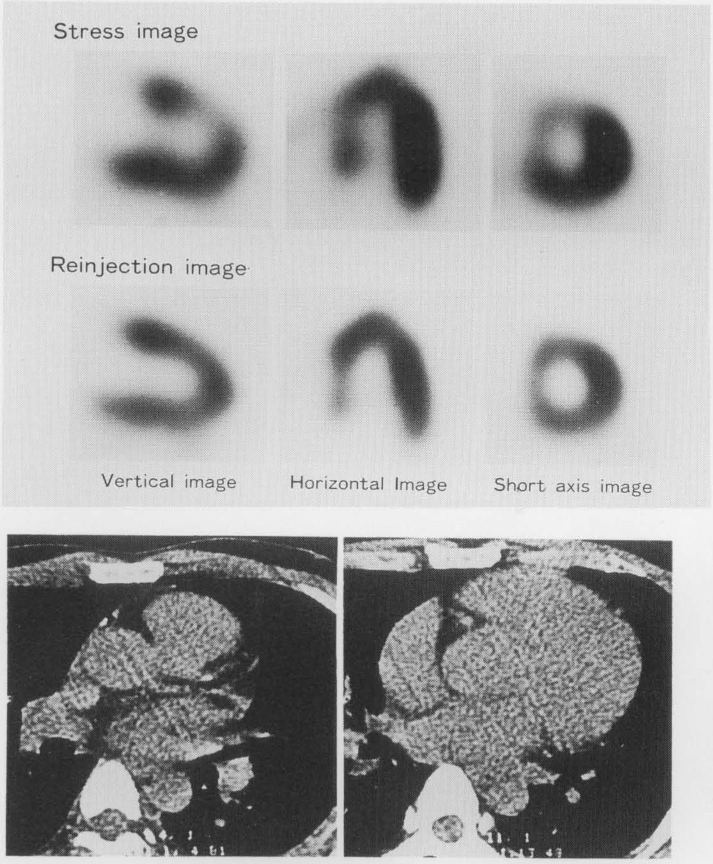


Fig. 4 a; myocardial ^{201}Tl SPECT, b; EBT. A 37 year-old male had been medicated for hypertension for 2 years and was hospitalized with a heart failure. Coronary arteriograms revealed 90% stenosis of left anterior descending artery, and dyskinesis of anterior wall and akinesis of septal wall were shown on echocardiograms. His SPECT score was 3 (a), and his log transformed total calcium index was 0 (b), showing true positive results on SPECT and false negative results on EBT for coronary artery disease.

a

b

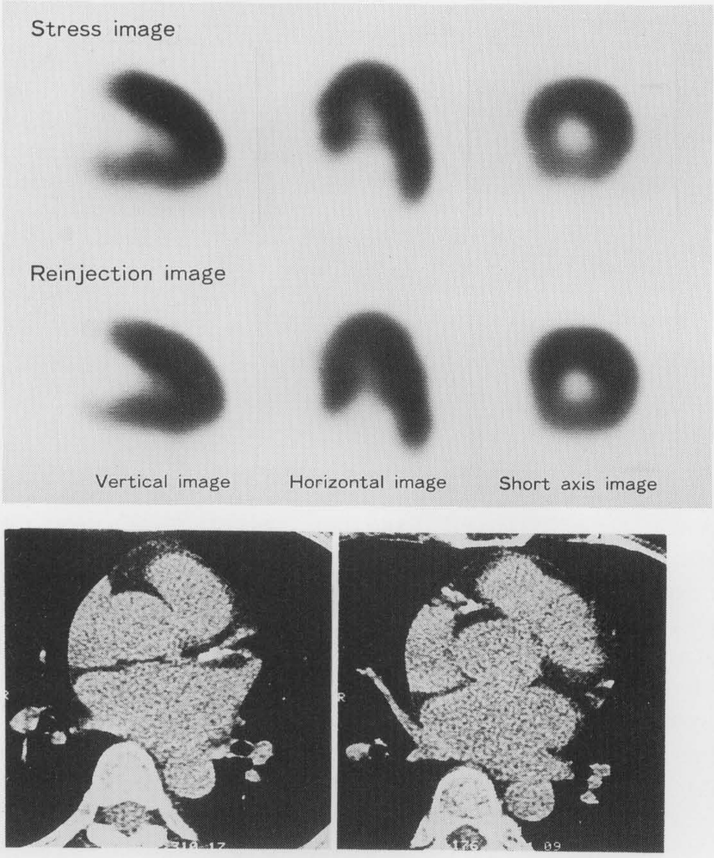


Fig. 5 a; myocardial ^{201}Tl SPECT, b; EBT. A 63 year-old male had been medicated for hypertension and diabetes mellitus and was hospitalized with chest pain. Coronary arteriograms revealed significant stenosis of only left circumflex artery (LCx). However EBT showed prominent high calcification score in left anterior descending (LAD) and right coronary artery (RCA) which were defined as false positive results. Calcium index in LCx was 5, which was defined as true positive. Normal ^{201}Tl SPECT myocardial perfusion images showed true negative result for LAD and RCA lesions and false negative result for LCx lesion.

patient basis of myocardial ^{201}Tl SPECT were almost the same as those previously reported,[1,4,7,8,21] and the sensitivity of EBT in this study for the diagnosis of CAD was also almost the same as that previously reported,[1,12,18,21] but the specificity of EBT was 38%, which was lower than that previously reported, due to low specificity in detecting LAD lesion. EBT can detect fine calcification more easily in LAD (Fig. 5b) than in LCx, which may lead to a high percentage of false positive results for LAD lesion.

With respect to the per-vessel basis, the sensitivity of exercise myocardial ^{201}Tl SPECT for detecting LAD, LCx, and RCA lesions was reported as 83%, 63% and 87%, and regarding EBT, 94%, 88% and 100%, respectively.[3,22,27] The specificity of myocardial ^{201}Tl SPECT for detecting LAD, LCx and RCA lesions was reported as 95%, 96% and 87%, and of EBT, 54%, 80% and 76%, respectively.[3,22,27] Sensitivity on a per-vessel basis of both exercise myocardial ^{201}Tl SPECT and EBT and specificity on a per-vessel basis of EBT was inferior to those previously reported, which may be due to the different age population and diagnostic criteria as the cutoff point for calcification.

The cutoff points for the calcium score determined by EBT varied among institutions.[1,28] Our cutoff point for the log transformed calcification score for predicting significant stenosis was 4.0 which was interpreted as 53.6 when using the Agaston method. In the report by Kajinami et al.[1] the cutoff point for the log transformed calcification score was 3.0 in all patients. Rumberger described the optimal cutoff point for the calcium score as 123 when using the Agaston method,[28] which was based on the receiver operating characteristic curve analysis. When we discuss the optimal cutoff points for the calcium score, we must pay attention to the age distribution of the patients described in previous studies.[1] In fact, since a constant cutoff point was employed regardless of age in the present study, the specificity of EBT was sacrificed along with age (Table 2).

Regarding the combined diagnosis of "myocardial ^{201}Tl SPECT and EBT," there was no improvement in diagnostic accuracy in sensitivity, specificity or accuracy, irrespective of age or gender. In our study, noticeably low sensitivity for detecting LCx lesions was observed in myocardial ^{201}Tl SPECT and EBT (Fig. 2a). With respect to myocardial ^{201}Tl SPECT, small area perfusion supplied through LCx might yield to sensitivity, but it might not be related to the sensitivity of EBT because of the evaluation of proximal coronary arteries. We anticipated that the detectability of LCx lesion by EBT may improve the low sensitivity of myocardial ^{201}Tl SPECT, but for LCx lesion, there was no significant difference of the sensitivity between myocardial ^{201}Tl SPECT and EBT.

Although sensitivity for detecting LAD lesions was reduced by combining the results of myocardial ^{201}Tl SPECT and EBT (Fig. 2a), the sensitivity of EBT in patients over 70 yr was significantly higher than that of myocardial ^{201}Tl SPECT. This may indicate the clinical usefulness of EBT examination. And the specificity of myocardial ^{201}Tl SPECT in detecting LAD and RCA lesions was superior to that of EBT. A previous study also reported that the specificity and accuracy of EBT were lower than those of myocardial SPECT with ^{99m}Tc-MIBI (specificity 77% vs. 95%; accuracy 71% vs. 85%).[29] From the viewpoint of screening tests for CAD, there was no reason to combine the results of SPECT and EBT.

CONCLUSION

The clinical usefulness of combined diagnosis with myocardial ^{201}Tl SPECT and EBT for CAD was investigated by statistical analysis for diagnostic accuracy. Although sensitivity in detecting LAD lesion in patients over 70 yr of age by means of EBT was significantly higher than that by means of myocardial ^{201}Tl SPECT, in the detectability of CAD, combined use of myocardial ^{201}Tl SPECT and EBT offers no improvement.

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