Comparative Study of Dobutamine Stress Electron-Beam Computed Tomography and Exercise Thallium Scintigraphy in the Diagnosis of Patients With Suspected Coronary Artery Disease

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To evaluate the diagnostic value of dobutamine stress electron-beam computed tomography (EBCT) as compared with exercise stress thallium-201 single-photon emission computed tomography (^{201}Tl -SPECT) for the detection of myocardial ischemia, 10 patients with proven or suspected coronary artery disease underwent both tests. Nine of the 10 patients also underwent coronary angiography. EBCT images were analyzed objectively to evaluate systolic wall thickening and analyzed segmentally to determine the distribution of the coronary arteries. Dobutamine stress EBCT revealed the presence of ischemia in 59 segments, whereas exercise stress ^{201}Tl -SPECT revealed ischemia in 51 segments (agreement=73%). The advantage of dobutamine stress EBCT was demonstrated in the inferior/posterior segments as compared with the results of exercise stress ^{201}Tl -SPECT. The overall sensitivity for detecting ischemic regions supplied by coronary arteries with significant stenosis (diameter stenosis >50%) was 83% for dobutamine stress EBCT and 79% for exercise stress ^{201}Tl -SPECT ($p=\text{NS}$), with specificities of 75% and 82% ($p=\text{NS}$). Thus, dobutamine stress EBCT presents a reasonable alternative to exercise stress ^{201}Tl -SPECT for the objective assessment of patients with suspected coronary artery disease. (*Jpn Circ J* 1998; 62: 83–90)

Key Words: Dobutamine stress EBCT; Exercise thallium scintigraphy; Myocardial ischemia; Systolic wall thickening; Segmental analysis

The ability to detect regional myocardial ischemia non-invasively would significantly aid the diagnosis and treatment of patients with coronary artery disease. Currently, exercise testing is performed to induce myocardial ischemia.^{1,2} Exercise-induced abnormalities in myocardial blood flow distribution can be detected by the traditional scintigraphic technique of thallium-201 single-photon emission computed tomography (^{201}Tl -SPECT).³ Recently, dobutamine stress testing has also been used to detect myocardial ischemia or significant coronary artery disease, mainly in conjunction with echocardiography.^{4–9} Dobutamine is a β -adrenergic agonist with positive inotropic and chronotropic effects that make it suitable for inducing myocardial oxygen demand and provoking myocardial ischemia in patients with coronary stenosis. The basis of stress echocardiography is that the occurrence of wall motion abnormalities is an early and sensitive marker for myocardial ischemia that precedes the development of ECG changes and anginal symptoms.^{10–12} Cine mode scanings of electron-beam computed tomography (EBCT) may potentially be as effective as echocardiography in detecting myocardial ischemia induced by dobutamine stress testing. Although several studies using EBCT have reported the detection

of coronary artery calcification or the measurement of myocardial blood flow,^{13–17} there are few reports of its use in the assessment of left ventricular wall motion abnormalities.^{18,19} The present study was designed to determine the value of dobutamine stress EBCT, as compared with exercise stress ^{201}Tl -SPECT, for the detection of myocardial ischemia.

Methods

Study Patients

The study group consisted of 10 Japanese patients who were referred for perfusion scintigraphy at the Second Department of Internal Medicine, Hiroshima University School of Medicine, for the evaluation of myocardial ischemia. The group comprised 6 men and 4 women aged 40–79 years (mean $\pm$ SD, 62 ± 13). Three patients had a history of previous myocardial infarction (postinfarction time >6 months). Five patients had previously received coronary angioplasty. At the time of study, no patients were receiving β -adrenergic blocking agents, but nitrates, calcium channel blocking agents, or both were administered. Informed consent was obtained from each patient prior to study.

Dobutamine Stress EBCT

Scanning was performed with an Imatron C-150 scanner (Imatron, South San Francisco, CA, USA). Each subject was placed in a supine position on the scanner couch, tilted 15° axially with the feet down, and was slewed 25° horizontally to the right to produce an approximate

(Received February 19, 1997; revised manuscript received June 27, 1997; accepted July 15, 1997)

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Fig 1. Schematic representation of 12 segments of basal, middle, and apical left ventricular levels, and coronary artery distribution. LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery.

short-axis view of the left ventricle. An intravenous cannula was inserted into the right antecubital vein for the administration of contrast medium, and another cannula was inserted into the left or right saphenous vein for the administration of dobutamine. The patient's hands were positioned above the head throughout the study. Scans were obtained 30 sec after administration of a bolus injection of contrast medium (iopamidol, 370 mg of iodine/ml), followed by the administration of a dose at 1.2–1.5 ml/sec, for a total of 30–50 ml. We used a cine mode protocol that repeatedly scans 1 target at a rate of 50 msec/scan with an 8 msec/scan interval. The scan of 10 continuous images in 1 target was triggered by the R wave of the ECG (approximating lead V₅). By using 4 targets and 2 detectors in sequence, we scanned 8 levels. One scanning covered 76 mm, as 1 level had a thickness of 8 mm, and there was a slice gap of 4 mm between each target. After the first scanning was performed at baseline, dobutamine was infused at a dose of 5, 10, 20, 30, and up to 40 µg/kg per min, being increased at 3-min intervals. The maximal dose of dobutamine was infused for 6 min. The ECG was monitored continuously throughout the dobutamine infusion, and a 12-lead ECG and cuff blood pressure were recorded each minute. The dobutamine infusion was discontinued if any of the following were observed: (1) a rise in systolic blood pressure to >230 mmHg and/or diastolic blood pressure >130 mmHg; (2) a decrease in systolic blood pressure to <80 mmHg; (3) depression of ST segment >2 mm 80 msec after the J point, or ST segment elevation; (4) development of ventricular tachycardia; (5) development of severe chest pain or other intolerable symptoms, or (6) achievement of the target heart rate of 85% of the age-predicted maximal exercise heart rate. Cine EBCT was performed at baseline and again at termination.

Computed tomograms were analyzed by 3 experienced investigators who were unaware of the scintigraphic, angiographic, and clinical data. For the purposes of wall motion analysis, 3 out of 8 short-axis images in 1 scanning were selected as representative of the basal, middle, and apical levels. Images were divided according to the vascular distribution of the major epicardial coronary arteries; 12 segments of basal, middle, and apical levels were obtained (Fig 1). The anterior and septal segments (Nos. 1, 2, 5, 6, 9, 10) were considered specific for the left anterior descending coronary artery distribution, the

lateral (Nos. 4, 8, 12) and the inferior region (Nos. 7, 11) for the left circumflex coronary artery and the right coronary artery distribution, respectively, whereas the posterior area (No. 3) was regarded as the territory of the left circumflex or right coronary artery, depending on the dominance of the right coronary artery. In EBCT, the field of view was 30 cm and the matrix size was 256 × 256. One pixel therefore measured 1.17 mm. Endocardial and epicardial boundaries in end-systolic phase images were traced manually with a track ball cursor. The endocardial boundary was traced excluding the papillary muscles and trabeculae. A reference point (0°) of the epicardial boundary at the anterior interventricular groove was selected. The center of end-systolic endocardial gravity was used to measure systolic wall thickness. The lengths of 36 radii each 10° from the center of gravity to the endocardial and epicardial boundaries were calculated by a computer linked to the system. The systolic wall thickness in each segment was calculated as the end-systolic distance from the endocardial boundary to the epicardial boundary at the center of each segment. For the objective assessment of myocardial contraction during dobutamine stress, the systolic wall thickness ratios (SWTRs) in each segment were calculated as the ratio of the value at the peak dobutamine infusion rate to that obtained at baseline. Because dobutamine increases myocardial contractility, the SWTR must exceed a value of 1 in the normal segment without myocardial ischemia. If there is a lack of viability in the myocardium as a result of a previous infarction, the SWTR will equal 1 because of the absence of myocardial contraction. In a segment with dobutamine-induced myocardial ischemia, the SWTR may be less than 1 or, if the ischemia is mild, it may be greater than 1 (but less than the value in the normal segments). Accordingly, to detect mild myocardial ischemia with a SWTR value greater than 1, the rate in each segment relative to the maximal SWTR was obtained for each patient and denoted as R-SWTR. Intrinsically, the R-SWTR in a segment with the definite SWTR was thought to be altered by the maximal SWTR. In this study, the criteria used to determine a positive dobutamine stress EBCT-detected myocardial ischemia were a SWTR ≤ 1 and/or a R-SWTR less than the threshold value. The adequate threshold of R-SWTR was estimated to detect myocardial ischemia.

Table 1 Results of Dobutamine Stress Electron-Beam Computed Tomography (EBCT), Exercise Stress Thallium-201 Single-Photon Emission Computed Tomography (²⁰¹Tl-SPECT) and Coronary Angiography

Case No	Age (Years)	Sex	Regional division	EBCT	²⁰¹ Tl-SPECT	Coronary angiography		Left ventriculogram	Previous myocardial infarction
				Ischemic segments	Ischemic segments	True ischemic segments	Stenosis location	Wall motion	
1	66	M	(Ant, Sept) (Lat) (Ip)	1,2 4,12 11	— — 3,7,11	— — —	None	Normal	No
2	67	M	(Ant, Sept) (Lat) (Ip)	1,2 — 3,11	2 — 3,7,11	— — 3,7,11	RCA(3)	Inferior and posterobasal hypokinesis	No
3	60	F	(Ant, Sept) (Lat) (Ip)	1,2,5,6,9,10 12 11	2,5,6,9,10 12 3,7,11	5,6,9,10 12 11	LAD(7) LCx(14) RCA(4), PD	Apical and septal hypokinesis	Yes (Ant)
4	43	M	(Ant, Sept) (Lat) (Ip)	1,2,5,6,9,10 4,8,12 3,7,11	1,2,5,6,9,10 8 3,7,11	1,2,5,6,9,10 12 3,7,11	LAD(6) LCx(14) RCA(3)	Normal	No
5	76	F	(Ant, Sept) (Lat) (Ip)	1,6 12 7	— — 7,11	Unknown	Unknown	Unknown	No
6	70	M	(Ant, Sept) (Lat) (Ip)	1,2,5,6,9,10 — 7,11	1,2,5,6,9,10 — 3,7,11	1,2,5,6,9,10 — 3,7,11	LAD(6)* — RCA(3)	Anterolateral, apical, inferior and septal hypokinesis	Yes (Ant)
7	79	F	(Ant, Sept) (Lat) (Ip)	6 12 —	— — —	— 8,12 —	LCx(12)	Normal	No
8	63	M	(Ant, Sept) (Lat) (Ip)	1,2,5,10 4,8,12 3,11	1,2,5,9 — 3,7,11	1,2,5,6,9,10 4,8,12 3	LAD(6) LCx(11)	Normal	No
9	40	F	(Ant, Sept) (Lat) (Ip)	2,9 — —	— — —	— — —	None	Normal	No
10	53	M	(Ant, Sept) (Lat) (Ip)	6,9,10 12 7	9,10 4,8,12 7,11	5,6,9,10 8,12 7,11	LAD(7)* LCx(12) RCA(4), PD	Apical and posterolateral hypokinesis	Yes (Ant)

M, male; F, female; Ant, anterior region; Sept, septal region; Lat, lateral region; Ip, inferior/posterior region; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; PD, posterior descending artery.

Segment(s) of the coronary arteries with an intraluminal narrowing of at least 50% are shown in parentheses (according to the American Heart Association Committee Report. *Circulation* 1975; 51: 5–40.).

*Coronary artery obstruction.

Exercise Stress ²⁰¹Tl-SPECT

Thallium tomography was performed in the week before the EBCT trial. Exercise stress was executed using a bicycle ergometer or a treadmill, and was discontinued when any of the previous criteria used for the termination of dobutamine infusion occurred, except for the maximal dose of dobutamine. The ECG was continuously monitored, and a 12-lead ECG and systolic cuff blood pressure were recorded each minute. Approximately 60 sec before the termination of the exercise stress, an injection of 148 MBq of ²⁰¹TlCl was administered. Imaging began 5–10 min after termination of the exercise stress, using a single-crystal rotating gamma camera (ZLC 7500, Siemens Medical Systems, Hoffman Estates, IL, USA) interfaced with a computer (Scintipac 7000, Shimadzu, Kyoto, Japan). A low-energy, high-resolution collimator was employed, with a total of 32 projections being obtained over an anterior 180° arc from a 45° right anterior oblique with an acquisition time of 25 sec/projection. Transaxial images of 6 mm slice thickness were obtained by back-projection using a Shepp-Logan filter, and were then reoriented into short-axis and vertical and horizontal long-

axis views. Delayed images were obtained in 4 h. The tomographic slices were interpreted visually by 3 experienced investigators who were unaware of the results of EBCT and coronary angiography and the clinical data. The initial and delayed images were compared qualitatively using the same segmentation as that employed for the EBCT. The same assumptions were made about the distribution of the coronary artery. Regions were interpreted as showing normal perfusion, a stress-induced perfusion defect, or a fixed perfusion defect.

Cardiac Catheterization

Selective coronary angiography and biplane left ventriculography were performed using the Judkins technique in the week before or after the EBCT trial. Films were read by 2 independent observers who were unaware of the results of EBCT and ²⁰¹Tl-SPECT and the clinical data. Segmentation of the coronary circulation was performed according to the recommendation of a committee of the American Heart Association in 1975²⁰. Narrowing of the coronary artery was expressed as percent diameter stenosis for each segment. Significant coronary stenosis was

defined as >50% narrowing of the lumen of the major epicardial coronary artery or major branch vessel.

Statistical Analysis

Continuous variables were expressed as means $\pm$ SD, and compared using the Wilcoxon signed-ranks test for paired data. Unpaired data were compared with the Mann-Whitney U test. Discrete variables were analyzed using McNemar's test for paired data and the chi-square

test with Yates' correction, or Fisher's exact test (depending on the sample size), for unpaired data. A *p* value <0.05 was considered statistically significant.

Results

Cardiac Catheterization

Angiographic data are listed in Table 1. One woman was excluded from this section of the study because of a lack of informed consent for the invasive procedure. Four patients demonstrated moderate hypokinesis of the left ventricle at rest during biplane ventriculography. Seven of 9 patients who underwent coronary angiography exhibited significant coronary stenosis (>50% diameter stenosis). Two of these 7 patients had single-vessel disease. An additional 2 patients had 2-vessel disease and 3 patients had triple-vessel disease. Two of the 7 patients had coronary artery obstruction and some collateral tracts toward the obstructed coronary arteries were seen. In the 2 remaining patients, no significant coronary stenosis was detected. One of these patients had a normal coronary angiogram, whereas the other had recently undergone balloon angioplasty with no significant coronary abnormality at the time of catheterization. Thus, as determined by coronary angiography, in 108 segments of the 9 patients, 48 were considered true ischemic regions that were supplied by coronary arteries with significant stenosis, whereas 60 were considered normal regions.

Feasibility of Dobutamine Stress and Exercise Stress Tests

The dobutamine stress and exercise stress tests were completed without serious complications in all patients. The clinical variables are shown in Table 2. Overall, dobutamine significantly increased heart rate and rate-pressure product, and decreased diastolic blood pressure.

Table 2 Clinical Parameters During Dobutamine Stress and Exercise Stress Tests

	Dobutamine stress test	Exercise stress test
Heart rate (beats/min)		
Baseline	70 $\pm$ 12	77 $\pm$ 15
Peak stress	120 $\pm$ 20 ^{†‡}	140 $\pm$ 21 [†]
Systolic blood pressure (mmHg)		
Baseline	144 $\pm$ 26	149 $\pm$ 18
Peak stress	132 $\pm$ 26 [§]	180 $\pm$ 30 [†]
Diastolic blood pressure (mmHg)		
Baseline	74 $\pm$ 18	
Peak stress	57 $\pm$ 11 [*]	
Rate-pressure product (mmHg/min)		
Baseline	10,244 $\pm$ 2,962	11,508 $\pm$ 2,917
Peak stress	16,014 $\pm$ 4,748 ^{†§}	25,280 $\pm$ 6,156 [†]
Peak THR(%)	76 $\pm$ 16	88 $\pm$ 13
Chest pain (No)	3	3
ST segment depression (No)	2	3
ST segment elevation (No)	1	2

Data are expressed as means $\pm$ SD or number of patients.

THR, theoretical maximal exercise heart rate.

^{*}*p* < 0.05, [†]*p* < 0.01 vs baseline.

[§]*p* < 0.05, [§]*p* < 0.01 vs exercise stress test.

Fig 2. Baseline images of electron-beam computed tomography (EBCT) at end-diastole (A) and end-systole (B) and the end-systolic images of EBCT with endocardial and epicardial outlines at baseline (C) and during dobutamine stress (D) in a patient with significant left anterior descending coronary artery stenosis. The baseline contraction demonstrated visible systolic wall thickening in a whole region (B). The contractile response to dobutamine infusion was considered normal in the lateral and inferior regions with a systolic wall thickness ratio (SWTR) >1 and a relative rate of systolic wall thickness ratio (R-SWTR) $\geq$ 70% (D). Myocardial ischemia induced by dobutamine was detected in the anterior and septal regions using the positive criteria of dobutamine stress EBCT (SWTR $\leq$ 1 and/or R-SWTR < 70%) (D, arrows).

Table 3 Comparison of Dobutamine Stress Electron-Beam Computed Tomography (EBCT) and Exercise Stress Thallium-201 Single-Photon Emission Computed Tomography (^{201}Tl -SPECT) for the Detection of Myocardial Ischemia

	Sensitivity	Specificity	PPV	NPV	OR	95% CI	p Value
<i>EBCT</i>							
(SWTR ≤ 1 and/or)							
R-SWTR $< 75\%$	88%	58%	63%	85%	3.1	2.0–5.4	< 0.0001
R-SWTR $< 70\%$	83%	75%	73%	85%	3.9	2.5–6.4	< 0.0001
R-SWTR $< 65\%$	73%	82%	76%	79%	3.5	2.2–5.6	< 0.0001
^{201}Tl -SPECT	79%	82%	78%	83%	4.1	2.7–6.8	< 0.0001

SWTR, systolic wall thickness ratio; R-SWTR, relative rate of systolic wall thickness ratio; PPV, positive predictive value; NPV, negative predictive value; OR, odds ratio; CI, confidence interval.

Exercise significantly increased heart rate, systolic blood pressure, and rate-pressure product. Peak heart rate, peak systolic blood pressure, and peak rate-pressure product were significantly lower during the dobutamine stress test than during the exercise stress test. On average, the heart rate achieved was for the dobutamine stress test 76% and for the exercise stress test 88% ($p=\text{NS}$) of the age-predicted maximal exercise heart rate.

Dobutamine Stress EBCT

The EBCT image quality was good in all 10 patients, allowing wall motion analysis (Fig 2). The baseline systolic wall thickening was visible in a whole segment of each patient. The SWTR values were 1.0 ± 0.3 for the segments considered to be true ischemic regions by cardiac catheterization vs 1.5 ± 0.5 for those segments considered to be normal regions ($p < 0.001$). The values of R-SWTR were $66 \pm 18\%$ in the true ischemic regions and $73 \pm 25\%$ in the normal regions ($p < 0.001$). Statistical correlates of the dobutamine stress EBCT at various thresholds of R-SWTR are listed in Table 3. For SWTR ≤ 1 and/or R-SWTR $< 70\%$, the sum of sensitivity and specificity for the detection of true ischemic regions based upon the angiographic findings was maximized with the highest odds ratio. Using this value, dobutamine stress EBCT revealed the following results compared with exercise stress ^{201}Tl -SPECT.

Relation Between Wall Motion and Myocardial Perfusion

Dobutamine stress EBCT was positive for myocardial ischemia in a total of 59 segments in the 10 patients (Table 1). A total of 42 segments had SWTR values of ≤ 1 and 46 had R-SWTR values of $< 70\%$. Twenty-nine segments had both SWTR values of ≤ 1 and R-SWTR values of $< 70\%$. The test results were negative in 61 segments. With exercise stress ^{201}Tl -SPECT, reversible perfusion defects were detected in 51 segments, but no fixed perfusion defects were detected. Test results were negative in 69 segments. The results of the 2 methods agreed in classifying 88 of the 120 segments (73%), with no significant difference observed between their diagnoses.

Relations Between Dobutamine Stress EBCT and Exercise Stress ^{201}Tl -SPECT and Coronary Angiographic Findings

In 9 patients who underwent coronary angiography, when compared with the angiographic data, dobutamine stress EBCT correctly predicted the presence or absence of myocardial ischemia in 78% of the anterior, septal, and lateral segments and in 81% of the inferior/posterior segments (Table 1). The corresponding values obtained with exercise stress ^{201}Tl -SPECT were 96% for the anterior

segments ($p < 0.05$), 81% for the septal segments ($p=\text{NS}$), 70% for the lateral segments ($p=\text{NS}$), and 74% for the inferior/posterior segments ($p=\text{NS}$). The 2 tests showed a false-positive rate of 29% for dobutamine stress EBCT and 0% for exercise stress ^{201}Tl -SPECT ($p < 0.05$) for the anterior segments, 36% and 14% ($p=\text{NS}$) for the septal segments, 22% and 11% ($p=\text{NS}$) for the lateral segments, and 14% and 50% ($p=\text{NS}$) for the inferior/posterior segments. The incidence of false-negative results was 15% for dobutamine stress EBCT and 8% for exercise stress ^{201}Tl -SPECT ($p=\text{NS}$) for the anterior segments, 8% and 23% ($p=\text{NS}$) for the septal segments, 22% and 67% ($p=\text{NS}$) for the lateral segments, and 23% and 0% ($p=\text{NS}$) for the inferior/posterior segments. Dobutamine stress EBCT revealed no significant differences between the incidence of false-positive and false-negative results in the 4 regional divisions. However, with exercise stress ^{201}Tl -SPECT, the incidence of false-positive results in the inferior/posterior segments significantly exceeded that in the anterior ($p < 0.01$) and lateral segments ($p < 0.05$). The incidence of false-negative results in the lateral segments was also significantly higher than observed in the other regional divisions ($p < 0.01$ for the anterior and inferior/posterior segments; $p < 0.05$ for the septal segments).

Overall, dobutamine stress EBCT detected 40 segments (29 with SWTR values ≤ 1 and/or 29 with R-SWTR values $< 70\%$, 18 had both criteria), whereas exercise stress ^{201}Tl -SPECT detected 38 segments of the 48 ischemic segments, based upon the angiographic findings. The sensitivity was 83% and 79% ($p=\text{NS}$), respectively (Table 3). The specificity was 75% for dobutamine stress EBCT and 82% for exercise stress ^{201}Tl -SPECT ($p=\text{NS}$), with overall accuracies of 79% and 81% ($p=\text{NS}$). The predictive value of the 55 positive EBCT results was 73%, compared with 78% for the 49 positive ^{201}Tl -SPECT results ($p=\text{NS}$). The predictive value of a negative EBCT was 85% and that of ^{201}Tl -SPECT was 83% ($p=\text{NS}$). The odds ratio for the detection of myocardial ischemia was similar for the 2 tests (3.9 and 4.1).

Discussion

Dobutamine stress echocardiography and perfusion scintigraphy have recently been used in the diagnosis of coronary artery disease, the assessment of the results of coronary angioplasty, or risk stratification before vascular surgery.^{21–24} However, in both echocardiography and scintigraphy, cardiac images can be easily influenced by the condition of the lungs, the presence of obesity, as well as by the subjective evaluation of the observer. We used EBCT to overcome these problems. With EBCT, the

endocardial and epicardial boundaries of the left ventricle were easily recognized in all cases. This property made it possible to assess left ventricular wall motion objectively. In this study, we used EBCT combined with the dobutamine stress test as a substitute for echocardiography. We also assessed the rationale for this method as compared with the scintigraphic technique. This appears to be the first study to compare dobutamine stress EBCT with exercise stress ^{201}Tl -SPECT in the detection of myocardial ischemia.

The determination of the relationship between regional myocardial perfusion and transmural function is a challenging problem. Tomoike et al²⁵ demonstrated experimentally the adverse consequences of limited coronary flow during heavy exercise in terms of regional contractile function in dogs that were instrumented to monitor myocardial segment lengths and left ventricular pressure. Similarly, several studies on myocardial blood flow and experiments on regional function have shown that insufficient blood flow leads to ischemia that is manifested by regional mechanical dysfunction²⁶⁻²⁹ Gallagher et al³⁰ demonstrated that systolic wall thickening provides a reliable index of the relative adequacy of myocardial blood flow under widely varying conditions in exercising dogs with varying degrees of coronary stenosis.

With EBCT, the observation of wall thickening was expected to be carried out easily because of the excellent recognition of the endocardial and epicardial boundaries of the left ventricle. Accordingly, in this study, we considered systolic wall thickening in the analysis of EBCT. For practical analysis, we used the systolic wall thickness and originally calculated its ratio (SWTR) during the infusion of dobutamine. To assess the spatial distribution of mild abnormalities of wall thickening, we defined the indicator 'R-SWTR' as the relative rate of SWTR in each segment normalized to the maximal value of SWTR in each patient. Even if the values of SWTR were the same for any 2 segments in different patients, the corresponding values of R-SWTR should differ because of the discordance of the maximal values of SWTR between the patients. However, in 1 patient, we thought that we observed a single segment with severe myocardial ischemia based upon the low SWTR and R-SWTR values (data not shown). In fact, we detected a considerable number of ischemic segments supplied by significantly stenosed coronary arteries using the positive criteria of dobutamine stress EBCT (SWTR ≤ 1 and/or R-SWTR $< 70\%$). However, in this trial, some segments had values of SWTR ≤ 1 or R-SWTR $< 70\%$ in the normal region, and those with values of SWTR > 1 and R-SWTR $\geq 70\%$ in the ischemic region, as determined by coronary angiography. We suspected that this discrepancy could be attributed to the following mechanisms. (1) In this trial, image slices of EBCT might not have been adjusted to the accurate short-axis view of the left ventricle, even though each patient was positioned on a scanner couch adjusted to the uniform direction. In addition, some difficulties were due to cardiac translation and rotation during the infusion of dobutamine. Further development of image-adjusting techniques on EBCT is required to circumvent these problems in future. (2) We traced the cardiac boundary manually because the automatic tracing system in EBCT was not sufficient for our needs. This led to the inclusion of observer bias in the data. Thus, in future,

tracings should be performed more accurately, and, preferably, automatically.

One limitation of our method of wall motion analysis is the absence of a normal control group. We determined the threshold of R-SWTR by comparing normal and ischemic regions. Future studies should determine the threshold of R-SWTR in subjects with and without coronary artery disease. Moreover, another potential limitation existed in the present analysis. If all segments were considered to be ischemic by coronary angiography and the maximal value of SWTR exceeded 1, we could not detect the segment with the maximal SWTR using our positive criteria of dobutamine stress EBCT. In this trial, at least 1 segment was considered to be a normal region in each of the 9 patients who underwent diagnostic coronary angiography. To circumvent this problem, future studies should refer to the lower limit of the normal range of SWTR.

Our group of patients was primarily referred for exercise stress perfusion scintigraphy to investigate chest pain. Dobutamine stress EBCT was positive for myocardial ischemia in 59 (49%) of the 120 segments, whereas transient perfusion defects of exercise stress ^{201}Tl -SPECT were detected in 51 of the 120 segments (43%). The agreement between the 2 tests for the detection of presence or absence of myocardial ischemia was 73%, whereas disagreement was reported in 32 (27%) of the 120 segments. This discrepancy may have been due to problems with image adjustment or tracing systems of EBCT. Other mechanisms could also be involved. For example: (1) it should be noted that the stress methods differed between the 2 tests. In this study, dobutamine significantly increased the heart rate and rate-pressure product on average in all patients just as in the exercise stress test. However, the peak heart rate, peak systolic blood pressure, and peak rate-pressure product were significantly lower during the dobutamine stress test than during the exercise stress test. Recently, McNeill et al⁸ using dobutamine stress echocardiography in the detection of coronary artery disease, reported the utility of atropine administration in patients who did not achieve an adequate heart rate response to dobutamine. If atropine had been used, the results of dobutamine stress EBCT and its concordance with exercise stress ^{201}Tl -SPECT may have been altered. (2) Visual images of ^{201}Tl -SPECT may have been influenced by the attenuation of thallium energy through the body mass, a weakness of ^{201}Tl -SPECT. In contrast, EBCT provides excellent imaging with high spatial and contrast resolution that is not affected by the patient's condition. We think that this is the unique advantage of EBCT, despite problems such as the risk of radiation exposure and the administration of a contrast medium. EBCT does not necessarily require the same technical skill or experience as echocardiography. Accordingly, we think EBCT can be used more easily and more widely than either echocardiography or ^{201}Tl -SPECT.

When compared with the angiographic data, the overall accuracy of dobutamine stress EBCT resembled that of exercise stress ^{201}Tl -SPECT. However, using a regional division approach, the accuracy of dobutamine stress EBCT, in the anterior segments, was significantly lower than that of exercise stress ^{201}Tl -SPECT. The incidence of false-positive findings in these segments was significantly higher with dobutamine stress EBCT; segment No 1, in

particular, contributed to this discrepancy. The incidence of false positives in the septal segments with dobutamine stress EBCT was 2.5 times that of exercise stress ^{201}Tl -SPECT, although the difference was not statistically significant. In this case, segment No 2 was the main contributor to this discrepancy. We believe that a possible explanation for these discrepancies is that, as a result of the incomplete image adjusting of EBCT, an accurate short-axis view of the left ventricle actually led to the images of slices in the direction of the long axis of the heart. We suspect that the image slices at the basal level occurred toward the base of the left ventricle where the wall contraction was anatomically restricted, especially at the anterior and septal segments (segments Nos 1 and 2), producing false-positive results. Improvement in the image adjustment of EBCT should prevent these problems in the future.

Exercise stress ^{201}Tl -SPECT had a false-positive rate in the inferior/posterior segments that was 3.5 times that of dobutamine stress EBCT, although this difference was not statistically significant. The false-negative rate observed in the septal and lateral segments with exercise stress ^{201}Tl -SPECT was 3 times that of dobutamine stress EBCT; once again, this difference was not statistically significant. With exercise stress ^{201}Tl -SPECT, the false-positive rate in the inferior/posterior segments and the false-negative rate in the lateral segments were significantly increased in the 4 regional divisions. These results suggest that the occurrence of myocardial ischemia in the inferior/posterior segments could easily be overestimated by exercise stress ^{201}Tl -SPECT, probably because of the thallium energy attenuation of these segments through the body mass. Conversely, the septal and, in particular, the lateral segments adjacent to the inferior/posterior segments tended to be underestimated. However, dobutamine stress EBCT did not reveal any significant differences in the incidence of false-positive and false-negative results between the 4 regional divisions. These results demonstrated the advantage of dobutamine stress EBCT for the detection of myocardial ischemia in the inferior/posterior segments as compared with exercise stress ^{201}Tl -SPECT.

The overall sensitivity and specificity of dobutamine stress EBCT for detecting myocardial ischemia resembled those of exercise stress ^{201}Tl -SPECT. The positive and negative predictive values of the 2 tests were also similar. Thus, dobutamine stress EBCT and the methodology presented here may be useful in detecting myocardial ischemia. Further investigation is necessary to verify the accuracy of dobutamine stress EBCT in a larger series of patients with coronary angiography. A modification of the centerline method that was previously described for echocardiography³¹ may prove to be useful in assessing regional wall motion on cine EBCT.

Dobutamine stress EBCT appears to present a reasonable alternative to exercise stress ^{201}Tl -SPECT for the assessment of patients with suspected coronary artery disease. However, EBCT trials using only short-axis tomograms may be insufficient for the assessment of apical myocardium. In this study, we detected the ischemic region supplied by coronary arteries with significant stenosis and obtained a sensitivity of 83% with an accuracy of 79% for dobutamine stress EBCT. These results are comparable to those of previous reports obtained using dobutamine stress echocardiography.

Recent studies of dobutamine stress echocardiography have reported sensitivities of 70–96% for detection of coronary artery disease^{4–9}. Additionally, McNeill et al⁸ reported an accuracy of 78% for dobutamine stress echocardiography. In other studies^{4–7,9} the reported level of accuracy (82–89%) slightly exceeded the result obtained in our study. With respect to accuracy, the difference between these studies and ours may be due to differing patient series or methods used in the assessment of myocardial ischemia. In this study, we included 3 patients with previous myocardial infarction after confirmation of the baseline systolic wall thickening in a whole segment of myocardium. Further investigation is needed to corroborate the accuracy of dobutamine stress EBCT in patients without previous myocardial infarction and to determine the utility of this new technique combined with exercise stress ^{201}Tl -SPECT in the diagnosis of coronary artery disease.

Conclusion

The results of the present study showed good agreement between dobutamine stress EBCT and exercise stress ^{201}Tl -SPECT for the detection of myocardial ischemia. Dobutamine stress EBCT has an advantage in the inferior/posterior region as compared with exercise stress ^{201}Tl -SPECT. Using coronary angiography as a standard, the overall results of the 2 tests were similar. Dobutamine stress EBCT therefore presents a reasonable alternative to exercise stress ^{201}Tl -SPECT for the objective assessment of patients with suspected coronary artery disease.

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