SIMULTANEOUS ASSESSMENT OF LEFT VENTRICULAR WALL MOTION AND MYOCARDIAL PERFUSION AT REST AND DURING EXERCISE BY TECHNETIUM-99M METHOXY ISOBUTYL ISONITRILE

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First-pass radionuclide ventriculography followed by myocardial SPECT with technetium-99m methoxy isobutyl isonitrile (Tc-99m MIBI) was performed on 12 patients with suspected coronary artery disease at rest and during exercise. Left ventricular wall motion and myocardial perfusion were assessed simultaneously and compared on a segment-by-segment basis. Segmental agreement between Tc-99m MIBI and TI-201 with regard to the presence of perfusion defects was 95% (57/60) at rest and 93% (37/40) during exercise. With respect to the assessment of myocardial ischemia and/or infarction, abnormalities in regional wall motion agreed with the presence of myocardial perfusion defects in 18 out of 21 segments (86%). Simultaneous evaluation of regional wall motion and myocardial perfusion by Tc-99m MIBI may provide useful information for the assessment of myocardial ischemia.

THALLIUM-201 myocardial imaging has widely been accepted as a useful, noninvasive technique for the diagnosis of coronary artery disease. However, the limitations of thallium-201 imaging in clinical practice include: 1) relatively low-energy photons of thallium-201 (68 to 80 KeV) are not adequate for current Anger camera systems; 2) the long half-life (73h) of the isotope limits the dose of application; and 3) the need for a cyclotron occasionally results in a lack of emergent availability. To overcome these problems, a number of technetium-99m labeled agents have been developed for imaging of myocardial perfusion. Among them, technetium-99m methoxy isobutyl isonitrile (Tc-99m MIBI) has been accepted as having the most favorable biological properties for myocardial imaging.6-7 The short half-life of technetium-99m (6h) and the favorable dosimetry of Tc-99m MIBI mean that a large dose can be administered. This higher injectable dose permits the simultaneous evaluation of both left ventricular function using the first-pass technique and myocardial perfusion by a single photon emission computed tomography (SPECT), which will improve diagnostic accuracy.

The goal of the present study was to assess the clinical application of Tc-99m MIBI for the simultaneous and segment-by-segment assessment of wall motion and myocardial perfusion in patients with coronary artery

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Twelve patients with suspected coronary artery disease were studied (Table I). They were all male with a mean age of 53 years and had chest pain associated with ischemic ST depression during exercise ECG tests. Exercise and delayed TI-201 myocardial SPECT and coronary arteriography were performed in all patients, as were first-pass RNV followed by myocardial SPECT with Tc-99m MIBI at rest. Exercise imaging by Tc-99m MIBI was performed in 8 out of 12 patients. All studies were performed after receiving informed consent. The study protocol was approved by the Yamagata University Committee on Human Research.

Three patients had single-vessel disease, 2 had double-vessel disease and 3 had triple-vessel disease. Three patients had normal coronary arteries and were considered as having syndrome X. The remaining patient had aortic regurgitation. Six patients had a previous myocardial infarction. None of the patients had previous coronary bypass surgery or percutaneous transluminal coronary angioplasty.

**Study protocol**

The exercise and delayed TI-201 myocardial SPECT was obtained before the Tc-99m MIBI imaging. Three days after the TI-201 studies, RNV and myocardial imaging with Tc-99m MIBI at rest were performed in 10

**METHODS**

**Subjects**

patients. Exercise studies with Tc-99m MIBI were performed in 6 of these 10 patients, 2
days after the studies at rest. In the remaining
2 patients, exercise Tc-99m MIBI studies were
obtained 5 days after the Ti-201 imaging, then 2 days later the Tc-99m MIBI
studies at rest were carried out. Coronary arteriography was performed within a week
after the radionuclide studies.

**Exercise Ti-201 imaging**

Antianginal medications were discontinued at least 24 h before the exercise tests, except for short-acting sublingual nitrates in episodes of anginal attack. Exercise was performed on a bicycle ergometer. Blood pressure was measured every minute at the left arm by the cuff method, and CMR-lead ECG was continuously monitored during the testing. The workload was started at 25 watts and increased by 25 watts every 3 min. Exercise was terminated when angina, dyspnea, ischemic ST depression, serious arrhythmia, or excessive fatigue appeared. A dose of 74 MBq of Ti-201 was injected 1 min before the termination of exercise. Myocardial perfusion imaging was begun 5 min after the Ti-201 administration. All studies were obtained on a rotating gamma camera (ZLC-7500 Digitrac, Siemens) equipped with a parallel hole, high resolution collimator. Energy discrimination was provided by a 20% window centered at approximately 70 KeV. Thirty-two planar acquisitions were performed during a 180° rotation from the 45° right anterior oblique to 45° left posterior oblique projection. Each 64×64 matrix was collected for 40 sec during each of the 32 steps and contained 15,000 to 20,000 counts. Delayed images were obtained 3h later. Patients were fasted between image acquisitions. Patients were carefully repositioned for the delayed image acquisition with a laser positioning device.

Data processing was performed on a nuclear medicine computer system (Scintipac-700, Shimadzu Co.) by means of a back-projection algorithm with filtering and no attenuation correction. Oblique, orthogonal tomographic slices, each 6 mm thick, were reconstructed parallel to the short axis, the vertical long axis and the horizontal long axis of the left ventricle.

**Tc-99m MIBI imaging**

Remedies for angina remained unchanged during the present study, and were discontinued in the same way as in the exercise Ti-201 studies. Exercise was performed on a bicycle ergometer and terminated at an equal duration to that achieved in the previous Ti-201 study.

First-pass radionuclide ventriculography (RNV): An 18-gauge teflon catheter was placed in an anterior-cubital vein and CMR-lead ECG was continuously monitored. The subjects faced a gamma camera (Ohio Nuclear Sigma 410S) equipped with a slant-hole collimator. A bolus dose of 555 MBq Tc-99m MIBI was injected and flushed rapidly with 20 ml saline at rest and at the peak level of exercise (Fig. 1).
TABLE III  THE RESULTS OF MYOCARDIAL PERFUSION, REGIONAL WALL MOTION AND
THE LEFT VENTRICULAR EJECTION FRACTION BY Tc-99m MIBI IN 12 PATIENTS

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<th>Myocardial perfusion</th>
<th>Regional wall motion</th>
<th>LVEF (%)</th>
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Ant: anterior, Api: apical, Inf: inferior, Ex: exercise, Re: rest, LVEF: left ventricular ejection fraction, uptake score: 2=normal, 1=reduced, 0=absent, wall motion score: 2=normal, 1=hypokinesis, 0=akinesis/dyskinesis, −: not performed.

Fig. 3. Segment-by-segment comparison of myocardial Tc-99m MIBI uptake and regional wall motion. Agreement in findings with regard to the presence or absence of myocardial ischemia or infarction was 18 out of 21 (86%) segments.
N: normal, IS: ischemia, MI: infarction

Fig. 4. Changes in regional wall motion score during exercise. In segments with ischemia, changes in the wall motion score were significantly smaller than those in normal uptake segments (p<0.01).
N: normal, IS: ischemia, MI: infarction

First-pass study was carried out at a standard 30° right anterior oblique view. When the tracer reached the left ventricular cavity, patients paused the exercise and held their breath for about 4 to 6 sec until the radioactivity passed the left ventricle. Radioactivity was gathered for 30 sec in a list mode onto a magnetic disk of a minicomputer (Gamma-11, DEC). The original data were reformed into a 32×32 matrix at a rate of 20 frames per cardiac cycle. Five to 8 beats were averaged to make up 1 cardiac cycle. Each matrix accumulated about 200–250 counts. The left ventricular contour was outlined according to Kuwahara's non-linear enhancement.10 After a background-correction, a left ventricular volume curve was constructed. The left ventricular ejection fraction was determined from this volume

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myocardial imaging (perfusion)  

exercise  

rest  

RNV (wall motion)  

exercise  

rest  

LVEF: 67%  

86%

Fig. 5. Myocardial perfusion imaging (left) and left ventricular wall motion (right) by Tc-99m MIBI in patients with anterior myocardial infarction and triple-vessel disease. Apical segment shows a persistent defect in myocardial perfusion imaging and is considered to be infarcted. In contrast, wall motion analysis reveals that the apical segment shows a transient wall motion abnormality during exercise, which suggests myocardial ischemia.

curve as the end-diastolic count (EDC) minus the end-systolic count (ESC), times 100 divided by the EDC: \((EDC-ESC) \times 100/EDC)\).

Myocardial imaging: Myocardial perfusion imaging was accumulated 3h after the Tc-99m MIBI injection, when the radioactivity ratio of myocardium to the background was at a maximum (Fig. 1). All patients ate a meal after the Tc-99m MIBI injection to hasten the excretion of the isotope through the gallbladder into the bowel. Patients were then repositioned by a laser positioning device at the same position as in the TI-201 studies. The process of image acquisition was the same as for TI-201 with the following exceptions: 1) the imaging time per projection was 30 sec; and 2) a 15% window was centered over the 140 KeV. Accumulated data were processed in a manner identical to the TI-201 studies. The short axis, the vertical long axis and the horizontal long axis images were reconstructed as reported.

Image interpretations

Myocardial uptake of TI-201 and Tc-99m MIBI: Two short axis slices at the basal and apical levels were selected for the comparison of myocardial uptakes between TI-201 and Tc-99m MIBI. To assess the apical uptake, a vertical long axis slice at the mid level was used. The left ventricular myocardium was divided into 5 segments: anterior, septal, inferior, lateral and apical. Myocardial uptakes of TI-201 and Tc-99m MIBI were assessed on a CRT by 3 independent observers who had no information regarding the clinical history and angiographic findings of the patients. A 3-point system was used to the level of myocardial perfusion: 2 = normal, 1 = reduced, 0 = severely reduced or absent. In interpreting stress and rest (or delayed) images, an uptake score at the stress images of less than 1 was defined as an initial defect. An increase of 1 or more in the uptake score at the rest (or delayed) images was defined as a transient defect and was considered to be ischemic. Uptake scores of 1 or 0 in both the rest (or delayed) and stress images were defined as a persistent defect, which was defined as the presence of myocardial infarction.

Left ventricular wall motion: For the evaluation of regional wall motion, first-pass RNV images were displayed on a CRT as an endless loop movie. The left ventricle was divided into 3 segments (anterior, apical and inferior). Each segment was assessed by 3

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independent observers who did not know the patients’ data. Regional wall motion was graded by a scoring system: 2=normal, 1=hypokinesis, 0=akinesis/dyskinesis. A transient wall motion abnormality present only during exercise was interpreted as ischemia. A persistent wall motion abnormality present both at rest and during exercise was defined as the presence of myocardial infarction.

Coronary arteriography
Coronary arteriography was carried out using a standard Judkins’ technique. All studies were assessed by 2 experienced cardiologists who had no information relating to the clinical history or radionuclide results of the patients. Significant coronary stenosis was defined by a luminal diameter narrowing of \( \geq 75\% \) in either main epicardial arteries or major branches.

Statistics
Statistical analysis was performed using Students’t-test. The values of the data were reported in terms of the mean \( \pm 1 \) standard deviation. A \( p \) value \(<0.05\) was considered significant.

RESULTS
Exercise duration, heart rate, systolic blood pressure and rate-pressure products achieved were similar in TI-201 and Tc-99m MIBI exercise studies (Table II).

Comparison between TI-201 and Tc-99m MIBI myocardial uptake studies
Myocardial uptake of Tc-99m MIBI was compared with that of TI-201 on a segment-by-segment basis (Fig. 2). Out of the 60 myocardial segments in 12 patients at rest, segmental agreement with regard to the presence of perfusion defects was 95% (57 segments). During exercise performed in 8 patients, an exact agreement between TI-201 and Tc-99m MIBI studies was observed in 37 out of 40 segments (93%).

Correlation of left ventricular wall motion and myocardial perfusion
Table III summarizes the results of myocardial perfusion, regional wall motion and the left ventricular ejection fraction in 12 patients, assessed by Tc-99m MIBI. RNV data during exercise were not analyzed in 1 patient (No. 3), because the count density was insufficient. A total of 36 segments in 12 patients at rest and 21 segments in 7 patients during exercise were used for analysis. All 3 patients with triple-vessel disease showed an abnormal response to exercise in left ventricular ejection fraction (less than 5% increase during exercise)\(^{12}\).

Segment-by-segment comparison of regional wall motion and myocardial perfusion is summarized in Fig. 3. Myocardial Tc-99m MIBI distribution was compared with regional left ventricular wall motion at rest and during exercise. A segment-by-segment analysis demonstrated that agreement between myocardial perfusion and regional wall motion was found in 18 out of 21 (86%) segments. In segments which were categorized as ischemic according to Tc-99m MIBI uptake, changes in the wall motion score (exercise-rest) were significantly smaller than those in segments with normal uptake of Tc-99m MIBI (\(-0.8 \pm 0.4\) vs. \(0.2 \pm 0.6\), \(p<0.01\), Fig. 4).

Case presentation
Figure 5 represents myocardial perfusion imaging (left panel) and left ventricular wall motion (right panel) assessed by Tc-99m MIBI. The patient had previous anterior myocardial infarction and triple-vessel disease was documented during coronary arteriography (No. 7 in Tables I and III). The apical segment showed a persistent perfusion defect and was considered to be infarcted. However, using wall motion analysis, the apical segment showed a transient wall motion abnormality during exercise, which suggested the presence of reversible myocardial ischemia.

DISCUSSION
In the present study, we have reported that both left ventricular wall motion and myocardial perfusion at rest and during exercise can be assessed using Tc-99m MIBI in patients with coronary artery disease.

Simultaneous assessment of regional wall motion and myocardial perfusion
A single dose of Tc-99m MIBI in the pre-
sent study was proved to be beneficial due to the lower exposure to radiation, comparing with that currently used Te-99m diethylene-triamine-pentaacetic acid (DTPA) first-pass RNV and TI-201 myocardial SPECT. In addition, the present protocol using Te-99m MIBI is advantageous especially in exercise studies, as it spares the patients a second stress test.

In patients with multi-vessel coronary artery disease, homogenous reduction of thallium-201 uptake sometimes results in difficulty in detecting regions of perfusion defects. Simultaneous evaluation of left ventricular function and myocardial perfusion may overcome such disadvantages. In this study, all 3 patients with triple-vessel disease showed an abnormally reduced left ventricular ejection fraction in response to exercise.

In the present study, both ventricular function and myocardial perfusion were concordant. Complete agreement between left ventricular wall motion and myocardial perfusion was observed in 86% of the segments. In a few cases, disagreement was observed. One segment was considered infarcted according to Te-99m MIBI myocardial SPECT, but ischemic by wall motion analysis (Fig. 5). Thus, simultaneous evaluation of regional wall motion and myocardial perfusion may improve functional descriptions of the diseased segments and permit the assessment of myocardial viability. Furthermore, simultaneous assessment of wall motion and myocardial perfusion can distinguish the stunned myocardium from similarly dysfunctioning but irreversibly damaged myocardium.

**Biological properties of Te-99m MIBI**

Te-99m MIBI has several advantages for myocardial imaging. Minimal lung uptake, prompt hepatic excretion, and rapid blood clearance result in a high myocardial to background ratio. Hepatic uptake of Te-99m MIBI is higher than that of TI-201; however, this does not interfere with the interpretation of myocardial perfusion imaging due to faster hepatic excretion and rather prolonged retention of Te-99m MIBI in the myocardium. In contrast to the myocardial images of TI-201, Te-MIBI lacks a redistribution. Therefore, the timing of imaging after injection is not as critical as with TI-201. We obtained myocardial SPECT 3 h after the Te-99m MIBI injection. Such properties make Te-99m MIBI more appropriate for SPECT imaging in practice.

**Technical limitations of the study**

Although a gated myocardial perfusion study using Te-99m MIBI is potentially suitable to assess both wall motion and perfusion, such a study requires a long period of data acquisition. The first-pass technique used in the present study requires only 30 sec for data acquisition. Thus, this method is practical for clinical purposes. We used a single crystal gamma camera, because it has advantages in resolution over a multi-crystal camera. We previously reported that the left ventricular ejection fraction measured by RNV correlated well with contrast left ventriculography. We used 555 MBq of Te-99m MIBI in this study. We think this level is lower than that required for assessing left ventricular function by the first-pass method. Consequently, data analysis could not be performed in 1 patient with syndrome X, in whom the peak heart rate achieved was 145 beats/min during exercise, because the count density was insufficient for data processing. For the evaluation of left ventricular function during exercise, a dose of 740 to 1110 MBq is required.

In this study, 50 of 60 segments at rest and 29 of 40 segments during exercise showed normal myocardial uptake of Te-99m MIBI and TI-201, because 3 patients with syndrome X were included in the 12 subjects. A greater number of patients may be required for more refined comparison of myocardial uptake of Te-99m MIBI and TI-201.

**Conclusion**

Myocardial uptake of Te-99m MIBI was similar to that of TI-201 at rest and during exercise. High agreement between regional wall motion abnormalities and myocardial perfusion defects in the present Te-99m MIBI studies predict the clinical usefulness of this isotope for patients with ischemic heart disease. Simultaneous evaluation of left ventricular function and myocardial perfusion by Te-99m MIBI improves characterization of myocardial ischemia.
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REFERENCES


4. ISKANDRIAN AS, HEO J, KONG B, LYONS E, MAR SCH S: Use of technetium-99m isonitrile (RP-30A) in assessing left ventricular perfusion and function at rest and during exercise in coronary artery disease, and comparison with coronary arteriography and exercise thallium-201 SPECT imaging. Am J Cardiol 1989; 64: 270


