

Perfusion and mechanical analysis with technetium-99m 2-methoxy-isobutyl-isonitrile in a case of dilated cardiomyopathy

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With technetium-99m 2-methoxy-isobutyl-isonitrile ($^{99m}\text{Tc-MIBI}$), regional wall thickening in a patient with dilated cardiomyopathy was analyzed by the first component Fourier method. The regional wall thickening was compared with thallium-201 and $^{99m}\text{Tc-MIBI}$ SPECT imaging. Thallium-201 SPECT images showed mildly reduced perfusion in the posterior wall and redistribution in the septum, whereas $^{99m}\text{Tc-MIBI}$ images showed heterogeneous accumulation around the left ventricular circumference. By means of phase analysis, diffusely decreased wall thickening and discontinuity of percent wall thickening in neighboring segments were observed throughout the left ventricle. Regional wall motion and wall thickening correlated roughly. However, discrepancies between the mechanical function and myocardial perfusion, and discrepancies in regional myocardial perfusion between thallium-201 and $^{99m}\text{Tc-MIBI}$ were observed.

Key words: technetium-99m 2-methoxy-isobutyl-isonitrile ($^{99m}\text{Tc-MIBI}$), single photon emission computed tomography (SPECT), wall thickening, phase analysis, dilated cardiomyopathy

INTRODUCTION

THALLIUM-201 is the most important and widely used cardiac radionuclide imaging agent for diagnosing coronary artery disease.¹⁻³ It is also used to evaluate the morphological features and myocardial perfusion abnormalities in cardiomyopathy.⁴⁻⁸

Technetium-99m 2-methoxy-isobutyl-isonitrile ($^{99m}\text{Tc-MIBI}$) is a recently developed ^{99m}Tc labeling cardiac imaging agent. This agent may be more optimal than thallium-201 because of its superior physical characteristics, such as an ideal 140-keV photopeak for current gamma camera imaging systems and large injectable doses due to the 6-hour half life. The diagnostic ability of $^{99m}\text{Tc-MIBI}$ for

ischemic heart disease is reported to be almost the same as that of thallium-201.⁹⁻¹³ In addition to detecting regional myocardial perfusion abnormalities, evaluations of left and right ventricular wall motion,^{14,15} and regional myocardial wall thickening^{16,17} can also be performed simultaneously. We describe the results of myocardial perfusion and regional wall thickening abnormality detected by newly developed $^{99m}\text{Tc-MIBI}$ myocardial scintigraphy in a case of dilated cardiomyopathy.

CASE REPORT

This patient (71 years old, male) had a history of cough and progressive shortness of breath. He developed severe chest oppression, palpitations, and diaphoresis lasting 20 minutes at rest, and was admitted to the hospital with suspected ischemic heart disease. Cardiomegaly had been detected by chest x-ray five years previously, but he had no history of myocarditis. The present cardiothoracic ratio was

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52%. Echocardiography showed generalized left ventricular hypokinesis, and severe hypokinesis of the inferoseptal wall. The percent fractional shortening was 20%. Significant left ventricular dilatation (left ventricular diastolic dimension: 50 mm) was not demonstrated, and left ventricular wall thickness (interventricular septal wall thickness: 10 mm, posterior wall thickness: 10 mm) was normal. Aortic regurgitation (grade 2: Cohn's classification) was present. Stress ECG demonstrated slight ST depression in V5, 6, and was judged as a borderline case.

Radionuclide examination

Resting radionuclide examination was done by both the first pass method and the equilibrium method with an intravenous bolus injection of 555 MBq (15 mCi) of ^{99m}Tc -pertechnetate and *in vivo* red blood cell labeling with stannous chloride pyrophosphate. Stress first pass radionuclide angiography (^{99m}Tc -MIBI, 740 MBq) was performed in the sitting position under maximal stress conditions. One hour after the injection of ^{99m}Tc -MIBI, 32 step SPECT myocardial images were gathered in 180° rotation from right anterior oblique to left posterior oblique projection (90 sec/view) on a rotating gamma camera (ZLC-7500, Siemens Co. Ltd.) with a gating ECG signal (40 msec interval from the R wave). A high resolution low energy (HRLE) parallel collimator was used. SPECT reconstruction was performed by means of 9 point smoothing and a Shepp & Logan filter. Images of a short axis, vertical long axis and horizontal long axis were generated by SCINTIPAC-700 (Shimadzu Co. Ltd., Japan). Two days later, resting studies without ECG gating were performed by intravenous injection of 370 MBq (10 mCi) of ^{99m}Tc -MIBI. Image acquisition time at each view was set at 30 sec with the same SPECT system. Stress examination with thallium-201 was also performed by the same protocol as for ^{99m}Tc -MIBI one week previously. The injected dose was 74 MBq. Images were obtained immediately after stress and 3 hr after thallium-201 injection.

Stress radionuclide angiogram with treadmill revealed severe generalized hypokinesis and stress induced akinesis in the apex. The ejection fraction (EF) decreased from 38.4% to 31% (Fig. 1). Equilibrium gated blood pool scintigram also demonstrated generalized hypokinesis and a left ventricular EF of 29%. Phase analysis showed that wall motion in the posterolateral wall was somewhat greater than that in the septum, and delayed contraction occurred in the basal septum.

Stress thallium-201 scintigram showed mildly reduced perfusion in the apex, inferior wall and posterior wall. Redistribution was seen in the basal septum (Fig. 2), whereas ^{99m}Tc -MIBI SPECT imag-

ing revealed heterogeneously reduced perfusion (Fig. 3). On stress ^{99m}Tc -MIBI imaging, reduced perfusion was shown in the anterior wall, septum, inferior wall, posterior wall, and apex. On resting ^{99m}Tc -MIBI imaging, severe reduced perfusion was seen in the posterior wall and inferobasal wall, and these regions seemed to undergo a change resembling reverse redistribution on the thallium-201 scintigram. Stress-induced hypoperfusion (redistribution on the thallium-201 scintigram) was noted in the anterior wall and apex. Reduced perfusion continued in the septum. Discrepancies were noted between the thallium-201 and ^{99m}Tc -MIBI images in the area of perfusion abnormality.

Cardiac catheterization

The ejection fraction (EF) of left ventriculography was 41% with severe generalized hypokinesis, and the end-diastolic pressure was 9 mmHg. Significant coronary stenosis was not seen on coronary arteriography (Fig. 4). Accordingly, this case was diagnosed as dilated cardiomyopathy.

Phase analysis of regional wall thickening with ^{99m}Tc -MIBI

Quantitative cardiac wall motion was analyzed by SCINTIPAC-2400 (Shimadzu Co. Ltd., Japan). The epicardial boundaries of the left ventricle at the end-diastolic phase were traced manually, and actual epicardial boundaries at every cardiac cycle were automatically determined by cutting threshold (40%) and fundamental Fourier boundary fitting. The area center of gravity of the left ventricular epicardial boundaries was calculated for every cardiac cycle. From this center, 12 radii at 30 degree intervals were generated, and a short axis image was then divided into 12 segments. Parameters such as percent wall thickening (%WT), amplitude (AMP) and phase, were calculated in each segment by means of the fundamental Fourier component, and functional images of regional myocardial wall thickening were generated.

%WT was calculated by the following formula.

$$\%WT = \frac{[\text{End-systolic counts}] - [\text{End-diastolic counts}]}{[\text{End-diastolic counts}]} \times 100$$

Functional images were set as 32 step color. In %WT, the maximal upper range was set as 50% (1.56%/color step) from gray to red. In %WT (700), each color step was set as 2.19%. For the AMP, the maximal value was set as the relative change normalized by the maximal value obtained at the end-diastolic phase. In the phase image, each color step was 15.6 (msec/color step) from gray to red.

Using ^{99m}Tc -MIBI, sequential ECG gate images are shown in Fig. 5. The first frame of this sequential image corresponds to an end-diastolic phase, and

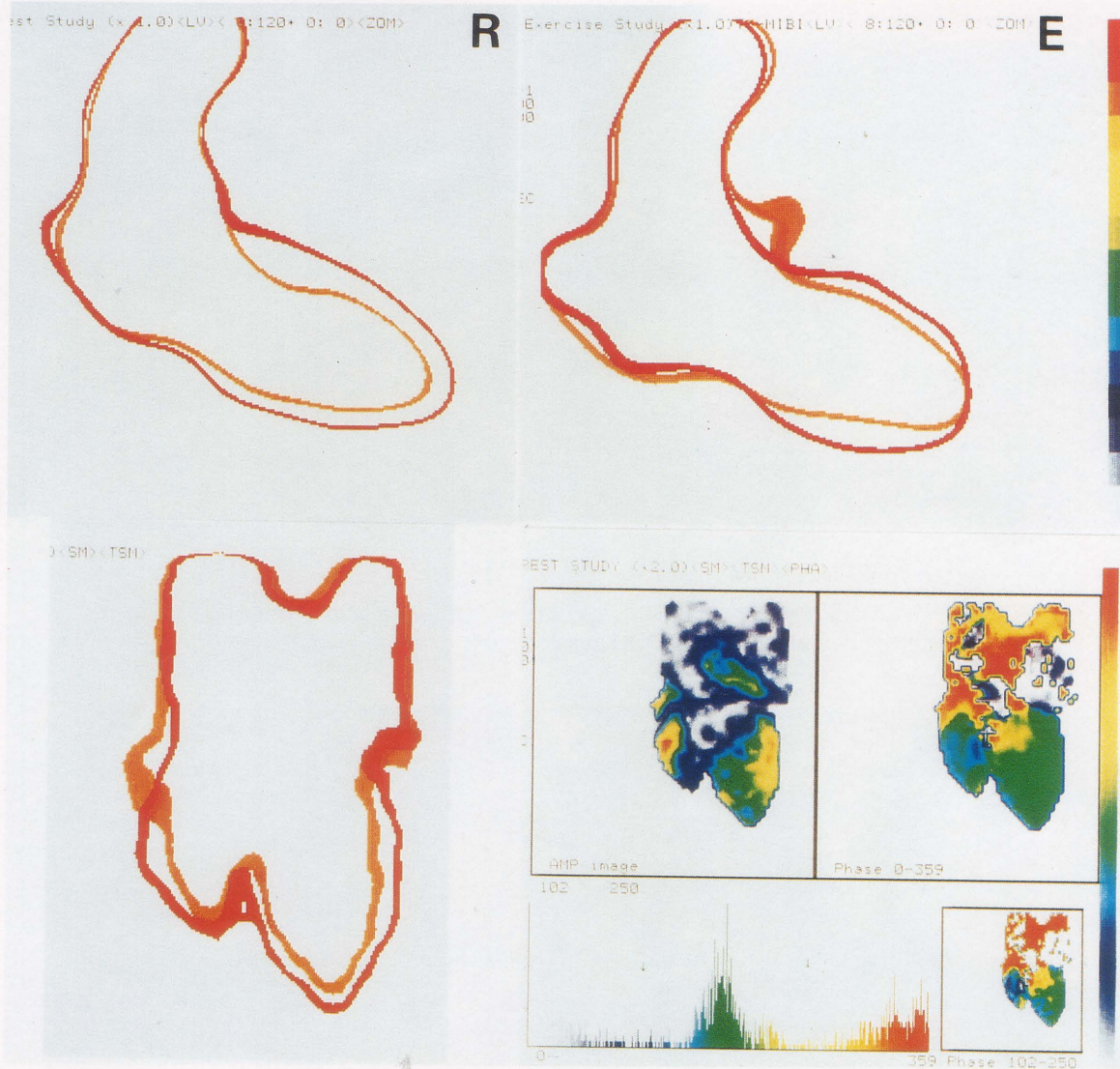


Fig. 1 Radionuclide angiography of stress and rest first pass, equilibrium ECG gated pool and phase images.

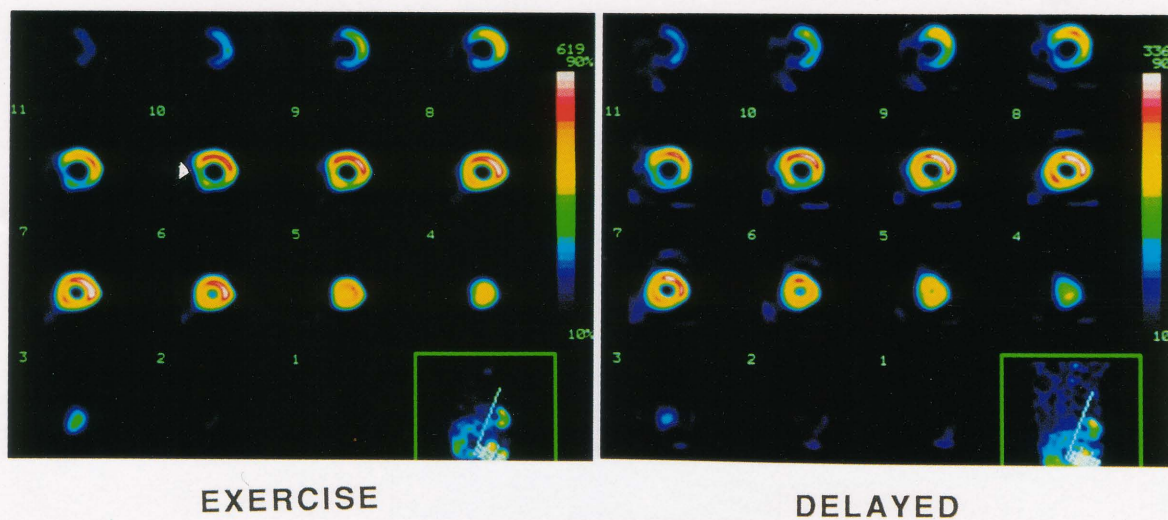
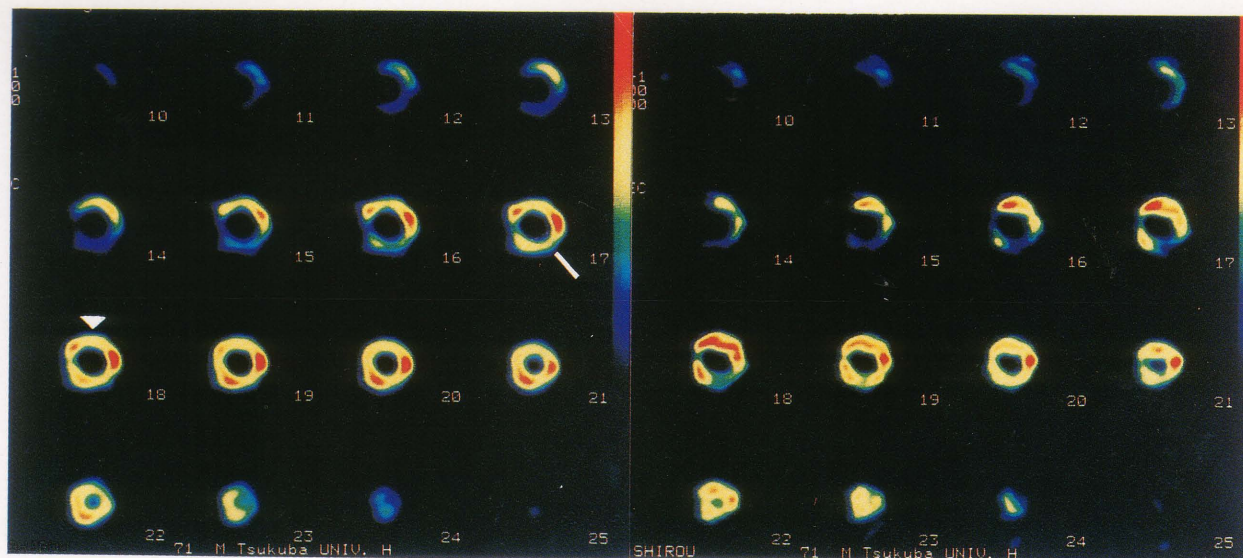


Fig. 2 Thallium-201 myocardial scintigram. arrow: redistribution.



EXERCISE

REST

Fig. 3 ^{99m}Tc -MIBI myocardial scintigram. arrow: stress induced hypoperfusion, bar: reverse redistribution like changes of thallium-201

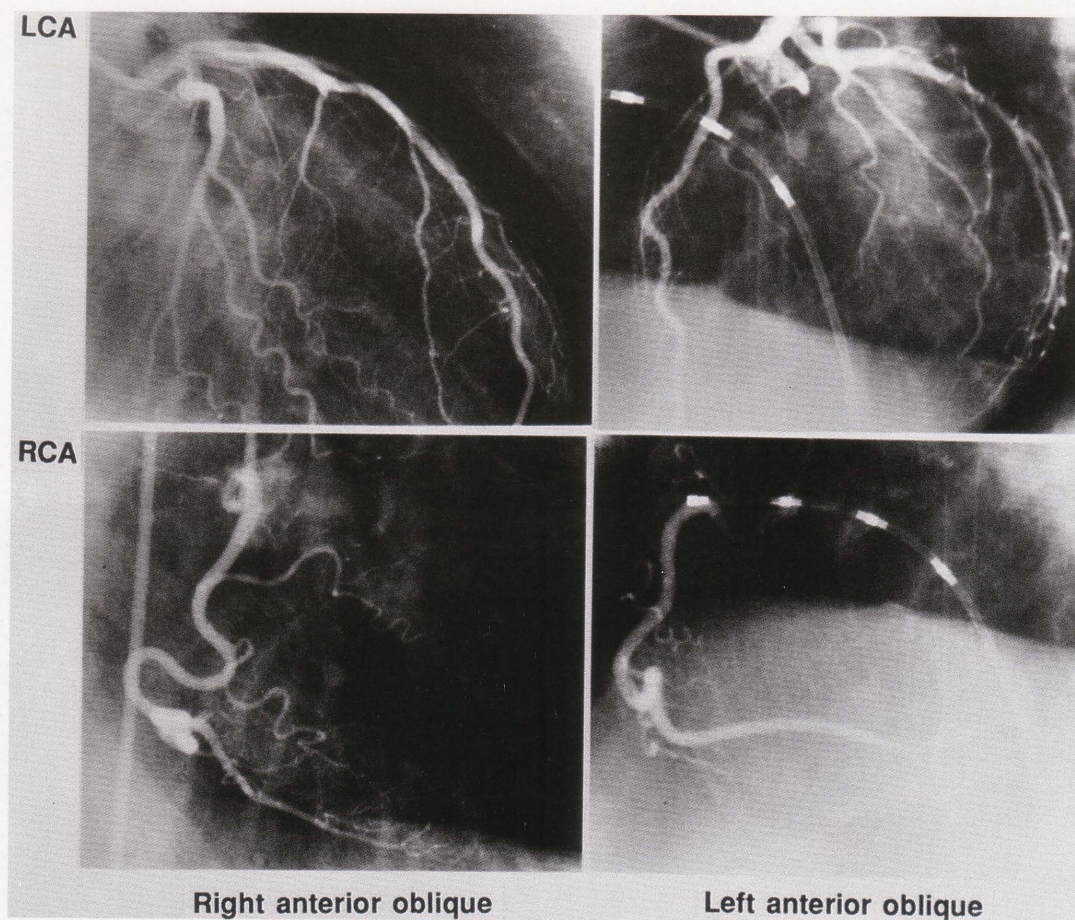


Fig. 4 Selective coronary arteriography.

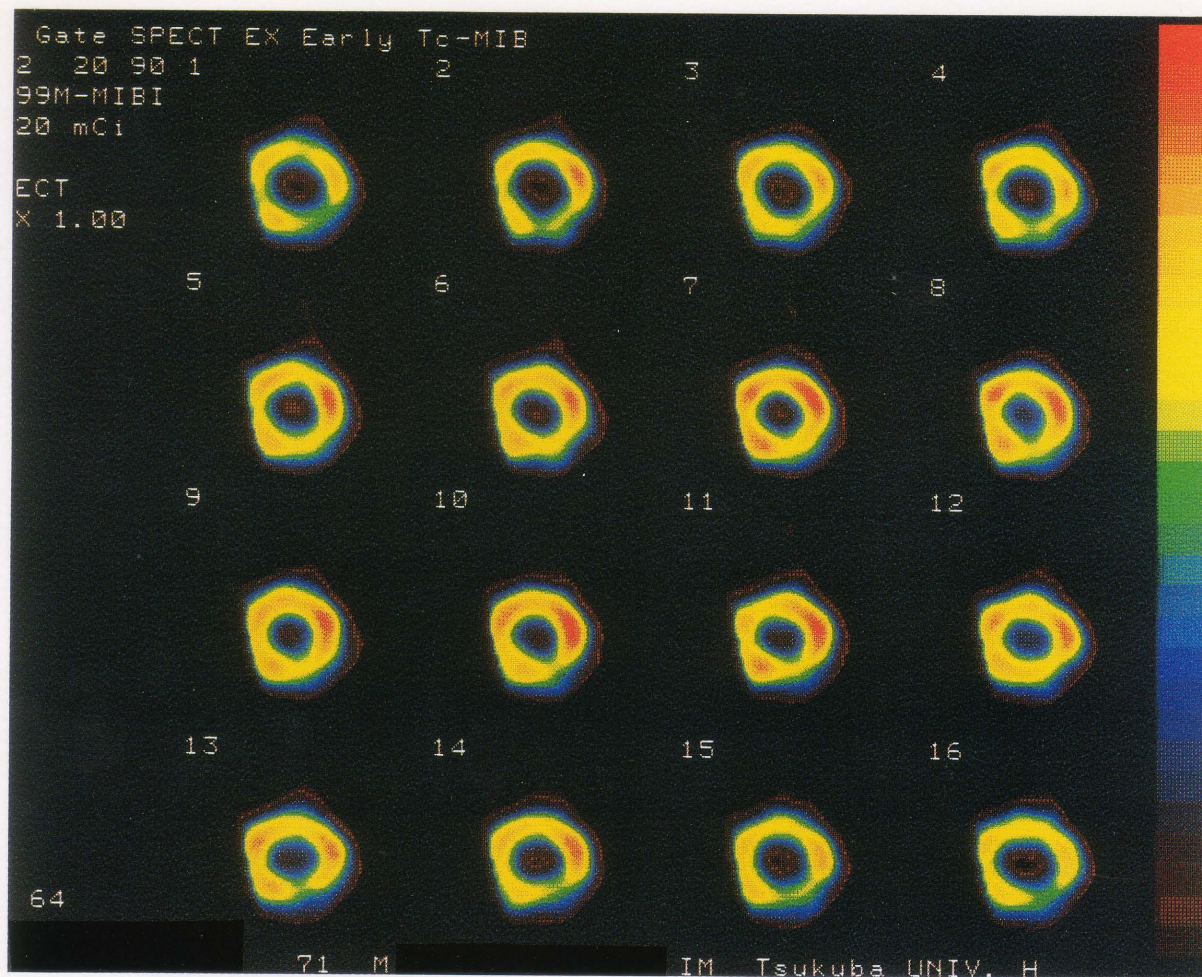


Fig. 5 Sequential ECG gated SPECT images with ^{99m}Tc -MIBI.

frame 10 is an end-systolic phase. An analysis with functional images of regional wall thickening revealed that %WT was diffusely reduced, especially discontinuity of %WT in neighboring segments which corresponded to regional heterogeneous contraction occurred throughout the left ventricle, and contraction was slightly delayed in the septum (Fig. 6). Quantitative phase analysis showed that severely reduced wall thickening occurred in the septum and inferior wall (Fig. 7). These changes in wall thickening corresponded roughly to those obtained with the gated blood pool scintigram. But discrepancies between the regional perfusion and regional wall thickening were identified especially in the infero-septum and posterior wall.

DISCUSSION

Consideration for myocardial perfusion

The ability of ^{99m}Tc -MIBI to detect dilated cardiomyopathy (DCM) has not yet been reported. To

assess dilated cardiomyopathy, thallium-201 is generally used to image the residual myocardium and perfusion abnormalities. Bulkley et al. first reported that patients with DCM demonstrated either normal perfusion or a defect amounting to <40% of the left ventricular circumference,⁶ whereas Dunn et al. showed widespread extensively reduced perfusion involving more than 40% of the left ventricular circumference, and that the number of segments involved, redistribution, lung uptake and ventricular size were similar in both DCM and severe coronary artery disease.⁸ A recent SPECT study revealed that significant perfusion abnormalities were shown compared to planar imaging.¹⁸ Redistribution (reversible defects) suggestive of myocardial ischemia were also found in about 40–60% of these patients, and segments with redistribution tended to show a lower incidence of abnormal wall motion.^{8,19–21}

First, we presumed that the perfusion abnormality shown by ^{99m}Tc -MIBI was the same as that shown by thallium-201. However, in this case, the accumu-

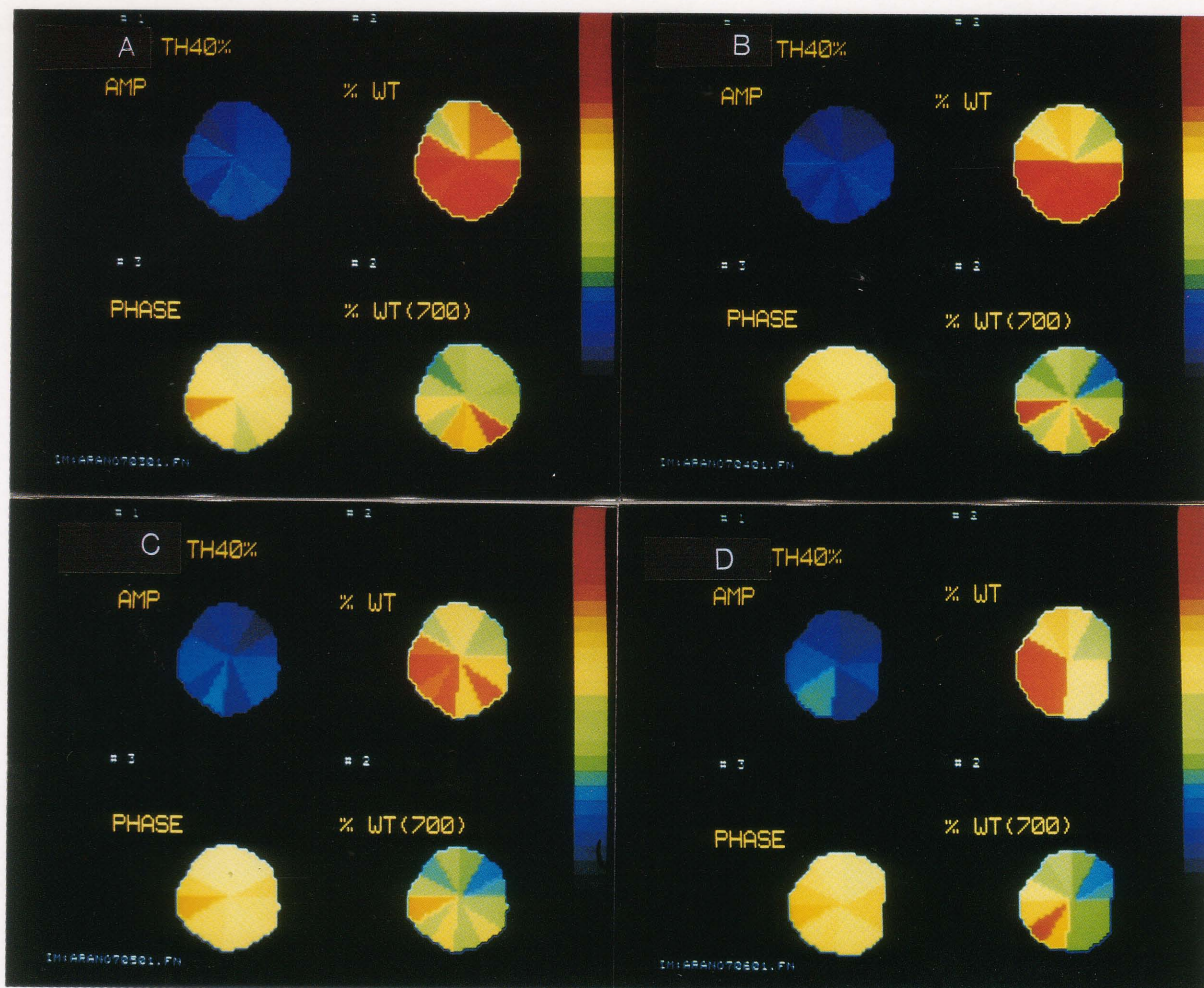


Fig. 6 Functional images of regional wall thickening obtained by first Fourier method with ^{99m}Tc -MIBI. A series of functional images in the mid-portion of the left ventricle are shown from base (A) to apex (D). Functional image in Fig. 6B was generated from the sequential image shown in Fig. 5 (slice number 18 in Fig. 3). amplitude (left upper), %wall thickening (right upper), phase (left lower), %wall thickening (700) (right lower)

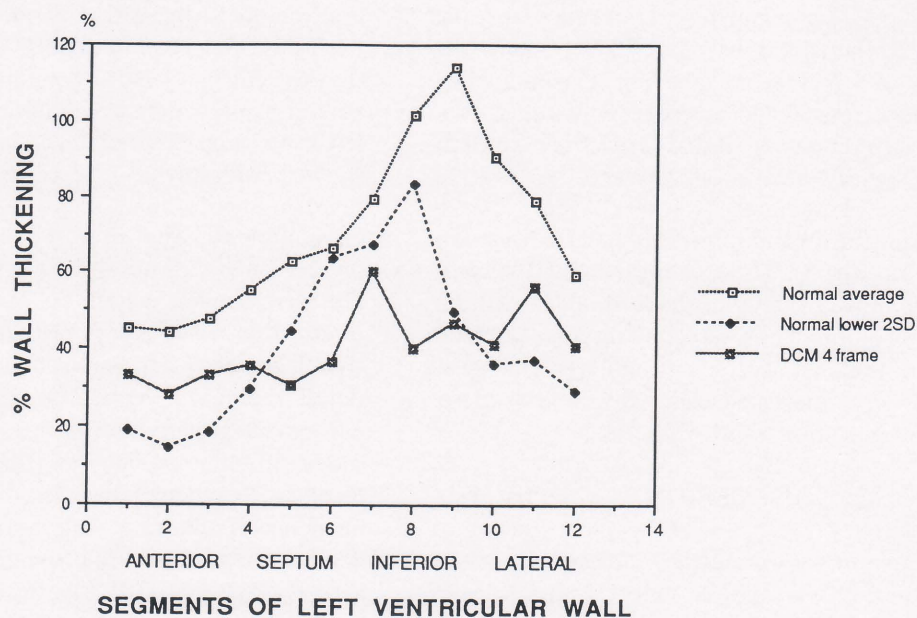


Fig. 7 Quantitative analysis of Fig. 5.

lation of radionuclide in the myocardium differed in ^{99m}Tc -MIBI and thallium-201. In the ^{99m}Tc -MIBI scintigram, the region of mildly reduced perfusion with a reverse redistribution-like change in thallium-201 (not quite a defect in the resting image) was shown as fixed mildly reduced perfusion in the thallium-201 scintigram. Other regions demonstrated as reduced perfusion by ^{99m}Tc -MIBI were shown as normal perfusion by thallium-201. A region of redistribution shown by the thallium-201 scintigram was demonstrated as fixed reduced perfusion by the ^{99m}Tc -MIBI, whereas stress induced hypoperfusion was revealed in the anterior wall by ^{99m}Tc -MIBI scintigram. The reason for these discrepancies is not known.

The causative mechanism underlying the production of reduced myocardial perfusion in patients with DCM is postulated. First, true myocardial ischemia may be present. Redistribution was noted in thallium-201, and this phenomenon was thought to be reduced coronary flow in DCM.¹⁹⁻²⁴ Second, foci of interstitial and replacement fibrosis are known to occur in DCM.^{25,26} The constant perfusion defect seen on the thallium-201 scan is thought to represent areas of myocardial fibrosis and scarring in patients with DCM.¹⁸⁻²⁰ Third, a primary abnormality at the myocardial cell membrane level, perhaps impairing thallium-201 and ^{99m}Tc -MIBI extraction, may exist at rest or be induced by exercise. Fourth, a change in left ventricular geometry may occur between the time of exercise and the delayed scan. Especially the difference between thallium-201 and ^{99m}Tc -MIBI in accumulation might be caused by a different mechanism of accumulation and retention in the myocardial cells.^{27,28} But ^{99m}Tc -MIBI was very helpful in diagnosing the DCM due to the heterogeneous reduced perfusion as a sign of DCM.⁸

Consideration for mechanical wall function

Left ventricular wall motion indicated severe generalized hypokinesis, and stress induced akinesis was demonstrated in the apex. Equilibrium gated pool scintigram combined with phase analysis showed that wall motion in the lateral wall was relatively greater than that in the septum. Functional analysis of wall thickening showed diffusely decreased wall thickening to be especially severe in the septum and inferoseptal wall. The regional wall motion abnormalities and wall thickening were well correlated. Especially wall thickening analysis could reveal regional heterogeneous contraction among the neighboring segments clearly.

Significant discrepancies were seen between the abnormal mechanical wall motion and myocardial perfusion. That is, in the septum and inferoseptal wall, reduced perfusion was not significant on either

thallium-201 or ^{99m}Tc -MIBI, whereas severe mechanical dysfunction was noted. In the posterior wall, perfusion with thallium-201 and ^{99m}Tc -MIBI was apparently reduced, whereas hypokinesis was mild. The cause of these discrepancies between abnormal wall motion and abnormal thallium-201 and ^{99m}Tc -MIBI perfusion is unclear. A comparative study of thallium-201 scintigraphy and echocardiography showed that the total abnormal regional wall motion segments did not correspond to those of reduced uptake on thallium-201, but the segments where regional wall motion was severely impaired demonstrated severely reduced uptake of thallium-201 and these regions contained fibrosis and myocardial scarring.¹⁸⁻²⁰ In addition to abnormalities of the radionuclide accumulation mechanism, a metabolic abnormality or energy-mechanical mismatch might occur in these regions.^{29,30}

Further assessment in patients with DCM is required in order to fully understand the clinical validity of this new radionuclide agent and this method of analysis.

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