Simultaneous Technetium-99m MIBI Angiography and Myocardial Perfusion Imaging

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Resting first-pass radionuclide angiography (FPRNA) was performed with the myocardial perfusion agent technetium-99m MIBI. In 27 patients, it was compared with technetium-99m diethylenetriamine pentaacetic acid FPRNA. A significant correlation was present in left ($r = 0.93$, $p < 0.001$) as well as right ($r = 0.92$, $p < 0.001$) ventricular ejection fraction measured with both radiopharmaceuticals. In 13 patients, MIBI derived segmental wall motion was compared with contrast ventriculography. A high correlation was present ($p < 0.001$), and qualitative agreement was found in 38/52 segments. In 19 patients with myocardial infarction a significant correlation was present between MIBI segmental wall motion and perfusion scores ($p < 0.001$). In ten patients with a history of myocardial infarction, 18 myocardial segments demonstrated diseased coronary vessels and impaired wall motion at contrast angiography. These segments were all identified by the MIBI wall motion and perfusion study. We conclude that MIBI is a promising agent for simultaneous evaluation of cardiac function and myocardial perfusion at rest.

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Decreased myocardial perfusion accompanied by left ventricular dysfunction constitute the landmarks of myocardial infarction. Radionuclide diagnosis of this condition is based on the presence of either abnormality at rest (*1–11*). Simultaneous assessment of wall motion and myocardial perfusion are desirable since the diagnostic specificity is higher when using two simultaneous tests instead of two consecutive ones (*12–14*). This strategy can be useful in evaluation of myocardial infarction (MI) for its early diagnosis or in stress studies for the evaluation of myocardium in jeopardy (*14*).

The recently developed technetium-99m- (^{99m}Tc) labeled cardiac imaging agent 2-methoxy isobutyl isonitrile (Cardiolite TM DuPont, DuPont Biomedical Products, No. Billerica, MA) (MIBI) labeled with ^{99m}Tc provides the capability of this simultaneity. We report on 31 studies in 31 patients with first pass radionuclide angiography (FPRNA) performed with [^{99m}Tc]MIBI followed by myocardial single photon emission computed tomography (SPECT). Because of lung and myocardial uptake, it was not clear that this agent could measure ventricular function and assess wall motion.

In this paper we report therefore on the following subjects:

1. Validation of right as well as left ventricular ejection fractions (RVEF, LVEF) measured with [^{99m}Tc] MIBI by correlating MIBI with ^{99m}Tc diethylenetriaminepentaacetic acid (DTPA) results in 27 patients.
2. Validation of [^{99m}Tc]MIBI left ventricular segmental wall motion by correlation with contrast ventriculography in 13 patients.
3. Correlation of myocardial perfusion and wall motion in 19 patients with myocardial infarction. We comment on a similar comparison in cardiomyopathy. Furthermore, we assess the value of resting [^{99m}Tc]MIBI study to identify myocardial infarction (ten patients).

PATIENTS AND METHODS

Resting FPRNA followed by myocardial SPECT studies were performed in 31 patients using [^{99m}Tc]MIBI. There were 18 males and 13 females with a mean age of 55+11 yr (mean

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± s.d.). Informed consent approved by the Human Subjects Committee of our institution was obtained prior to [^{99m}Tc] MIBI injection. Twenty-seven of these patients had a second examination with [^{99m}Tc]DTPA within 24 hr.

Clinical classification was as follows:

Group I included 19 patients with myocardial infarction. Diagnosis had been made on the presence of at least one of the following criteria: (a) clear history of myocardial infarction (patient hospitalized and treated as such), (b) presence of Q waves on ECG, (c) significant rise in specific enzymes (MB>6%total CK). Diagnosis was confirmed angiographically when possible: 12 of these patients had undergone coronary angiography and ten out of 12, contrast ventriculography.

Group II included ten patients with cardiomyopathy. Seven patients had a dilated cardiomyopathy. Coronary angiography demonstrated normal coronary arteries in three of them. Three other female patients had no risk factor for CAD and were being treated for congestive heart failure. In the last patient, the clinical diagnosis was idiopathic dilated cardiomyopathy based on a history of heart failure episodes. His ventricular function was normal at the time of the study, however. One patient had biopsy proven myocarditis with normal coronary arteries. Two young patients presented with a history of severe hypertension, exertional fatigue, and no other risk factor for CAD. Rest LV function was borderline in one and mildly depressed in the other.

Group III included two normal patients: one young healthy female volunteer and another one with normal coronary angiography.

Procedure

For each two patients a MIBI Kit was prepared in the following manner: a vial containing 1 mg of MIBI salt was labeled with 70 to 80 mCi ^{99m}Tc and then placed in boiling water for 10 min. Labeling efficacy was tested by chromatography prior to injection, and was classified as <90% (0 preparations), between 90% and 95% (7% of preparations), and over 95% (93% of preparations). Administration was performed 53 ± 10 (mean ± s.e.m.) minutes after ^{99m}Tc labeling of MIBI.

Data acquisition. FPRNA was performed supine at rest after intravenous bolus injection of 20 mCi of MIBI with the patient positioned for a 30-degree right anterior oblique view. The data were acquired in list mode on a digital camera (Elscint Apex 415, Elscint, Inc., Brea, CA) interfaced to a computer (Simis V Sopha Computer, Baltimore, MD).

Two hours later, 32 SPECT images were gathered in 180° rotation from left posterior oblique to right anterior oblique projection (40 sec per view) on a rotating gamma camera (Technicare Omega 500, Solon, OH) with a general all purpose collimator which was interfaced to the same computer. The patient was advised to have a meal 30 min before the SPECT study in order to decrease the amount of [^{99m}Tc]MIBI present in the gallbladder. In 27 patients a FPRNA was also performed at rest using 20 mCi [^{99m}Tc]DTPA within a 24-hr period, (one patient from Group I, two patients from Group II, one from Group III were not available for the repeat [^{99m}Tc]DTPA study). Patient's medication was not changed between the two evaluations.

Data processing. RVEF was calculated as described in (*12*) once, whereas LVEF was derived twice for each radiopharmaceutical injection (*15*). An end-diastolic, end-systolic LV edge image was generated automatically. Segmental wall motion was also assessed on a pixel by pixel LVEF image displayed on a relative color scale (0 to 100%) (*16*). Wall motion was scored on a scale of 2-0: normal = 2; hypokinesis = 1; akinesis or dyskinesis = 0, and it was assessed in four different segments: anterior, apical, inferior, and inferobasal (Fig. 1). Both functional EF and edge images were used. Dyskinesis was diagnosed either by edge overcrossing or by a 0% segmental EF. Akinesis was called when there was diastolic and systolic edge superposition or <20% segmental EF. Hypokinesis was either a segmental EF drop of 30% or more compared to any adjacent segment, or, for anterior, apical and inferior segments, an inter-edge distance less than the inferobasal inter-edge distance.

SPECT reconstruction was performed in a conventional way using pure Ramp filtering and three-dimensional spatial smoothing (19 points) (*17*). Three sets of 1.2-cm-thick cuts were generated (Fig. 2): (a) horizontal long axis cuts from top to bottom of the myocardium, (b) vertical long axis cuts from lateral to septal wall, (c) short axis cuts from apex to base. The maximum counts per pixel of each cut was normalized to a value of 100%. Segmental perfusion defects were quantitated on the cut demonstrating maximal decrease in counts per pixel. Perfusion was considered normal if the color scale denoted no more than a 40% diminution of the maximum

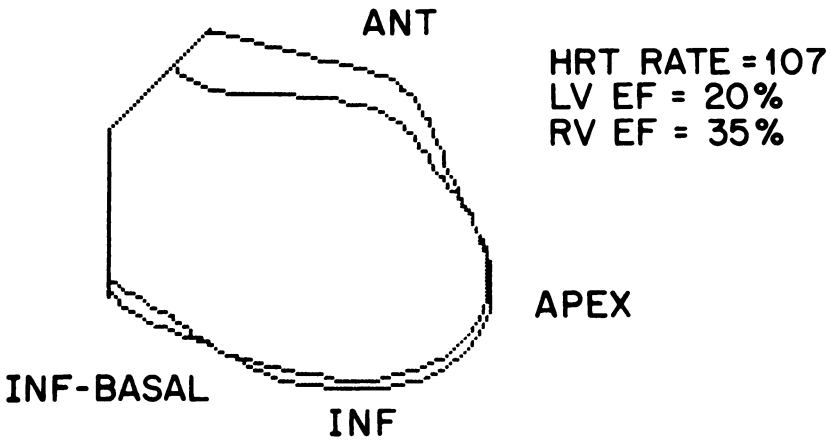

FIGURE 1
MIBI first-pass radionuclide angiography in a patient with triple vessel coronary artery disease and anteroapical MI. Left ventricular edges at end diastole and end systole are displayed. Anterior and infero-basal wall hypokinesis are present as well as apical and inferior akinesis.

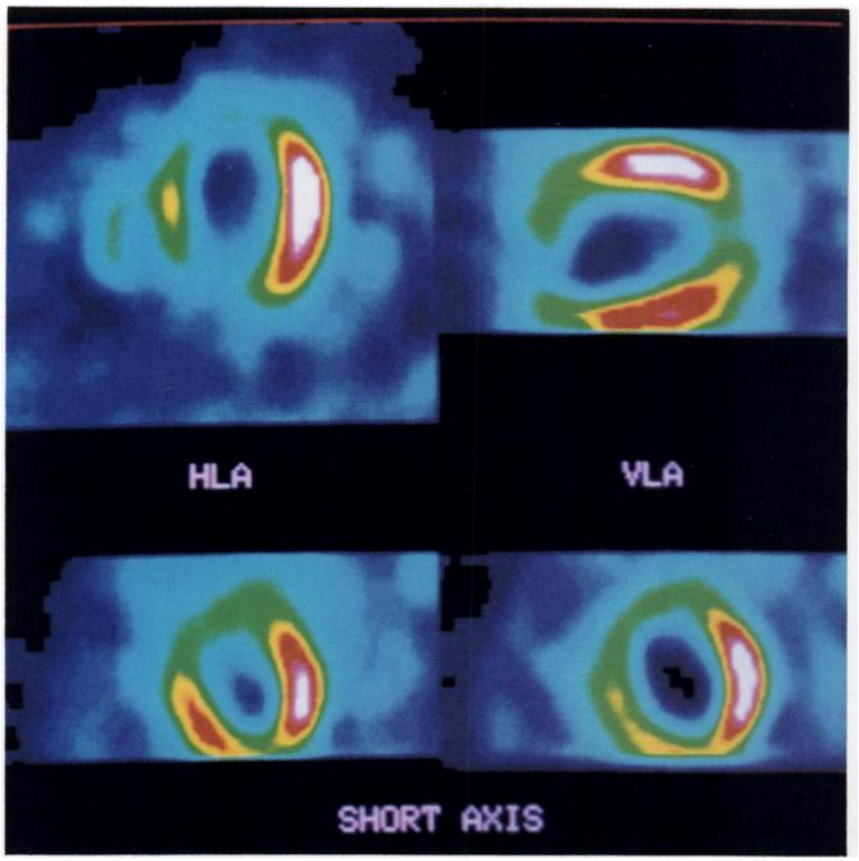

FIGURE 2
Simultaneous MIBI myocardial perfusion SPECT image. A horizontal long axis (HLA) cut, a vertical long axis (VLA) cut and two short axis cuts are displayed. Perfusion is absent at the apex and decreased in the anterior and inferior wall.

activity in the myocardium (score = 2), decreased perfusion if color scale indicated a diminution of perfusion of 40% to 70% (score = 1), or absent if perfusion was diminished more than 70% of maximum (score = 0). These threshold values provide a semiquantitative display of MIBI SPECT images and provide additional information to direct visual inspection of these images.

Contrast left ventriculogram in the right anterior oblique projection was analyzed by drawing end diastole and end systole ventricular edges. Wall motion was then scored either normal, hypokinetic, akinetic, or dyskinetic in any of the four segments described on FPRNA. Coronary angiography was considered abnormal if critical artery stenosis >70% was present in the segmental distribution. The scores in segmental wall motion and perfusion were compared in the four segments assessed by FPRNA to the results of contrast ventriculogram and coronary angiography. The septum, posterior, and lateral wall are blind regions in the FPRNA and were therefore not accounted for.

Statistical analysis. Product moment correlation (Pearson's r) was used to assess linear correlation between ejection fraction measurements. Paired t-test was also used. Differences in observed score frequencies between groups were assessed by chi-square test and correlation between scores by Kendall's test for ranked categories.

RESULTS

Comparison of Ejection Fraction Measured with MIBI and DTPA in 27 Patients

Recorded total field counts of MIBI FPRNA were similar to those published in (*12*).

Right ventricle. The ejection fraction measured with MIBI and DTPA were not significantly different (no bias was present). Pearson's r was 0.92 ($p < 0.001$) and the s.e.e. was five ejection fraction units (Fig. 3).

Left ventricle. The first calculation of MIBI LVEF was not significantly different from the second one, Pearson's r was 0.99 ($p < 0.001$) and the s.e.e. was two ejection fraction units. The first calculation of DTPA LVEF was also not different from the second one. Pearson's r was 0.99 ($p < 0.001$) and the s.e.e. was two ejection fraction units. The first calculations with MIBI and DTPA were then compared. LVEF measured with MIBI was not significantly different from LVEF measured with DTPA. Pearson's r was 0.93 ($p < 0.001$) and the s.e.e. six ejection fraction units (Fig. 4). There was no difference in segmental wall motion scores assessed with either radiopharmaceutical.

Comparison of MIBI and Contrast Derived Wall Motion

Comparison was performed in 13 patients (ten from Group I, two from Group II, one from Group III). A highly significant correlation between the two sets of scores was present ($p < 0.001$, Fig. 5). There was complete agreement in 38 segments (73%), whereas a one point score difference was present in 14/52 segments (27%).

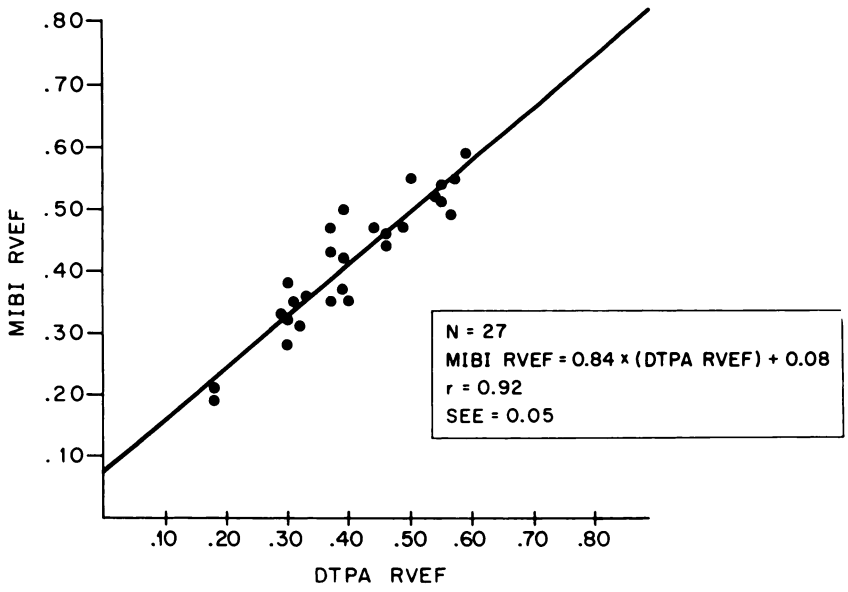

FIGURE 3
Correlation between right ventricular ejection fraction measured with [^{99m}Tc]DTPA and [^{99m}Tc]MIBI in 27 patients.

MIBI to Identify Myocardial Infarction

Correlation between FPRNA wall motion and MIBI myocardial perfusion. In Group I a highly significant correlation was present ($p < 0.001$) (Fig. 6). Of the 76 segments analyzed in the 19 patients of Group I, 53 (70%) demonstrated complete agreement between the two scores (match). Thirteen segments had perfusion worse than wall motion and ten perfusion better than wall motion. Correlation was not significantly different in the anterior, inferior, inferobasal wall, and the apex. Conversely in Group II (cardiomyopathies) there was no correlation between wall motion and perfusion: while wall motion appears significantly impaired and ejection fraction diminished, myocardial perfusion appeared homogeneously distributed.

Comparison of MIBI study with contrast angiography. Comparison was performed in ten patients from Group I. At contrast angiography, 18 segments presented abnormal wall motion accompanied by 70% to 100% stenosis of the involved coronary vessel. These 18 segments were correctly identified by the simultaneous MIBI wall motion perfusion study (Fig. 7, top row). Six segments presented abnormal wall motion and myocardial perfusion with normal coronary artery. Some of them probably represented infarction followed by recanalization, thus accounting for abnormal MIBI

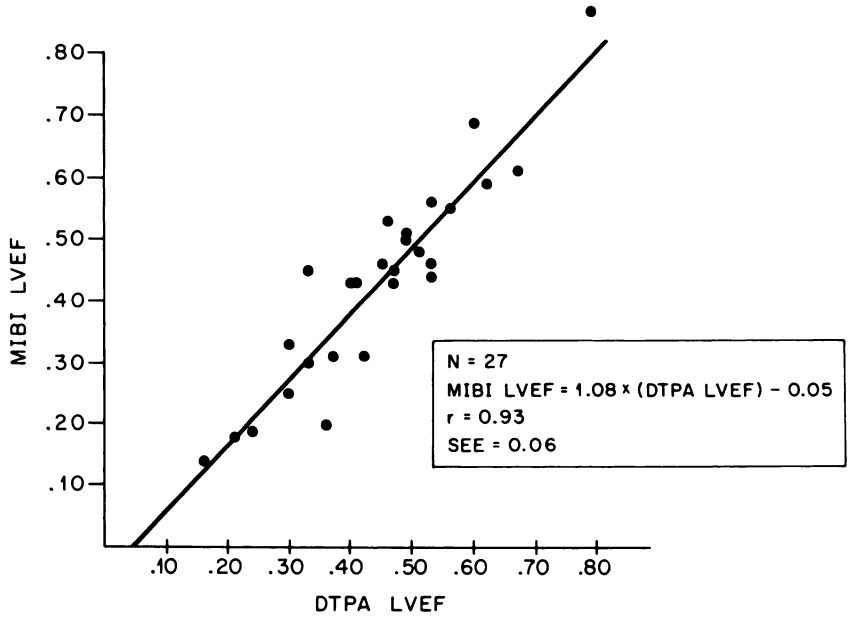

FIGURE 4
Correlation between left ventricular ejection fraction measured with [^{99m}Tc]DTPA and [^{99m}Tc]MIBI in 27 patients.

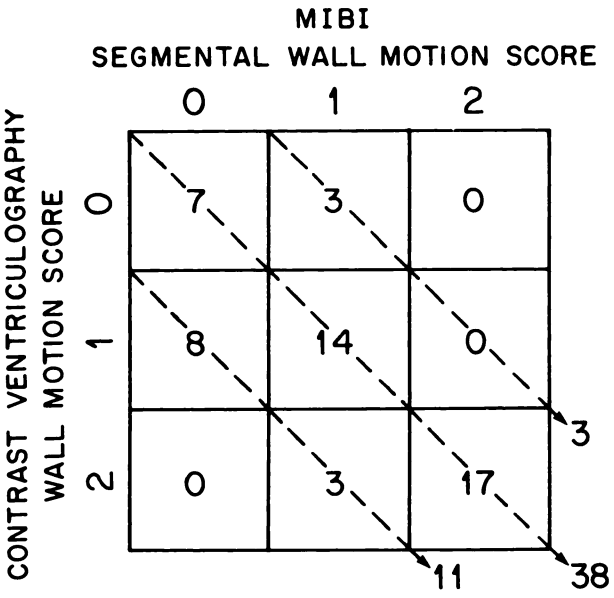

FIGURE 5
Comparison of MIBI and contrast ventriculography derived segmental wall motion in 52 segments (13 patients). Score 0 = akinesis, 1 = hypokinesis, 2 = normal. In each cell is represented the number of segments with a given wall motion score at contrast (vertical scale) or MIBI (horizontal scale) angiography.

MIBI STUDY

CONTRAST ANGIOGRAPHY		ABNORMAL WALL MOTION		NORMAL WALL MOTION	
		ABNORMAL MYOCARDIAL PERFUSION	NORMAL MYOCARDIAL PERFUSION	ABNORMAL MYOCARDIAL PERFUSION	NORMAL MYOCARDIAL PERFUSION
ABNORMAL WALL MOTION	ABNORMAL CORONARY ARTERY	17	1	0	0
	NORMAL CORONARY ARTERY	5	1	0	0
NORMAL WALL MOTION	ABNORMAL CORONARY ARTERY	1	0	3	5
	NORMAL CORONARY ARTERY	0	0	0	7

FIGURE 7
Comparison of contrast ventriculography and coronary angiography with MIBI derived wall motion and perfusion in ten patients with myocardial infarction who underwent contrast angiography. Forty segments are compared.

uptake and wall motion (Fig. 7, second row). The majority (5/9) of segments with normal wall motion and stenotic coronary artery were not identified by the MIBI study. This could be expected since the latter was performed at rest (Fig. 7, third row).

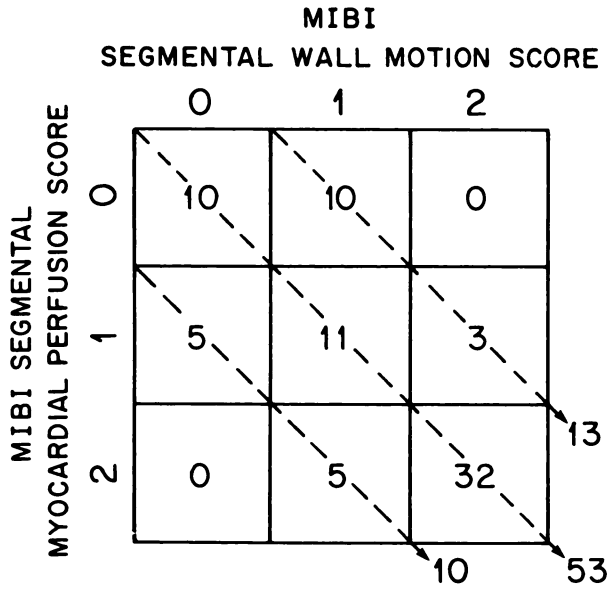

FIGURE 6
Comparison of MIBI segmental wall motion and perfusion in 76 segments of 19 patients with myocardial infarction. Score 0 = absent, 1 = reduced, 2 = normal.

DISCUSSION

MIBI is a lipophilic monovalent cation that localizes in the myocardial cells by simple diffusion without active transport and is reported to bind to a small molecular weight cytosolic protein (*18*). Unlike thallium it does not redistribute over time (*19*). Hepatic uptake is also present but since MIBI is excreted by the biliary tract, myocardium to liver ratio increases over time (*20*). A good agreement between thallium-201 and MIBI myocardial imaging has been reported (*21–25*). But it was unclear that MIBI could measure RVEF, LVEF, and segmental LV wall motion because of lung and myocardial uptake observed by us during the first passage of the MIBI bolus.

The advantages of simultaneous studies are multiple.

1. Single dose entails low radiation exposure to the patient, lower than the currently used [^{99m}Tc]DTPA FPRNA combined with thallium-201 SPECT (Table 1).

2. Discrepancies of wall motion and myocardial perfusion do exist (*14*) and could be explained by a time factor in nonsimultaneous studies. It is well known that numerous factors can modify ventricular function assessment: timing after a meal, mental status, etc. (*26, 27*). Such notorious discrepancies have been reported in cardiomyopathies with very abnormal ventriculographic findings in the presence of relatively homogeneous myocardial perfusion. We have reported also discrepancies of wall motion and myocardial perfusion in CAD (*16*) and so have others (*9*). In many instances,

TABLE 1

	Target organ	Rad
[^{99m}Tc]MIBI	Thyroid	1.9 (20 mCi)
[^{99m}Tc]DTPA	Kidney	0.6 (20 mCi) best case
^{201}Tl	Large intestine	1.8 (3 mCi) best case

the clinical significance of these discordances is often unclear and warrants, therefore, further research.

3. In exercise studies, the simultaneity is clearly advantageous as it saves the patient a second stress test with all the inconvenience and cost entailed.

4. The simple procedure described in this paper offers global information on cardiac function and perfusion that is not available with any other noninvasive imaging procedure. The maximal usefulness and limitations of this approach will be the subject of research once this radiopharmaceutical is approved by the Food and Drug Administration for clinical routine use.

FPRNA assessment of LVEF and left ventricular wall motion is acknowledged to be fairly reproducible and highly correlated with LVEF determined by contrast ventriculography (*12,16,28*). Our results indicate that there is no significant difference between MIBI and DTPA LVEF measurement, and the s.e.e. of six ejection fraction units agrees with results from the literature (*12, 14,16,29*). Moreover, agreement between MIBI and contrast derived wall motion is excellent. Lung and myocardial uptake of MIBI did not result in a significant change in background when compared to DTPA. There is no significant uptake of MIBI by the myocardium during the initial washout phase of the left ventricle; therefore, myocardial uptake does not interfere with LVEF measurement. Another source of concern could be MIBI hepatic activity present at the time of DTPA injection that would result in increased background. However, there was no significant difference when MIBI was injected before DTPA (Pearson's r = 0.92 in 12 patients) or DTPA before MIBI (Pearson's r = 0.95 in 15 patients).

In the MIBI studies, correlation of simultaneous abnormal wall motion and perfusion was present in the segments of myocardium that had suffered infarction. This observation has been described by others (*9–11, 30*). Note that myocardial perfusion could be assessed on three sets of cuts, whereas one view only was available for wall motion assessment. Remarkably, this correlation holds also in the inferior and inferobasal wall, in spite of the following: (a) FPRNA is less sensitive because of possible right ventricle superposition in right ventricular failure (*28,31*), and (b) hepatic uptake of MIBI can obscure inferior wall hypoperfusion. Imaging at 2 hr after injection of MIBI minimized this problem. The quality of the perfusion images was excellent and the resting counts per pixel were three to six times higher than with stress ^{201}Tl imaging. Simultaneous assessment of wall motion and perfusion may be a very sensitive procedure to assess the presence of acute myocardial infarction in its earliest stage. These studies can be performed on admission to determine the need for ICU care (*32*).

In conclusion, MIBI can precisely and simultaneously measure RVEF, LVEF and assess segmental wall motion as well as myocardial perfusion. This new ^{99m}Tc-labeled myocardial imaging agent is a promising radiopharmaceutical for the global evaluation of cardiac function.

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