ASSESSMENT OF MYOCARDIAL PERFUSION WITH SINGLE PHOTON EMISSION TOMOGRAPHY

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In order to compare Tc-99m-Sestamibi to T1-201 in the assessment of myocardial perfusion in the presence of coronary artery disease, 100 patients were studied with single photon emission computerized tomography (SPECT). Segmental analysis was carried out on 77 patients who underwent cardiac angiogram. The overall sensitivity and specificity rates in patients with myocardial infarction were respectively 92.5% and 98% for MIBI, 86.6% and 95% for T1; whereas in patients with chest pain, they were respectively 76.7% and 80% for MIBI, 69.8% and 70.5% for T1. Tc-MIBI correctly detected 11 lesions that were normal on T1-201, whereas the latter detected one lesion that was missed by Tc-MIBI. Concluding, we have the impression that Tc-MIBI not only correlated well with T1-201 but also showed marginal superiority over T1-201. Thus, Tc-MIBI is a valid alternative to T1 whenever the latter is not available. *Ann Saudi Med 1994;14(2):97-101.*

Technetium 99m-hexakis-2-methoxyisobutyle isonitrile (Tc-MIBI) was shown to be a suitable alternative to T1-201 in the assessment of myocardial perfusion and the diagnosis of coronary artery disease.[1,2] Human biodistribution, safety, and dosimetry of Tc-MIBI were evaluated and proved to be suitable for detection of coronary artery disease.[3] Compared to T1-201, Tc-MIBI showed some advantages such as better image quality for high photon flux, good myocardial uptake, and availability.[1,3] The potential applicability of a one-day imaging protocol with Tc-MIB[4,5] has added a further advantage over T1-201. Tc-MIBI was shown valuable when it was used to estimate areas of myocardium at risk due to severe ischemia[6] and to assess the response to thrombolytic therapy in myocardial infarction (MI).[7,8] Ability of Tc-MIBI to assess myocardial reperfusion was evaluated and compared to that of T1-201.[9] The optimal physical and chemical characteristics of Tc-MIBI such as the suitable photon energy, the physical half life, and the large usable dose allowed combination of myocardial perfusion imaging and assessment of ventricular function.[10,11] Tc-MIBI uptake and clearance by the myocardium in transient ischemia and reperfusion have been studied[12-14] and showed how this redistribution pattern is different from that of T1-201. The present work aims at showing clinical utility and usefulness of Tc-MIBI amid comparing it to T1-201 in terms of diagnosis of ischemic heart disease in patients complaining of chest pain with and without prior MI and identification of disease in individual coronary artery. To our knowledge, this work is the first of its kind in Saudi Arabia.

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Patients and Methods

A total of 100 patients, 17 females and 83 males, were referred for exercise-rest myocardial perfusion study with both T1-201 and Tc-MIBI within two to four weeks between the two studies. Their ages were between 35 and 78 years, average of 52 ± 4. The reasons for referrals were post MI angina (46 patients), chest pain being typical of angina or atypical (45 patients), as well as post percutaneous coronary angioplasty (PTCA), four patients, and post coronary artery bypass graft (CABG), five patients, in order to assess patency, reperfusion, or restenosis. Seventy-seven patients underwent coronary angiogram within one to two months after or before either Tc-MIBI or T1-201 study. The other 23 patients, 12 with post MI angina and 11 with chest pain, did not undergo coronary angiograms because of no evidence of reversible perfusion pattern. Therefore, these patients were not included in the comparative results.

Exercise Protocol

Treadmill exercise was performed according to the standard Bruce protocol with 12-lead electrocardiogram (ECG) monitoring throughout the exercise time. The time duration of exercise was observed to be not significantly different in both studies. In some patients, the exercise was terminated because of chest pain, ST-segment changes, or fatigue. All patients were asked to discontinue medications affecting exercise tolerance such as β-blockers for 48 hours before exercise. In 21 hypertensive patients, β-blockers were substituted for an alternate antihypertensive drug.

Tl-201 Study

Two to three mCi were injected at or near achievement of the predicted maximum heart rate. The exercise continued for one minute after injection. Imaging started 10 minutes post injection. Delayed images were taken 2.5 to 3 hours post injection. When reinjection technique was used, another set of images was produced within 30 minutes of the reinjection of about 1 mCi of Tl-201.

Tc-MIBI Study

Twenty to 25 mCi were injected at the predicted maximum heart rate. The exercise was carried out for another minute post injection. The patients were asked to drink 250 to 300 ml of milk to accelerate excretion of Tc-MIBI from the hepatobiliary system. Imaging began 60 minutes after the injection. The rest study was performed within two to three days of the exercise study with a similar dose.

Scanning

Single photon emission computerized tomography (SPECT) studies were performed using a rotating large field of view gamma camera (GE Starcam XCT) with a low energy all-purpose collimator. Thirty-two projections of 40 seconds each were obtained over a semicircular 180° arc that extended from the 45° right anterior oblique to the left posterior oblique. A 20% energy window centered on the 68 and 80 KeV peak for Tl-201, and on the 140 KeV for Tc-MIBI imaging was used. All images were stored on 64x64 matrix. The raw data were initially smoothed with a nine-point algorithm and then reconstructed to produce a transverse slice using back projection method (Ramp filter). Tomographic slices for the long and short axes of the left ventricle were then extracted from the filtered transaxial tomograms. No correction for attenuation or scatter was applied. As soon as acquisition was completed, the 32 planar acquired data were reviewed in order to detect potential patient movement and soft tissue attenuation or activity in structures overlying the heart. Findings were noted and taken into account before interpretation was performed.

Cardiac Angiogram

Seventy-seven patients underwent coronary angiogram and left ventriculogram using the Judkin technique with multiple views of the right and left coronary arteries. The findings were interpreted without knowing the results of the scintigraphic studies. Significant coronary artery stenosis was determined by qualitative evaluation and was defined as equal to or greater than 50% reduction in the luminal diameter.

SPECT Visual Interpretation

A four-point scoring system was followed, as numbers were given to each perfusion pattern; zero for normal, one for mild decrease, two for moderate decrease, and three for absent perfusion. Equivocal patterns were excluded. Abnormal perfusion was defined as less than score 2. Tomographic cuts of each study were divided into eight segments (Figure 1) which is based on the work of Kiat et al.[2] These segments were assigned to six evenly divided regions in the apical, mid ventricular, and basal cuts of the short axis images and the inferoapical segments in the vertical long axis. The horizontal long axis completes the set, showing segments that have already been seen on the other cuts. The perfusion pattern was interpreted by two observers as normal, decreased, or absent. Reversibility of the perfusion was described as complete, minimal, partial, or nonreversible. Discrepancies between the two observers were resolved by consensus. As seen in Figure 1, the territory of the left anterior descending artery included the anterior, anteroapical, and anteroseptal walls (respectively segments #1, 2 and 7). The territory of the right coronary artery included the inferoseptal or septal, inferior, and inferoapical walls (respectively segments #3, 4 and 8). The territory of the left circumflex artery included the anterolateral and inferolateral or posterolateral that are respectively the segments #6 and #5.

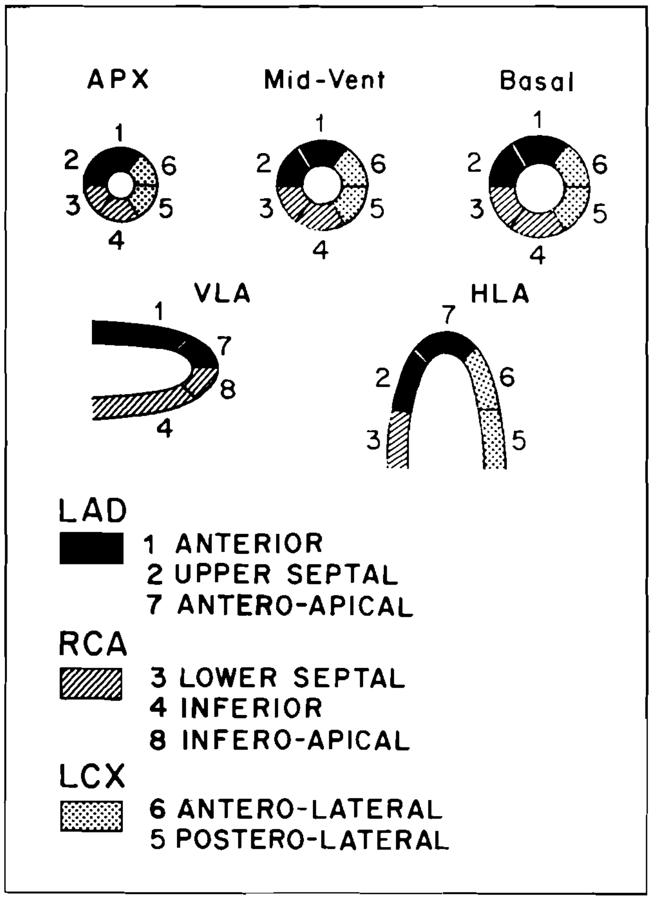

FIGURE 1. A schematic segmental representation of myocardial walls with assignment to coronary arteries. LAD = left anterior descending; RCA = right coronary artery; LCX = left circumflex; VLA = vertical long axis; HLA = horizontal long axis.

It is important to understand that this assignment of vascular territories should be looked upon as a flexible mapping because of anatomical variation that may require reassigning of segments, especially those supplied by more than one coronary artery.

Data Analysis

Segmental analysis was applied to the 77 studies with the two agents and expressed in terms of sensitivity and specificity. In respect to the coronary angiograms, true positive and negative as well as false positive and negative results were made available. To make this point clearer, it is important to define these terms in the group of patients with post myocardial infarction angina. Irreversible and reversible perfusion patterns were considered true positives in segments infarcted or supplied by significantly diseased arteries. In these segments, normal perfusion was considered false negative. Normal perfusion was considered true negative in segments not infarcted or supplied by normal arteries. In these segments, irreversible and reversible perfusion were considered false positives. Agreement between Tc-MIBI and T1-201 was expressed in terms of percent ratio of segments that appeared similar on both agents to the total number of segments.

Results

Patients with Post Myocardial Infarction (MI) Angina

The results in this group are summarized in Table 1. There were no false positive results. Ischemic changes associated with the infarction were found and indicated in the same table. The total number of abnormal segments as found with the coronary angiograms was 134. Therefore, the sensitivity rate was 92.5% for MIBI and 86.6% for T1-201. In order to calculate the specificity rates for both agents, the number of diseased segments is subtracted from the overall number of segments in this group that is equal to 368 (46x8) segments, yielding 234, which can represent the number of true negative segments. Therefore, the rate of specificity was 98% (234-5/234) for MIBI and 95% (234-11/234) for T1-201.

Patients with Chest Pain

The results for this group are summarized in Table 2. The sensitivity rate was 76.7% for Tc-MIBI and 69.8% for T1-201 whereas the specificity rate was 80% for Tc-MIBI and 70.5% for T1-201. The rates of false results in this group were substantially high.

Identification of Diseased Coronary Vessels

The rate of sensitivity of each agent to detect the diseased coronary arteries is shown in Table 3 and expressed in terms of percentage in each group of patients. However, the overall sensitivity rate was 82.7% for MIBI and 77.9% for T1-201.

TABLE 1. *Results of segmental analysis in 34 patients with post MI angina (Group I).*

	MIBI			T1		
	MI	Isc	All (%)	MI	Isc	All (%)
T +ve	99	25	124/134 (92.5%)	92	24	116/134 (86.6%)
F -ve	4	6	10/134 (7.5%)	14	4	18/134 (13.4%)
F +ve	0	5	5/234 (2%)	0	11	11/234 (4.7%)

T=true; +ve=positive; F=false; -ve=negative; Isc=ischemia; MI=myocardial infarction.

TABLE 2. *Results of segmental analysis in 34 patients with chest pain (Group II).*

	MIBI		T1	
T +ve	33/43	(76.7%)	30/43	(69.8%)
F -ve	10/43	(23%)	13/43	(30%)
T -ve	49/61	(80%)	43/61	(70.5%)
F +ve	12/61	(19.7%)	18/61	(29.5%)

T=true; F=false; +ve=positive; -ve=negative.

TABLE 3. *Rate of identification of diseased vessels.*

	MIBI		T1		%MIBI		%T1	
	I	II	I	II	I	II	I	II
Detected	57	48	54	45	81	84	77	79
Missed	13	9	16	12	19	16	23	21
Total	70	57	70	57	100	100	100	100

I=post myocardial group; II=chest pain group.

Identification of Diseased Segments

The rates of agreement and disagreement were respectively 74% and 26% in group 1 and 87.5% and 12.5% in group 2. The overall agreement and disagreement rates were 80% and 20%, respectively.

Which Agent Showed Lesions Missed by the Other One?

MIBI showed 11 lesions that were shown normal by T1 whereas the latter showed one lesion that was missed by the former. Interestingly, the lesion seen by T1 corresponded to an area of infarction in the inferior wall. False positives were not included in this comparison.

Post PTCA and CAGB Group

Tc-MIBI images of better quality offered more confidence in the interpretation. However, both agents were able to provide further evidence to the outcome of the interventional procedures in showing patency of flow in dilated or bypassed arteries. Both agents, by showing reversible perfusion, enabled the study to explain the chest pain in these patients. In summary, the results by both agents were identical and helpful in this group.

Discussion

The performance of SPECT studies allowed conditions for both agents to have comparable pharmacokinetics because of the relatively short time of SPECT acquisition. Redistribution of T1-201 can potentially occur during the

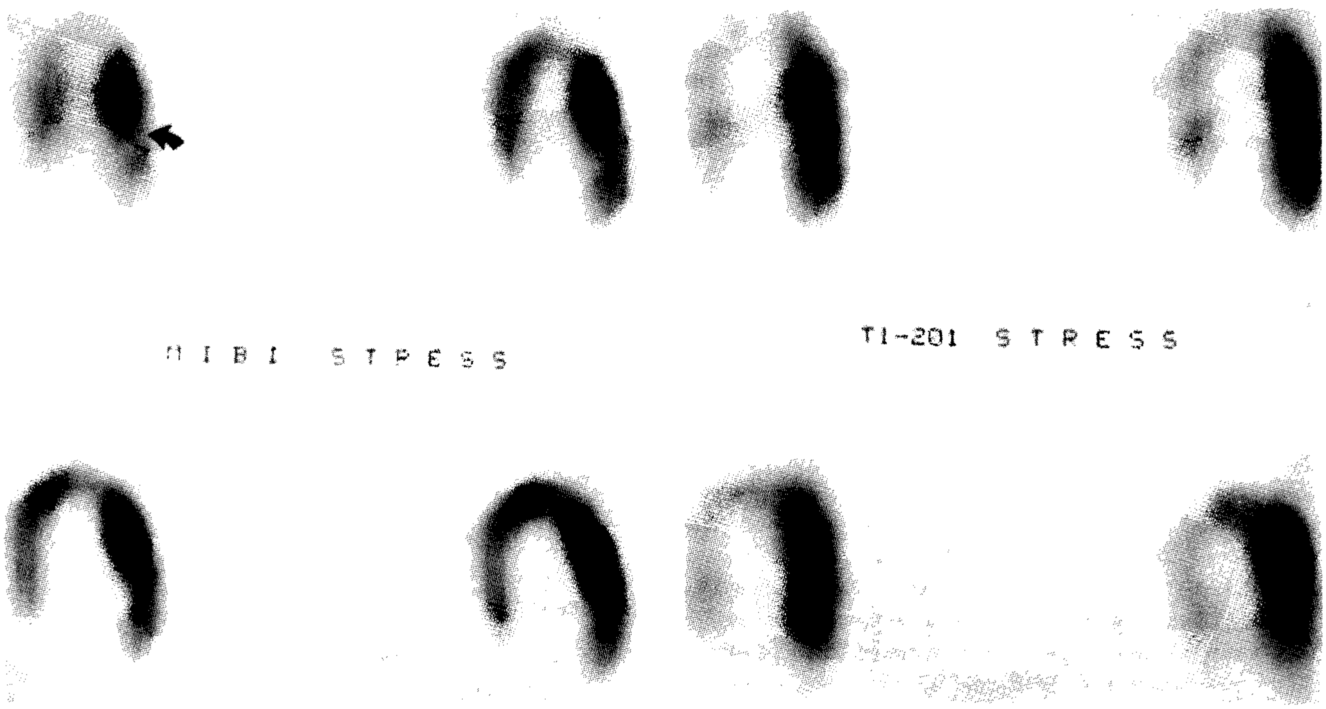

FIGURE 2. (A) MIBI showing hypoperfusion in the inferolateral area (curved arrow) that was not seen on T1-201. (B) The patient had myocardial infarction and, among other lesions, had 40% stenosis in the left circumflex artery.

35 minutes that pass between injection and completion of SPECT sequence[15] whereas Tc-MIBI has minimal redistribution.[1,16] Defect intensity is the same on SPECT of either agent.[17] The size of defect was not considered a parameter for comparison in this study and thus it is not an issue for argument. For all the above mentioned, we believe that our work was so designed that a scientifically fair comparison could be carried out. That is, the better rates of sensitivity and specificity by Tc-MIBI cannot be attributed to, for example, referral bias. In contrast to the results of Frans et al,[3] our results showed that Tc-MIBI detected more lesions than T1-201, particularly among patients with post myocardial infarction angina (Figure 2). This is to be added to the value to Tc-MIBI in the assessment of myocardium at jeopardy. The value becomes more important and vital when the results are going to dictate alterations in the patient's plan of management.

Clearance of Tc-MIBI is faster in normal than in ischemic myocardium (26% and 15% respectively).[13] This delay may cause an underestimation of the myocardium risk. On the other side, Iskandrian[14] stated that the clearance rate was almost the same in normal and ischemic myocardium and it was in the range between 10% and 15%. We noted the pattern of "inhomogeneous" perfusion at rest in five elderly patients with chest pain and history of long-standing hypertension and/or diabetes mellitus and in one young patient who suffered typical chest pain. Our impression was that cardiomyopathy might have had some role in producing such a pattern of apparently different clearance or washout of Tc-MIBI in the same area. In all the patients included in this study so far, both agents showed good to excellent rates of sensitivity and specificity and correlated well with each other. However, in group 1, Tc-MIBI appeared more sensitive as it detected more infarctions and 11 more lesions than T1-201. Two of the 11 lesions were caused by stenosis of 40%. Despite the fact that the stenosis was 40%, yet with Tc-MIBI we were able to detect the significance of such degree of narrowing. This agrees with the substantial interobserver variability (frequently is ± 20%) noted by Zir et al[18] in the visual quantification of moderate stenosis (i.e., 60%) between 40% and 80%. This range of stenosis is particularly important as stenosis of 50% (75% cross sectional area) is barely hemodynamically significant at peak coronary flow whereas stenosis of 70% (90% cross sectional area) is quite severe at the same peak of coronary flow.[19,20] Tc-MIBI also scored lower false negatives and lower false positives than T1-201, indicating that interpretation of Tc-MIBI images may be more reliable because the better resolution yielded less equivocal images (Figure 3). This inference is true as well in group 2 where Tc-MIBI again scored better with lower false results than with T1-201. The rates of false results in this group appeared high. This may be due to the relatively small number of segments when these are divided into two sets of segments to calculate sensitivity and specificity. The results in group 3 were identical for both agents. This may be due to the fact that these studies were carried out to complement the work of the interventional therapy only. Therefore, for this, either agent

FIGURE 3. Hypoperfusion to the apex appeared sharper on MIBI images (A) than on T1-201 images (B).

can be helpful in providing evidence supporting the outcome of interventions in terms of reperfusion or restenosis.

In conclusion, Tc-MIBI correlated well with T1-201 and showed slightly better overall results due to its favorable physical and chemical properties. Nevertheless, we believe that Tc-MIBI may not replace T1-201 completely, at least in our institution. In Riyadh, Saudi Arabia, T1-201 is being produced and made easily available to meet our needs. The cost of T1-201 was cheaper when compared to MIBI. When T1-201 no longer becomes available, then MIBI will be recommended to be used for its favorable radiochemistry.

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