

COMPARISON OF ^{99m}Tc -MIBI AND ^{99m}Tc -TETROFOSMIN MYOCARDIAL PERFUSION TOMOGRAPHERIES IN MULTIVESSEL CORONARY ARTERY DISEASE

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Radionuclide myocardial imaging is an important diagnostic technique for evaluation of patients with suspected or known coronary artery disease. The aim of the present study was to compare the results of ^{99m}Tc -MIBI and ^{99m}Tc -tetrafosmin in patients with multivessel coronary artery disease.

The study group consisted of 21 patients (18 male, 3 female) with a mean age of 58.2 ± 4.7 years. Eleven patients had a two vessel and the rest of them had a three vessel disease. Thirteen patients had evidence of previous myocardial infarction. Patients with recent (< 2 weeks) myocardial infarction and unstable angina pectoris were excluded from the study. Bruce protocol was applied to all of the patients. ^{99m}Tc -MIBI and ^{99m}Tc -tetrafosmin were applied in a previously described way and results were read separately by two investigators reaching a consensus.

There was a good segmental correspondence between ^{99m}Tc -MIBI and ^{99m}Tc -tetrafosmin (kappa values ranged from 0.73 to 1.00). Overall concordance was 95%. Both of them identified all of the patients with a previous myocardial infarction. With ^{99m}Tc -tetrafosmin, fixed defects were reported in 8 patients, and partially reversible defects in 5 patients; while with ^{99m}Tc -MIBI, fixed defects were reported in 7 patients and partially reversible defects in 6 patients. In conclusion, ^{99m}Tc -tetrafosmin, just as ^{99m}Tc -MIBI, is an agent to be used to obtain high quality images with fast liver clearance in patients with multivessel disease.

Key words: ^{99m}Tc -tetrafosmin, coronary artery disease, myocardial scintigraphy

Stress radionuclide myocardial perfusion imaging is a well established modality for diagnostic and functional evaluation of patients with suspected or known coronary artery disease (1).

Thallium-201 (^{201}Tl) has been used as a conventional myocardial perfusion imaging agent since its clinical introduction in 1976 (2). Recently, Tc- $^{99\text{m}}$ labeled myocardial perfusion agents have become available. Tc- $^{99\text{m}}$ labeled radiopharmaceuticals offer certain advantages over ^{201}Tl . These include extemporaneous reconstitution from a kit when required, more suitable photons (140keV) for gamma camera imaging, and due to its shorter half life (6.30hr) reduced patient radiation dose with a higher injected activity. It was claimed that a technetium -based agent could significantly improve the image quality compared to ^{201}Tl (3). $^{99\text{m}}\text{Tc}$ -MIBI planar and SPECT imaging are now widely used (4). $^{99\text{m}}\text{Tc}$ -tetrafosmin has been developed recently as a cationic, lyophilic myocardial perfusion agent. Initial results from clinical trials have demonstrated high quality images and good correlation with ^{201}Tl scintigraphy for the detection of coronary artery disease (CAD). These findings are similar to the other the findings that demonstrated the diagnostic concordance between ^{201}Tl and $^{99\text{m}}\text{Tc}$ -MIBI (5). The aim of the present study was to evaluate and compare the results of $^{99\text{m}}\text{Tc}$ -MIBI and tetrafosmin perfusion scintigraphies in multivessel CAD.

MATERIAL AND METHODS

Patients:

The study population consisted of 21 patients (18 men, 3 women; mean age 58.2 ± 4.7 years, age range 32-78 years) with multivessel CAD. All patients had more than one coronary artery lesions with 70% or greater stenosis graded by visual analysis. Ten patients had three-vessel disease, while 11 patients had two-vessel disease. Thirteen of the patients had a previous Q wave myocardial infarction. Scintigraphic studies and coronary arteriography were performed in all patients within two weeks. Patients were excluded from the study if they

had recent acute MI (in < 2 week) or (manifested) unstable coronary artery disease, significant clinical congestive heart failure, valvular disease, LBBB, congenital heart disease, significant noncardiac illness. Females with child bearing potential were also excluded (Table 1).

Stress test:

In all patients treadmill exercise tests were performed using standard Bruce protocol, with 12-lead ECG recording for each minute of exercise and continuous monitoring of leads DII, V2 and V5. Beta adrenergic blocking agents, calcium antagonists and long acting nitrates were withheld before the stress test as far as possible. Exercise end points were ≥ 3 mm horizontal or down sloping ST depression, physical exhaustion, development of severe angina, sustained ventricular arrhythmia, significant dyspnea, or hypotension due to exercise.

Imaging protocols:

Each patient underwent a $^{99\text{m}}\text{Tc}$ -tetrafosmin stress/rest imaging study on a one day protocol. Radiotracer (5 to 8 mCi) was injected at peak exercise. Patients were asked to continue exercise for an additional minute after injection. Approximately 4 hours after the initial injection, patients underwent a second $^{99\text{m}}\text{Tc}$ -tetrafosmin injection (15-24 mCi). Imaging was carried out between 15 and 60 minutes after each $^{99\text{m}}\text{Tc}$ -tetrafosmin injection. A light meal or a glass of milk was given to all patients.

Same patients underwent a $^{99\text{m}}\text{Tc}$ -MIBI rest/stress imaging study on another one day protocol. Radiotracer (5-8 mCi) was injected at rest. Images were taken 30-60 minutes after rest. Three hours after the initial injection, patients underwent a second injection at peak exercise (18-26 mCi). Patients continued to exercise for an additional minute after injection. A light meal or a glass of milk was given to all patients. For imaging, the gamma camera was equipped with low energy-all purpose (LEAP) parallel hole collimator. The camera energy window (20%) was symmetrically set on the 140keV peak of $^{99\text{m}}\text{Tc}$.

Tomography was obtained with a rotational single head gamma camera (Sophy Camera

DS7) collecting 32 views over 180° (30 sec/frame stress, 20 sec/frame rest for ^{99m}Tc-tetrofosmin; 30 sec/frame rest, 20 sec/frame stress for ^{99m}Tc-MIBI).

Image interpretation:

For each study, left ventricular myocardium was divided in to five large segments: anterior, septal, inferior, lateral and apical (anterior, apical and septal segments include the left anterior descending (LAD) artery territory, lateral segments include the left circumflex (LCx) artery territories, and inferior segments include the right coronary artery (RCA) territories). The ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin images were separately interpreted and uptake of the tracer in each segment was scored by consensus of the two experienced observers using a four point grading system (3= normal, 2=mildly reduced, 1=moderately reduced, and 0=defect) without knowing the clinical history and results of coronary arteriography findings. A segment was considered abnormal when stress score was ≤2. A reversible defect was defined as an abnormal segment showing an improved score on the resting scans.

Coronary Angiography:

Coronary angiogram and left ventriculography were performed by Judkins technique. Coronary lesions were analyzed qualitatively by two observers blind to the clinical or scintigraphic data.

Statistical method:

Student t test and kappa analysis were used in statistical analysis. ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin concordance was assessed by kappa analysis.

RESULTS

None of the patients experienced a cardiac event in the interval between SPECT studies and coronary angiography.

Exercise Data:

The physiological exercise parameters for the ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI exercise studies are shown in Table 2.

Exercise workload and duration were not significantly different during the two procedures. Mean duration of exercise for ^{99m}Tc-tetrofosmin was 7.35±2.1 min, (ranged from 4.15 to 11.3 min), while it was 7.21±1.7 min (ranged from 4.3 to 10.18 min) for ^{99m}Tc-MIBI; achieved maximum heart rate was virtually identical.

In ^{99m}Tc-MIBI and ^{99m}Tc-tetrofosmin groups, angina occurred in 8 and 9 patients, while ST-segment depression was observed in 11 and 13 patients, respectively.

Abnormal ST segment depression on exercise was observed in 5 of 8 patients without previous myocardial infarction.

Imaging Results:

Comparison of the diagnosis derived from the ^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI images was performed overall and for each segmental group. Overall segmental concordance was 95%. Discordance predominates in the inferior region (75%), where as concordance was better in the anterior (100%) and anteroseptal (100%) regions (Table 3).

^{99m}Tc-tetrofosmin and ^{99m}Tc-MIBI identified an abnormality in all of the patients with previous MI. With ^{99m}Tc-tetrofosmin, fixed defects were reported in 8 patients, and partially reversible defects in 5 patients; while

Table 1. Clinical characteristics of patients.

| | |
|--|--|
| Patients | 3 Female, 18 male |
| Mean age (years) | 58±4.7 (range 32-78) |
| Previous MI | 13pts (61%) |
| Coronary artery vessel with >70 % stenosis | 11 pts (52%) 2 vessel disease 10 pts (48%) 3 vessel disease |

Table 2. Hemodynamic parameters during treadmill exercise tests.

| | ^{99m} Tc-MIBI | ^{99m} Tc-tetrofosmin | p |
|-------------------------|------------------------|-------------------------------|----|
| Max Heart Rate / min | 127.8 (87-172) | 131.5 (90-176) | NS |
| Max Systolic BP (mmHg) | 175.4 (145-240) | 186.5 (150-240) | NS |
| HRxBP product | 23107 (12086-33690) | 22845 (11687-34310) | NS |
| Exercise duration (min) | 7.3±1.7(4.30-10.18) | 7.35± 2.1 (4.15-11.3) | |

with ^{99m}Tc -MIBI, fixed defects were reported in 7 patients and partially reversible defects in 6 patients.

Abnormalities in non-infarcted territories were recognized with both tracers in all (21/21) patients presenting with coronary lesions involving vessels unrelated to the infarct (Figure 1 and 2).



Figure 1. Mixed defect images of the patient.



Figure 2. Anteroseptal myocardial infarction and viable tissue, ischemia in septal infarct zone.

Table 3. Concordance data of all patients.

| | Reversible | Fixed | Mixed |
|-------------|------------|-------|-------|
| MIBI | 21 | 7 | 6 |
| Tetrofosmin | 21 | 8 | 5 |

DISCUSSION

There have been many studies conducted on ^{99m}Tc -tetrofosmin in the past few years, but these studies mostly compared ^{99m}Tc -tetrofosmin tomography with angiography, and thallium tomography in patients with coronary heart disease (6). However, when it comes to the comparison of ^{99m}Tc -tetrofosmin and ^{99m}Tc -MIBI in clinical usage, there are not many studies and the data is limited. In the present study, we compared ^{99m}Tc -MIBI and ^{99m}Tc -tetrofosmin in patients with multivessel coronary heart disease; thus, this is one of the few clinical studies conducted with such a procedure.

Thorley et al, administered ^{99m}Tc -tetrofosmin in 40 patients with multivessel coronary heart disease. Though they found high sensitivity both in ^{99m}Tc -tetrofosmin tomography and angiography, they did not compare ^{99m}Tc -MIBI with ^{99m}Tc -tetrofosmin (7). In the present study, the comparison of ^{99m}Tc -MIBI and ^{99m}Tc -tetrofosmin imaging data was found to be satisfactory.

As previously reported with other tracers, including thallium, ^{99m}Tc -MIBI, teboroxime, cesium, rubidium, potassium, as well as other PET tracers, ^{99m}Tc -tetrofosmin's ability to recognise and localize MI is excellent (8-10). In the present study, ^{99m}Tc -tetrofosmin result of one patient was different from ^{99m}Tc -MIBI result (while a fixed defect was seen in ^{99m}Tc -tetrofosmin, a mixed defect was observed in MIBI); however this discordance was not statistically significant.

^{99m}Tc -tetrofosmin and ^{99m}Tc -MIBI SPECT imaging provides high quality images. However, since there is a high initial hepatic activity with relatively slow clearance after injection of ^{99m}Tc -MIBI, there is a need for a delay of 0.5-2 hours before the imaging procedure. In some cases, high residual hepatic and gastrointestinal tract activity can make image interpretation impossible (especially in inferior regions) (11). This was the case in the present study as well, causing the majority of false interpretations to occur in the inferior wall of the myocardium.

^{99m}Tc -tetrofosmin was shown to have a good myocardial uptake and relatively slow clearance while back-ground clearance was

rapid. This rapid clearance from liver provides excellent heart-liver ratios for imaging (11). Preparation of ^{99m}Tc -tetrafosmin does not require heating, but only 15 minutes of incubation at room temperature. The relatively simple kit formulation, and possibility of imaging within 30 minutes after injection suggests a potential role for imaging in acute coronary disease. Such a role could involve imaging of acute infarction, resting ischemia and assessment of thrombolysis, and early diagnosis of infarction in the emergency department (12).

Although some studies utilized stress-redistribution protocol in comparison of ^{99m}Tc -tetrafosmin and thallium, we concluded that some comparative studies with ^{99m}Tc -tetrafosmin and ^{99m}Tc -MIBI were needed to identify viable tissue. Therefore, comparative studies on thallium re-injection or thallium rest injection are needed as well.

In conclusion, ^{99m}Tc -tetrafosmin, just as ^{99m}Tc -MIBI, is an agent to be used to obtain high quality images with fast liver clearance in patients with multivessel disease. However, it is recommended that further studies should be conducted on tissue viability.

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