Effect of Time on Liver Clearance of Technetium-99m-Tetrofosmin in Patients with Acute Chest Pain: When Should Imaging Begin?

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Objective: Due to stable myocardial retention and technetium imaging characteristics, ^{99m}Tc-tetrofosmin has been considered potentially useful for acute chest pain imaging. Tetrofosmin also has favorable biokinetics with reported rapid liver clearance, 5 min poststress and 30–45 min post-rest injection. Since comparable data are not available, the effect of time on liver clearance was evaluated in patients with acute chest pain.

Methods: One hundred six patients received an intravenous injection of 25–30 mCi ^{99m}Tc-tetrofosmin to evaluate acute chest pain. SPECT imaging was performed 15–120 min after injection of the tracer. Patient images were grouped according to the time of acquisition after acute injection: 15–30 min, 31–45 min, 46–60 min, 61–90 min and >90 min. Quantitative analysis was performed on a similar anterior projection for each patient consisting of a 6 × 6-pixel region of interest over the myocardium and adjacent liver. Average counts per pixel were determined and a heart/liver (H/Li) ratio was calculated.

Results: The mean H/Li ratio was < 1.0 for patient images acquired 15–45 min after injection, and > 1.0 for patient images acquired after 45 min. The difference was statistically significant ($p < 0.05$).

Conclusion: Quantitative analysis suggests that the optimal imaging time should be at least 45 min after the injection of ^{99m}Tc-tetrofosmin to allow adequate liver clearance before image acquisition of acute chest pain syndromes.

Key Words: technetium-99m-tetrofosmin; liver clearance; acute chest pain; myocardial perfusion imaging; ischemic coronary artery disease

J Nucl Med Technol 1998; 26:186–190

Technetium-99m-tetrofosmin is a recently approved myocardial perfusion imaging agent that has clinically insignificant myocardial redistribution (*1*). This property, in addition to the short half-life (6 hr) and 140-keV energy emission of technetium, allows tetrofosmin to be an effective myocardial perfusion imaging agent (*2*). It has been reported that tetrofosmin also has favorable biokinetics with rapid liver clearance, which allows imaging to be performed as early as 5 min after stress and 30–45 min after rest injection (*2–4*).

Technetium-labeled myocardial perfusion imaging agents, such as ^{99m}Tc-sestamibi, have proven to be useful in evaluating acute chest pain syndromes (*5*). For example, in patients with no history of myocardial infarction, a positive image has a high positive predictive value for unstable angina and acute myocardial infarction, while a negative image has a very high negative predictive value for these events (*6*). Due to the stable myocardial retention and favorable biokinetics, ^{99m}Tc-tetrofosmin also may be useful for evaluating patients with suspected acute ischemic coronary artery disease (*7*).

Although images obtained from patients injected with a radiopharmaceutical during chest pain may reflect ischemia, physiologic conditions differ from exercise stress since significant hemodynamic changes generally do not occur in these patients. Thus, it is unclear whether liver clearance of tetrofosmin follows the kinetics of a stress or rest injection. As a result, the optimal time for image acquisition is unknown. The purpose of this study was to evaluate the effect of time on liver clearance when using ^{99m}Tc-tetrofosmin for myocardial perfusion imaging in patients with acute chest pain syndromes.

MATERIALS AND METHODS

Study Design

This was a substudy of a multicenter trial evaluating the use of ^{99m}Tc-tetrofosmin for acute myocardial perfusion imaging (*8–9*). Patients enrolled in the multicenter trial at one site (Hartford Hospital) had SPECT imaging 15–270 min after injection of the tracer. A heart-to-liver ratio was determined for each patient.

Study Population

One hundred six patients evaluated in the emergency department with symptoms consistent with ischemic coronary artery disease were enrolled into the study. Entry criteria were:

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the ability to give written informed consent; a history of chest pain less than or equal to 6 hr; normal or nondiagnostic electrocardiogram; and the patient had to be admitted to the hospital for further evaluation independent of the image results. Excluded from the study were patients with: acute myocardial infarction; history of previous myocardial infarction; history of unstable angina; and female patients who were pregnant, lactating or of childbearing potential without confirmation of absence of pregnancy.

Acquisition Parameters

After intravenous injection of 25–30 mCi ^{99m}Tc-tetrofosmin in the emergency department, patients were transported to the nuclear cardiology laboratory for imaging. SPECT image acquisition was performed 15–270 min after injection of tracer using an ADAC (Milpitas, CA) single-head Cirrus gamma camera equipped with a low-energy high-resolution collimator, or an ADAC dual-head Vertex gamma camera, locked at a 90° angle and equipped with low-energy, high-resolution collimators. Sixty-four projections were acquired at 25 sec per projection, using a 64 × 64 × 16 matrix over 180° arc, beginning at a 45° right anterior oblique, rotating clockwise to a 45° left posterior oblique. The Cirrus acquisition was performed using a circular orbit and a full field of view. The Vertex acquisition was performed using a noncircular orbit with a roving zoom of 38 cm^2.

Processing Parameters

Images were reconstructed using an ADAC Pegasys computer. A Butterworth filter was applied using a frequency cutoff of 0.6 with an order of 5.0 and a slice thickness of 1.0 pixel. A standard three-view display was created consisting of short axis, vertical long axis and horizontal long axis slices.

Quantitation

Quantitative analysis was performed on each image to determine heart-to-liver (H/Li) ratios. The same anterior projection that best visualized the myocardial and hepatic uptake was chosen for each patient (Fig. 1). A 6 × 6-pixel region of interest was drawn over both the myocardium and liver and average counts per pixel were determined. A heart-to-liver ratio then was calculated by dividing average counts per pixel in the myocardium by the average counts per pixel in the liver.

RESULTS

Patient Demographics

Of the 106 patients enrolled into the study, 52 patients (49%) were female. The mean age of the patients was 58 ± 13 yr and the mean weight was 84 ± 7 kg.

Imaging Data

Patients were separated into five groups according to acquisition time after injection of the ^{99m}Tc-tetrofosmin (Table 1). Forty-six percent of the patients were imaged less than 45 min after injection, with a mean tetrofosmin dose of 28.6 ± 0.80 mCi.

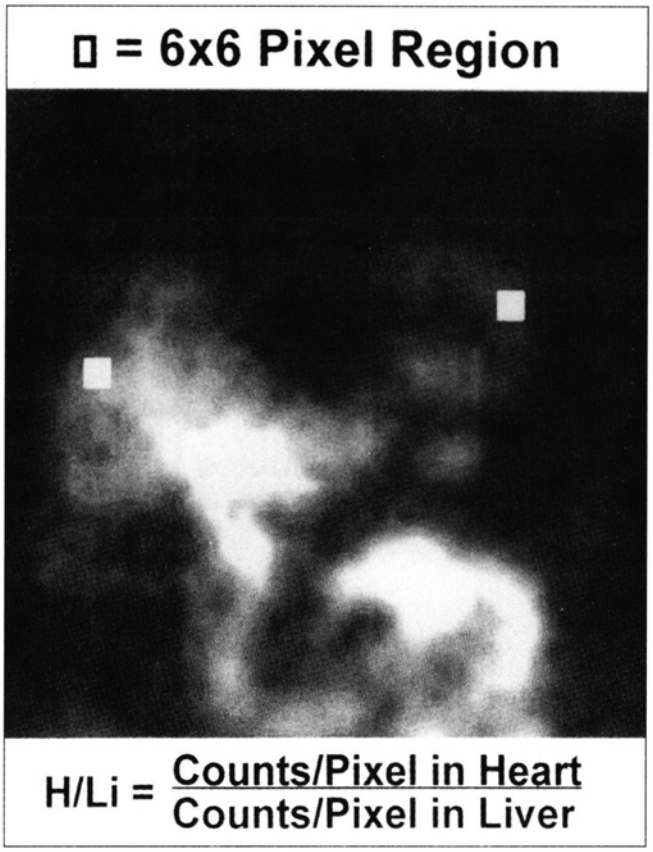

FIGURE 1. Formula for calculating heart-to-liver ratios and an example of the regions of interest in one patient.

Quantitative Analysis

The mean heart-to-liver ratios were calculated for each time interval and were significantly less in patients whose images were acquired ≤ 45 min after injection than in patients acquired ≥ 46 min ($p < 0.05$; Fig. 2). In general, the mean ratio was ≤ 1.0 if image acquisition began 15–45 min after injection and was ≥ 1.0 if images were acquired more than 45 min after injection of the tracer.

Patient Examples

Patient 1 was a 67-yr-old woman who was evaluated in the emergency department with chest pain and a nondiagnostic

TABLE 1
Data from 106 Patients Who Had Technetium-99m-Tetrofosmin SPECT Myocardial Perfusion Imaging for Acute Chest Pain Syndromes

Time from injection to initiation of acquisition	Number of patients (n)	Mean injected activity (mCi)	% of patients injected during chest pain
15–30 min	29	28.0	41.4%
31–45 min	20	28.1	20.0%
46–60 min	25	28.1	64.0%
60–90 min	22	28.8	50.0%
> 90 min	10	29.9	40.0%
	21.2 ± 7.1	28.6 ± 0.80	43.0 ± 16.0

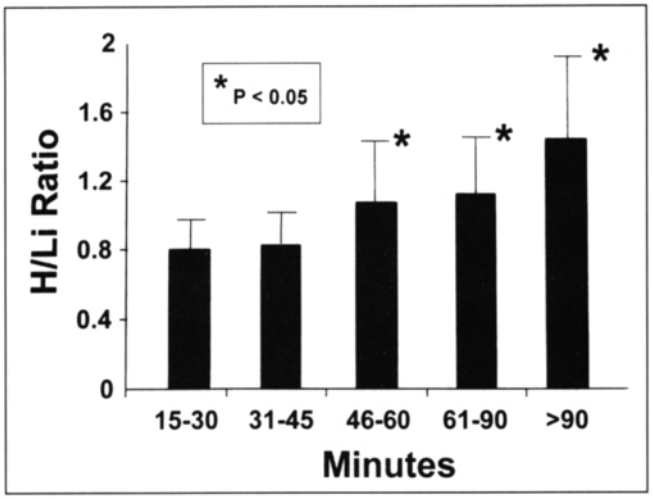

FIGURE 2. Mean heart-to-liver ratio for each time interval. The value $p < 0.05$ when compared with 15–45 min.

electrocardiogram. The patient was injected 5 hr following complete resolution of symptoms with 29.2 mCi ^{99m}Tc-tetrofosmin. SPECT images were acquired 15 min after injection and the calculated heart-to-liver ratio was 0.71. Myocardial perfusion images revealed a small inferioposterior defect on both the short axis and vertical long-axis views and increased hepatic uptake was observed on the unprocessed projection data (Fig. 3). Thus, an inferior defect was present, which may have been due to attenuation from the liver or cardiac ischemia. Further evaluation revealed no evidence of coronary artery disease in this patient.

Patient 2 was a 50-yr-old woman who was evaluated in the emergency department with chest pain and a nondiagnostic electrocardiogram. The patient was injected 5 hr following the complete resolution of symptoms with 30.3 mCi ^{99m}Tc-tetrofosmin. SPECT images were acquired 60 min after injection and the calculated heart-to-liver ratio was 1.5. Myocardial perfusion images revealed normal distribution of tetrofosmin and no increased hepatic activity was observed on the unprocessed projection data (Fig. 4).

DISCUSSION

The optimal time to begin image acquisition after injection of ^{99m}Tc-tetrofosmin during acute chest pain is unknown. This study examined the effect of time on the relative uptake of ^{99m}Tc-tetrofosmin in the heart and liver after injection of the tracer in patients with chest pain and nondiagnostic electrocardiograms. For the 106 patients studied, the heart-to-liver ratio was ≤ 1.0 if image acquisition occurred less than 45 min after injection of the radiopharmaceutical and ≥ 1.0 if image acquisition occurred more than 45 min after radiopharmaceutical injection. These findings suggest that the biokinetics of ^{99}Tc-tetrofosmin during acute chest pain injection are similar to a rest injection and image acquisition should not begin until 45 min after injection of the tracer to ensure optimal imaging results (*3,10*).

Liver attenuation may be a source of error in interpreting myocardial perfusion images. When hepatic activity occurs, it cannot be eliminated from the acquisition by placement of a lead shield or other devices. This problem most often occurs after rest and pharmacologic stress injections, as with an exercise injection, due to a lack of blood shunting from the abdominal viscera to the working skeletal musculature (*11*). Radiopharmaceutical uptake in the liver may degrade SPECT images through the superimposition of the liver and inferior wall of the myocardium (*11*). Artifactual defects may occur during backfilter projection processing, causing apparently hypoperfused areas in the inferior regions of the myocardium

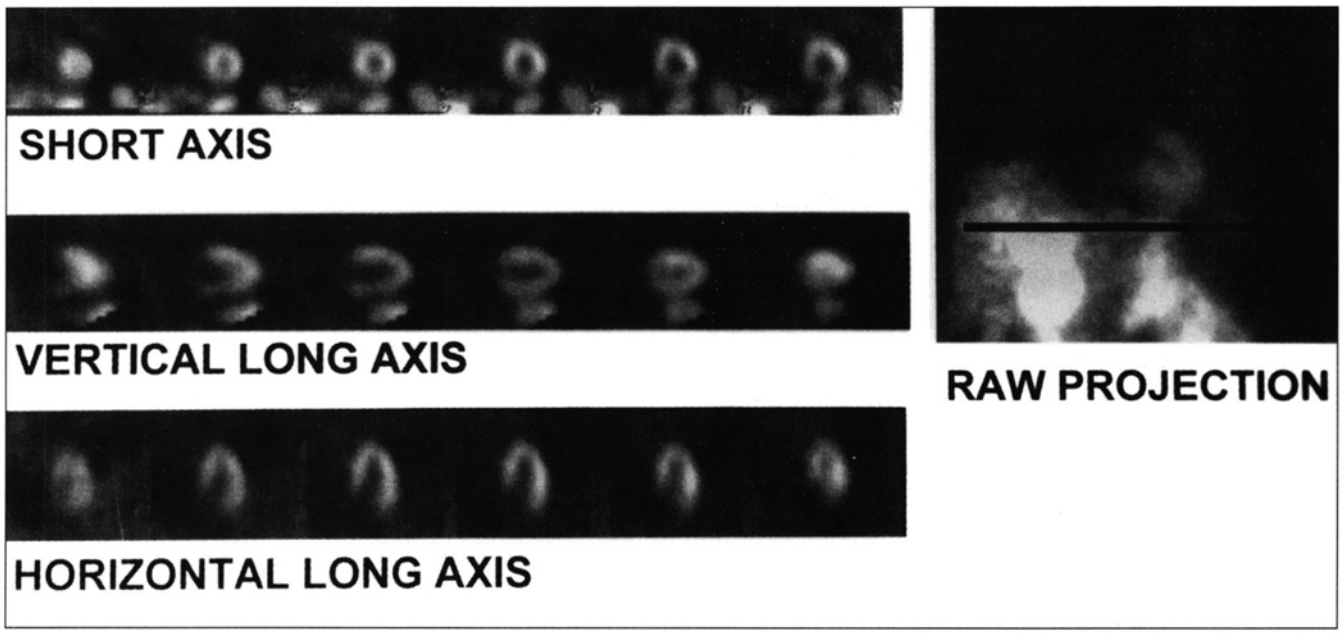

FIGURE 3. Inferioposterior defect with increased hepatic activity in a patient whose image acquisition began 15 min postinjection.

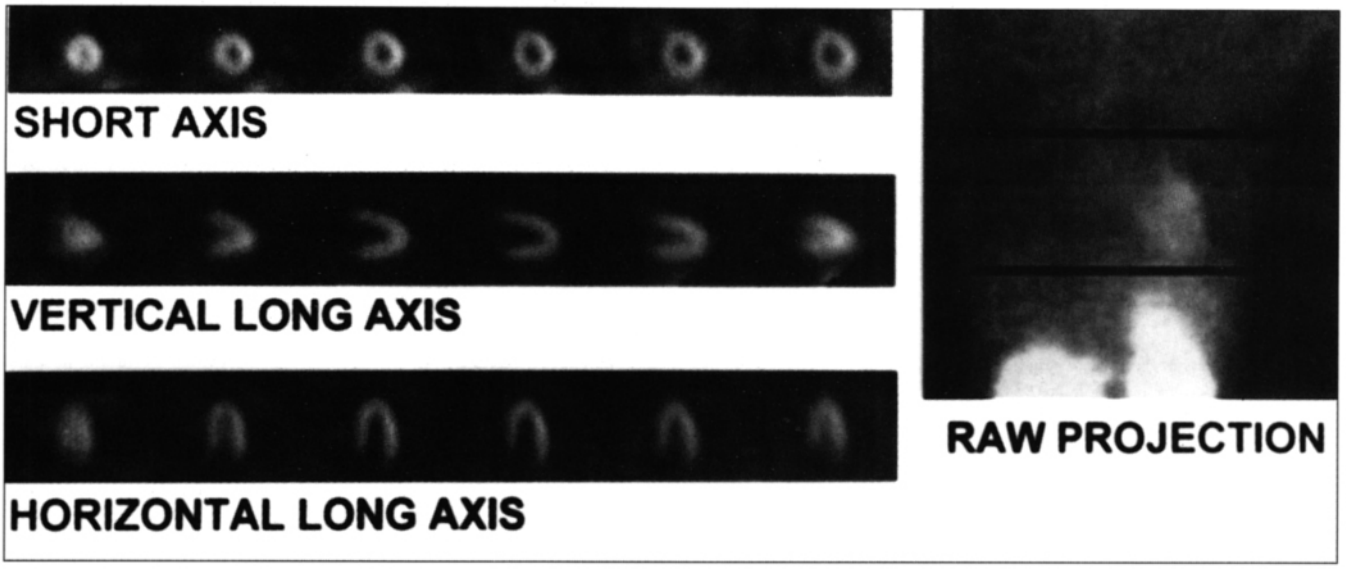

FIGURE 4. Normal perfusion with minimal hepatic activity in a patient whose image acquisition began 60 min postinjection.

which are difficult to distinguish from myocardial ischemia (*12–13*). Incorrect normalization during quantitative analysis and polar plot generation also may occur. Activity in the superimposed region may make other areas of the myocardium appear count deficient and defects may be identified incorrectly as consistent with coronary artery disease (*11*).

The biokinetics for tetrofosmin suggest rapid liver clearance when used with exercise myocardial perfusion imaging with heart-to-liver ratios of > 1.0 as early as 5 min after injection (*3*). However, liver clearance was not as rapid when pharmacologic stress was performed, during which heart-to-liver ratios did not reach 1.0 until 30–45 min after injection (*10*). Biokinetics for tetrofosmin after a rest injection were comparable to pharmacologic stress, with heart-to-liver ratios reaching 1.0 after 45 min (*3*). These results are similar to biokinetic data for ^{99m}Tc-sestamibi, which suggests heart-to-liver ratios ≥ 1.0 as early as 5 min after injection during exercise stress and 45–60 min after injection for both pharmacologic stress and rest myocardial perfusion imaging (*10,14*).

When performing myocardial perfusion imaging to evaluate patients with acute chest pain syndromes, it is important to allow adequate time for liver clearance since only one image set is being interpreted to make a clinical decision. Maturnari et al. (*15*) concluded that it is best to perform late imaging in patients with suspected coronary artery disease using ^{99m}Tc-tetrofosmin. Without adequate liver clearance, a false-positive study may result. Such an interpretation may inappropriately result in a patient unnecessarily being hospitalized and/or undergoing cardiac catheterization. Conversely, an abnormal study may be misinterpreted as liver attenuation and the patient could be inappropriately discharged without further evaluation.

Limitations

Image acquisition was performed once for each patient rather than in a repetitive fashion which may have resulted in greater variability. However, due to the number of patients enrolled in this study, the data consistently demonstrated a significant difference in heart-to-liver ratios in patients undergoing image acquisition more than 45 min after injection.

CONCLUSION

Adequate liver clearance is achieved 45 min after injection of ^{99m}Tc-tetrofosmin for acute myocardial perfusion imaging. To optimize SPECT imaging in the acute setting, proper liver clearance should be achieved to eliminate the possibility of interpreting a false-positive study due to artifacts caused by increased hepatic activity using ^{99m}Tc-tetrofosmin. Thus, optimal image acquisition should begin at least 45 min after acute injection in patients with symptoms suggestive of myocardial ischemia.

ACKNOWLEDGMENTS

This study was supported in part by a grant provided by Amersham/Medi-Physics, Arlington, Illinois and was performed as a substudy of a multicenter trial. This study was presented in part at the 1996 Society of Nuclear Medicine Annual Meeting in Denver, Colorado.

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