

QUANTITATIVE ASSESSMENT OF CORONARY PERFUSION RESERVE ON NORMAL AND ABNORMAL MYOCARDIUM WITH Tc-99m HEXAMIBI, COMPARISON WITH Tl-201.

ERKAN IBIS*
GÜNER ERBAY*
GÜLSEREN ARAS*
ASIM AKIN*

SUMMARY: In 12 cases with normal coronary angiogram and 29 patients with abnormal coronary angiogram, 15 mCi Tc-99m hexamibi and 2 mCi Tl-201 were injected during exercise on separate days and planar imaging was applied. A second injection of 15 mCi of Tc-99m hexamibi was performed with the patients at rest one day later. Rest Tl-201 scintigraphy was performed 3 to 4 h later following exercise imaging without a second injection. Quantitative assessment of both Tc-99m hexamibi and Tl-201 were performed in 205 left ventricle segments and coronary perfusion reserve (cpr) of each segment was calculated on Tc-99m hexamibi and Tl-201 studies, from exercise to rest. There was good correlation for the cpr of normal or abnormal myocardium with two radiopharmaceuticals Myocardial defect uptake was nearly identical, yielding agreement in 93.8% of the myocardial segments in patients with coronary artery disease (CAD) and 88.3% of the myocardial segments in normal patients. We conclude that Tc-99m hexamibi is a sensitive myocardial flow marker. However, a second injection was needed to assess regional cpr within this protocol.

Key Words: Myocardial perfusion scintigraphy, Tc-95m, Tl-201.

INTRODUCTION

Thallium-201 chloride (Tl-201) served for many years as the agent of choice to evaluate myocardial perfusion of patients with coronary artery disease (CAD), during exercise and rest (1,2,4). However, the physical and biological properties of Tl-201 are not ideal for imaging purposes. Rapid serial evaluation of perfusion is not possible, because of its long physical half-life and slow myocardial clearance. Image quality is marginal because of its low energy radiation. Furthermore its myocardial distribution reflects flow for only a short time after stress because of redistribution (4,6,17,18,22). For these reasons, researchers have focused their attention on myocardial perfusion agents labeled with Tc-99m isonitrile analogs have recently been synthesized that demonstrate cardiotropic properties (5,6,19). One of the most

promising these analogs at the present time is the Tc-99m-methoxy-isobutyl-isonitrile (Tc-99m hexamibi) (16). As Tl-201, the distribution of Tc-99m hexamibi reflects the myocardial blood flow, but unlike Tl-201 there is no evidence of significant myocardial redistribution following injection (7,14,20,22). Since it does not redistribute, two separate injections of Tc-99m hexamibi are needed in order to differentiate transient ischemic defects from fixed myocardial defects (22).

This present study was undertaken in patients with CAD, executing a typical exercise-rest protocol to determine the cpr in myocardium with Tc-99m hexamibi and Tl-201 studies, and to compare these radiopharmaceuticals.

MATERIALS AND METHODS

Myocardial perfusion images were performed in 41 patients with specific or non-specific chest pain in Ankara University Medical School, Nuclear Medicine Department, over six months.

*From Department of Nuclear Medicine, Ankara University, School of Medicine, Ankara, Türkiye.

period. There were single-vesel disease in 12 patients, double-vesel disease in 12 patients, and triple-vesel disease in 5 patients. Coronary angiograms were found normal in 12 patients.

The pathologic group included 29 males whose ages ranged from 33 to 68 years (mean: 51.2). In the patients with CAD, 60% or higher stenosis in one or more major arteries was detected on coronary angiography.

There were 7 males and 5 females whose ages ranged from 25 to 55 years (mean: 40.0) in the normal group.

Tc-99m hexamibi and TI-201 studies were applied in all cases instructed to fast after midnight and stopped cardiovascular drugs for 24 h prior to studies. The exercise protocol was similar for each patient. The exercise were performed using a bicycle ergometer to the Bruce protocol. Each patient was taken to the same level of exercise or the Tc-99m hexamibi and TI-201 stress studies. Blood pressure and heart rate per minute were controlled both prior and after the exercise. Any symptom (such as angina, arrhythmia) for stopping exercise were not observed in any patients. Although patients were submitted to two maximal or submaximal stress tests, serious complications such as worsening of angina, or myocardial infarction did not occur in a period of less than two weeks, during myocardial perfusion studies.

For the exercise Tc-99m hexamibi scintigraphy, 15 mCi (550 MBq) of Tc-99m hexamibi was given as a compact bolus into an antecubital vein at peak exercise. Exercise was continued for another 60 seconds. Imaging was commenced one hour later, after injection. Each image was obtained with 450.000 counts. After exercise scintigraphy, a second injection of 15 mCi of Tc-99m hexamibi was performed at rest 24 h later. Imaging was started 60 to 120 minutes later following injection. Those subjects who had exercised underwent rest imaging for the same preset time.

At least one week after Tc-99m hexamibi studies, the patients were re-exercised and injected with 2 mCi (74 MBq) of TI-201 in the same manner, same protocol and the same level achieved during Tc-99m hexamibi stress test. Imaging was started in less than 5 minutes following TI-201 injection. Each image contained 350.000 counts collected with the same gamma camera. Rest images were performed 3 to 4 h later from TI-201 injection for the same time. Images of Tc-99m hexamibi and TI-201 were obtained with the patients supine in the 45° left anterior oblique (LAO), anterior, and 85° left lateral (LL) projections. Myocardial perfusion studies were performed using scintiview imaging console and pho gamma IV camera equipped with a low energy, all purpose, parallel hole collimator. The energy setting was centered at 140 keV for Tc-99m hexamibi, and 75 keV for TI-201 with a window of 20%. All data were stored on magnetic disk in a 128 x 128 matrix for quantitative

analysis. All myocardial images were interpreted qualitatively. The left ventricle was arbitrarily divided into five segments which were septum, anterior, apex, inferior and lateral walls.

Quantitative assessment was made using linear profile technique which has been developed by Dr. Watson and *et al.* (23,24). Briefly, the technique employs modified background subtraction from each image, and establishment of four profile lines through each image. Each resultant curve consists of two peaks. The heights of the two peaks are approximately equal in a normal perfusion study, i. e. the count activity in the two walls is similar. A difference of 25% or more between the two peaks is an indication of perfusion defect. If there is no change in the profile ratios on the rest study, the abnormality is considered 'fixed' and suggestive of myocardial scar. Reversion of the pattern toward

Table 1: Comparison of Tc-99m hexarnibi and TI-201 myocardial perfusion imaging: segmental analysis in 29 patients with CAD.

Perfusion studies	Myocardial Segments (145)		
	Normal	Ischemia	Scar
Tc-99m hexamibi	76	11	58
TI-201	79	10	56

Table 2: Comparison of Tc-99m hexarnibi and TI-201 myocardial perfusion imaging: segmental analysis in normal patients.

Perfusion studies	Myocardial Segments (60)		
	Normal	Ischemia	Scar
Tc-99m hexamibi	58/60 (96.6%)	-	2
TI-201	53/60 (88.3%)	2	5

Table 3: Comparative data cpr both for Tc-99m hexamibi and TI-201.

Myocardial Segment	cpr %		
	Tc-99m hexamibi	TI-201	
Normal	4.3 ± 5.2	5.3 ± 8.3	p>0.05
Abnormal	8.2 ± 11.1	12.0 ± 12.1	p>0.05

Table 4: Tc-99m hexamibi vs. TI-201: comparative results in CAD.

Authors	Tc-99m hexamibi	TI-201
Stirner <i>et al.</i> (20)	39.8 ± 24.9	36.1 ± 24.4
Watson <i>et al.</i> (25)	44 ± 12	41 ± 19
Maddahi <i>et al.</i> (7)	12 ± 12	11 ± 8

normal (both peaks have similar heights) on the rest study suggests myocardial ischemia (8). The perfusion defect only in apical segment was not commented on abnormal.

Cpr % illustrates regional perfusion change from efor to rest in each segment. Statistical analysis were made using a paired t-test. Data were presented as mean ± standard deviation.

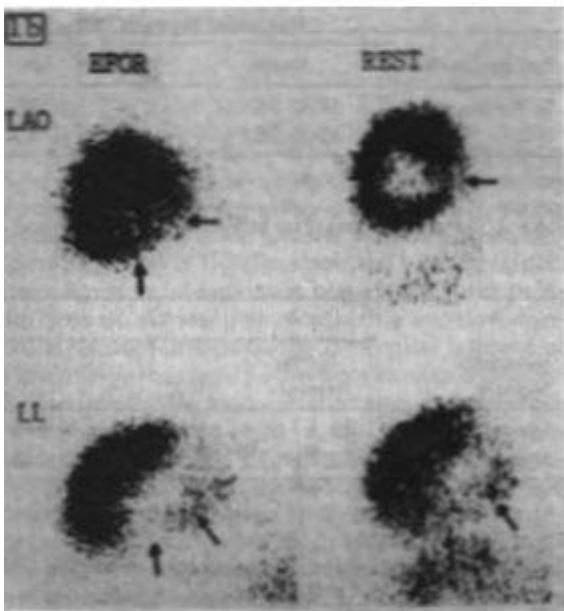
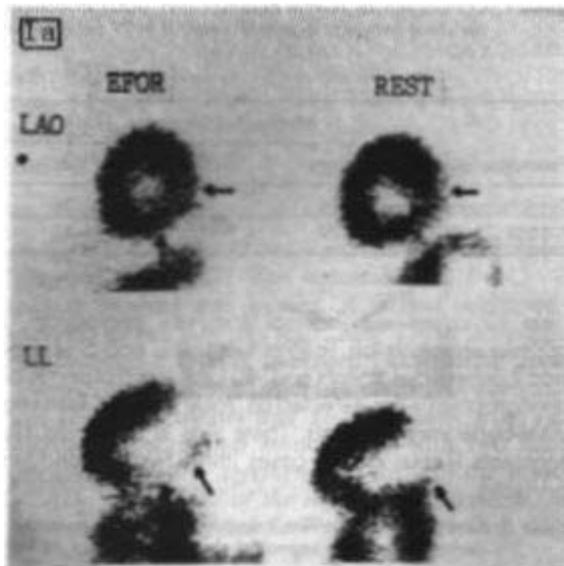


Figure 1a, 1b: In a 56- year-old-man with severe double vessel (LCx+RCA) CAD, 1a and 1b depict the myocardial perfusion images with Tc-99m hexamibi (1a) and TI-201 (1B) in 45° LAO, and 85° LL views. Both scintigraphies demonstrate perfusion defects of inferior, inferoapical, and lower part of lateral wall.

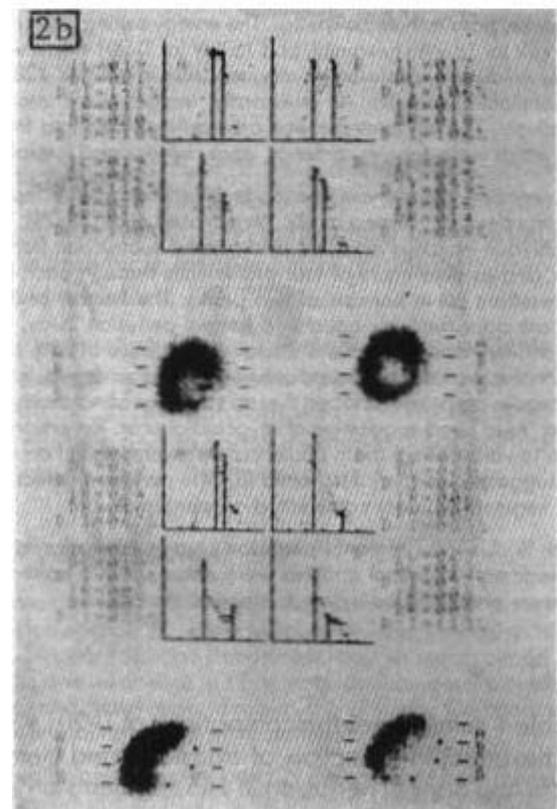
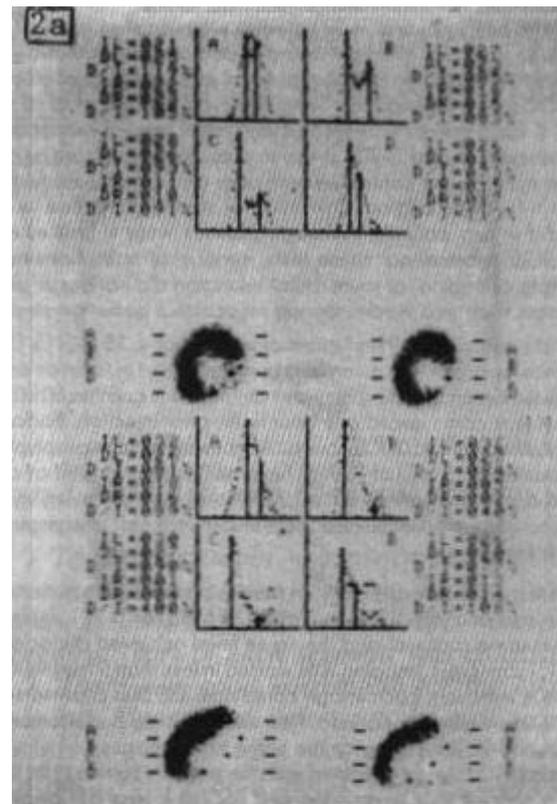


Figure 2a, 2b : The quantitative analysis of Tc-99m hexamibi (2a) and TI-201 scintigraphies with linear profile technique.

RESULTS

Table 1 summarizes the comparison of TI-201 with Tc-99m hexamibi in detection of transient, and persistent defects and normal perfusion in 145 segments on 29 patients with CAD. There was agreement in 136/145 (93.8%) segments. The total number of ischemic segments (11 for Tc-99m hexamibi vs 10 for TI-201) and scarred segments (58 for Tc-99m hexamibi vs 56 TI-201) determined by both agents are similar. The number of segments that were normal with one agent and ischemic with the other (1 each) or normal with one and scar with the other (2 for Tc-99m hexamibi).

In 12 cases with normal coronary angiogram, 2 scarred segments on Tc-99m hexamibi, and 5 scarred and 2 ischemic segments on TI-201 myocardial perfusion scintigraphies were detected as 'false positive' with segment-by-segment analysis. There was in 53/60 (88.3%) segments (Table 2). In 5 cases (three females and two males) on TI-120 images, and in two (one female and one male) of those 5 cases on Tc-99m hexamibi images had false positive myocardial perfusion defects. Three female cases had hyperthyrophic mammary glands. For comparative evaluation of Tc-99m hexamibi and TI-201 kinetics, slices (Figure 1a, 1b) and target (Figure 2a, 2b) were visually screened. Table 3 illustrates comparative data of cpr both for Tc-99m hexamibi and TI-201. Mean cpr% were found 4.3 ± 5.2 for Tc-99m hexamibi and 5.3 ± 8.3 for TI-201 in normal segments, and 8.2 ± 11.2 for Tc-99m hexamibi and 12.0 ± 12.1 for TI-201 in defect area.

DISCUSSION

The current radiotracer of choice for the myocardial perfusion studies is TI-201. While this tracer has performed well, it is not ideal. It has some disadvantages as a myocardial perfusion agent. Low energy characteristics of its x-rays are not ideal for Anger camera imaging. Their attenuation by soft tissues is high, markedly reducing the efficiency with which activity in deep structures is measured. The long half-life of TI-201 limits serial studies to frequencies of a day more. On the other hand redistribution and washout (WO) of TI-201 in myocardium is an important problem to calculate coroner perfusion reserve (2,4,6,20-22). For the above reason, development of myocardial perfusion agents labeled with Tc-99m is essential. A Tc-99m labeled tracer has some important advantages; 1)it is more readily available in kit form and inexpensive, 2)it has good physical characteristics for

imaging such as short half-life, higher photon flux and better suited to standard imaging equipment than TI-201, resulting in better image quality with less attenuation of photon from deeper tissues.

From the most recent animal work, we know that Tc-99m hexamibi is taken up from the myocardial cell by diffusion, and the main myocardial cellular binding is to cytosol (11-13, 20). Tc-99m hexamibi had excellent, and rapid and stable heart uptake that was proportional to blood flow, showed rapid and stable heart uptake that was proportional to blood flow, showed rapid clearance from the blood and lung and also cleared in a suitable time from the liver via the biliary tract in to urine through the kidneys (9,16,22). Cpr of mixed scar and ischemia quantitated by the % change in perfusion defect intensity from efor to redistribution (TI-201) and efor to rest (Tc-99m hexamibi) were found similar for TI-201 and Tc-99m hexamibi (Table 4). On the other hand, cpr in normal myocardium was 6.7 ± 10.2 for TI-201 from efor to redistribution, and 5.4 ± 5.9 for Tc-99m hexamibi from efor to rest by Stirner *et al.* (20). We confirmed that there were no statistically significant differences in the distribution of tracer uptake or extent of redistribution indicated by delayed TI-201 imaging or alternatively by a second hexamibi injection at rest in normal, scarred or ischemic myocardium. Our results of perfusion reserve in patients with CAD are lower than Stirner's and Watson's results. These could relate to most of our patients having myocardial scarred tissues. In one ischemic, two scarred, and six normal myocardial segments, different ratios of cpr were detected with Tc-99m hexamibi and TI-201 studies. This difference may be due to Tc-99m hexamibi which has low rates of redistribution and WO in myocardium, to the contrary TI-201. High WO rates of TI-201 may maske perfusion changing of ischemic myocardium from exercise to rest.

CONCLUSION

From these preliminary results, we conclude that the diagnostic performances of Tc-99m hexamibi is a sensitive myocardial flow marker. A second injection of Tc-99m hexamibi may be additionally used to assess the coronary perfusion reserve.

ACKNOWLEDGEMENTS

We gratefully acknowledge the assistance of Ayfer Soylu, Ph. D., preparation of Tc-99m hexamibi, and nuclear medicine technologists of our institution.

REFERENCES

1. Becker CL : Myocardial perfusion. In Harbert J and Rocha AFG (eds): *Textbook of Nuclear Medicine*, Philadelphia, Lea and Febiger, pp 383-405, 1984.
2. Dash H, Osbakken DM, Reeves WC : Myocardial perfusion studies. In Osbakken DM, Reeves WS, Flickinger FW (eds): *Techniques, Diagnostics, and Advances in Nuclear Cardiology*. Illions, Charles C Thomas Publisher, pp 173-179, 1983.
3. Deutsch E, Glavan KA, Sodd VJ, Nishiyama H, et al : Cationic Tc-99m complexes as potential myocardial imaging agents. *J Nucl Med*, 22:897-907, 1981.
4. Gerson MC : Myocardial perfusion imaging: Kinetics and planar methods. In Gerson MC (Ed) *Cardiac Nuclear Medicine*, New York, McGraw-Hill Book Comp., pp 1-24, 1987.
5. Holman BL, Jones AG, Lister JJ : A new Tc-99m labeled myocardial imaging agent, hexakis (t-butylisonitrile) technetium (I): initial experience in the human. *J Nucl Med*, 25:1350-1355, 1984.
6. Holman LB, Sporn V, Jones AG, et al. : Myocardial imaging with Tc-99m CPI: Initial experience in the human. *J Nucl Med*, 28:13-18, 1987.
7. Maddahi J, Merz R, Van Train KF, et al. : Tc-99m hexamibi (RP-30) and Tl-201 myocardial perfusion scintigraphy in patients with coronary disease; Quantitative comparison of planar and tomographic techniques for perfusion defect intensity and defect reversibility. Presented at: 34th Annual meeting, Toronto, 1987.
8. Makler PT, Osbakken DM : Computers in nuclear cardiology. In Osbakken DM, Reeves WS, Flickinger FW (Eds): *Techniques, Diagnostics, and Advances in Nuclear Cardiology*. Illions, Charles C Thomas Publisher, p 27, 1983.
9. McKusick K, Beller G, Berman D, et al : Initial clinical results with Tc-99m hexamibi. Presented at: 36th Annual Scientific Session of the American College of Cardiology, New Orleans, 1986.
10. McKusick KA, Rigo P, Holman BL, et al : Three Tc-99m isonitriles for cardiac imaging. Presented at: 4th Congress International Federation of Biological Nuclear Medicine, 1986.
11. Mousa SA, Cooney JM, Williams SJ : Regional myocardial distribution of RP-30 in animal models of myocardial ischemia and reperfusion. Presented at: 34th Annual Meeting, Toronto, 1987.
12. Mousa SA, Maina M, Brown BA, et al : Retention of RP-30 in the heart may be due to binding to a cytosolic protein. Presented at: 34th Annual Meeting, Toronto, 1987.
13. Mousa SA, Maina M, Williams SJ, et al : Myocardial uptake and retention of Tc-99m RP-30. Evidence for specificity. Presented at: 33rd Annual Society of Nuclear Medicine Meeting, 1986.
14. Mousa SA, Williams SJ : Studies of mechanisms of uptake and retention of Tc-99m hexakis isonitriles in the heart. Presented at: European Nuclear Medicine Congress, 1986.
15. Nishiyama H, Deutsch E, Adolph RJ : Basal kinetic studies of Tc-99m DMPE as a myocardial imaging agent in the dog. *J Nucl Med*, 23:1093-1101, 1982.
16. Okada R, Williams S, Glover D, et al : Myocardial kinetics of Tc-99m hexamibi. A new cardiac imaging agent. Presented at: American College of Cardiology Meeting, New Orleans, 1987.
17. Rothendler JA, Okada RD, Wilson RA, et al : Effect of a delay in commencing imaging on the ability to detect transient thallium defects. *J Nucl Med*, 26:880-883, 1985.
18. Schwartz JS, Ponto R, Carlyle P, et al : Early redistribution of thallium 201 after temporary ischemia. *Circulation*, 57:332-335, 1978.
19. Sia STB, Holman BL, Campbell, et al : The utilization of Tc-99m CPI as a myocardial perfusion imaging agent in exercise studies. *Clin Nucl Med*, 12:681, 1987.
20. Stirner H, Buell U, Kleinhans E, et al : Tc-99m hexakis (2-methoxy-isobutyl-isonitrile) vs Tl-201. A quantitative comparison with SPECT in CAD. *Nucl Med Comm*, 9:15, 1988.
21. Taillefer R, Dupras G, Sporn V, et al : Myocardial perfusion imaging with a new radiotracer, technetium-99m-hexamibi (methoxy isobutyl isonitrile): comparison with thallium-201 imaging. *Clin Nucl Med*, 14:89-96, 1989.
22. Taillefer R, Laflamme L, Dupras G, et al : Myocardial perfusion imaging with Tc-99m-methoxy-isobutyl-isonitrile (MIBI): comparison of short and long time intervals between rest and stress injections. *Eur J Nucl Med*, 13:515-522, 1988.
23. Watson D, Beller G, Read M, et al : Quantitative standards for thallium-201 myocardial distribution and washout. *J Nucl Med*, 21:64, 1980.
24. Watson D, Campbell N, Read E, et al : Spatial and temporal quantitation of plane thallium myocardial images. *J Nucl Med*, 22:577, 1981.
25. Watson DD, Smith WH, Teates CD, Beller GA : Quantitative myocardial imaging with Tc-99m MIBI: comparison with Tl-201. Presented at: 34th Annual Meeting, Toronto, 1987.

Correspondence:
 Erkan IBIS
 Department of Nuclear Medicine,
 Faculty of Medicine,
 Ankara University,
 Cebeci, Ankara, TURKIYE.