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Dobutamine stress tetrofosmin SPECT; evaluation of short rest-stress protocol and head to head comparison with MIBI in detection of coronary artery disease

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Objective: The purpose of the present study was to evaluate the feasibility and diagnostic accuracy of same day short rest-dobutamine stress Tetrofosmin (TF) SPECT imaging protocol and to compare TF SPECT results with MIBI SPECT in the same subjects who were unable to perform treadmill exercise or were unsuitable for pharmacological vasodilator stress. ***Methods:*** The study group consisted of 19 patients (2 female and 17 male, with a mean age of 53.8 ± 7.9 yrs) in whom coronary artery disease (CAD) had been proven or excluded at coronary angiography (CA). MIBI SPECT imaging was performed first. TF SPECT images were obtained one week after MIBI imaging. Immediately after the rest SPECT imaging in both of the MIBI and TF studies, patients underwent dobutamine stress tests. Rest-stress radiotracer doses and dobutamine doses were the same for both TF and MIBI studies. While 60 min waiting periods were applied for MIBI study, only 30 min waiting periods were applied for TF study after the rest and stress injections. Images were evaluated by visual and quantitative analysis. ***Results:*** Dobutamine stress parameters were similar for both studies. Although in TF study, the time between radiopharmaceutical injection and imaging was shorter than in MIBI study, there was no significant difference between heart-to-liver (H/Li) and heart-to-lung (H/Lu) ratios. According to CA results, diagnostic accuracy was similar for TF and MIBI. While sensitivity, specificity and accuracy for TF study were calculated as 82%, 84% and 82%, respectively, the corresponding values for MIBI were 82%, 88% and 84%, respectively. This clinical study has shown comparable diagnostic performance for the detection of CAD between MIBI and TF. Good correlation was found between segmental analysis for both studies. ***Conclusion:*** MIBI and TF showed similar perfusion defects and good segmental correlation during dobutamine stress with the same quality images. Both radiopharmaceuticals may be acceptable with this imaging protocol. Besides this, TF study showed better reversibility degree (55%) in a shorter time when compared to MIBI study (25%) in perfusion defects (especially in segments with severely decreased perfusion or no uptake).

Key words: sestamibi, tetrofosmin, dobutamine, SPECT, coronary artery disease

INTRODUCTION

CHOOSING an ideal myocardial perfusion imaging agent for the diagnosis of CAD and for detection of ischemia and viability, is an important issue in nuclear cardiology. Tc-99m methoxyisobutyl isonitrile (sestamibi or MIBI) and Tc-99m 1,2-bis[bis(2-ethoxyethyl)phosphino]ethane (tetrofosmin or TF) are currently the most widely used alternative flow tracers to conventional thallium-201 (Tl-201). Protocols completed in a shorter time are preferred for myocardial perfusion imaging especially in busy nuclear medicine departments. Separate- and same day, rest/stress and stress/rest protocols have been employed with very similar diagnostic accuracy for MIBI for CAD.

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In TF studies, the possibility of earlier imaging after injection to obtain high quality myocardial images has been suggested by some authors.[1] Because of faster clearance of TF from lung and liver than MIBI, the waiting period from injection to acquisition for rest and stress is shorter for studies using TF, as compared to studies using MIBI. Imaging can be performed from after the fifth min of injection following exercise and as soon as 30 min after injection for rest or pharmacological stress studies.[1–3] On the other hand, recommended optimum imaging time for MIBI is 1–2 hours after tracer injection.[1,2] So the total study time is longer for studies using MIBI.[1,3]

It is known that both MIBI and TF have a 4-fold greater uptake then Tl-201, and they are washed out of cells through similar kinetics, at slower rates than Tl-201.[4] It has been reported that, regional MIBI or TF activity closely correlates with that of Tl-201, indicating that these tracers may be used as a marker of viability.[5] Beside this, there are a limited number of reports comparing MIBI and TF in clinical practice. In an *in-vivo* pig model, Matsunari et al. found nearly identical uptake ratios in a direct head-to-head comparison of retention of MIBI and TF.[6]

It has not yet been determined which tracer is an alternative agent for reversibility or viability and discordant results have been reported. Despite the difference in fractional mitochondrial retention between MIBI and TF, Schaefer et al. reported that the initial cellular uptake of these tracers should be the same.[7] Although, both have similar properties, MIBI seems to be more suitable than TF for the detection of myocardial reversibility and viability since it accumulates mostly inside the mitochondria.[7]

Certainly, besides radiopharmaceutical selection and imaging protocols, the clinical condition of the patient and stress techniques are also important in myocardial perfusion imaging. Although both tracers have similar physiologic characteristics, to our knowledge, adequate clinical investigations which simultaneously compare the diagnostic effectiveness of these tracers in CAD especially in patients unable to perform treadmill exercise or unsuitable for pharmacological vasodilator stress testing have yet to be performed. In such patients, dobutamine is considered as a safe and appropriate agent for the pharmacological stress during the myocardial perfusion SPECT.

In this clinical study, we evaluated the feasibility and diagnostic accuracy of the same day short rest-dobutamine stress TF SPECT protocol and head to head compared TF SPECT results with MIBI SPECT in the same patients with suspected or known CAD who had limitations to perform treadmill exercise or pharmacological vasodilator stress testing.

MATERIAL AND METHOD

Patient Population: The study group consisted of 19 patients [2 female (10%) and 17 male (90%) with a mean age of 53.8 ± 7.9 years, range: 41–69] with suspected or known CAD who had limitations to perform treadmill exercise or pharmacological vasodilator stress referred to Gazi University Hospital, Dept. of Nuclear Medicine for myocardial perfusion SPECT. Six patients had severe orthopedic problems, 13 patients had mild physical problems (4 of 13 also had a history of chronic obstructive pulmonary disease or bronchospasm with exercise and 3 other of 13 patients had also low systolic blood pressure), which limited them to perform treadmill exercise or pharmacological vasodilator stress testing. Nine of the 19 patients (47%) had no previous myocardial infarction, whereas 10 (53%) of the study group had historical and/or electrocardiographic (ECG) criteria for prior myocardial infarction. Two of 10 also had aneurysms (Table 1). None of the patients had undergone previous percutaneous transluminal coronary angioplasty and/or coronary artery bypass grafting surgery. Patients with stable myocardial infarction or a history of typical angina or angina-like chest pain were included in this study. All patients underwent CA using standard percutaneous techniques within 2 weeks of the radionuclide studies. Significant stenosis was considered as ≥50% luminal narrowing in major coronary vessels. Exclusion criteria were unstable diseases such as recent infarction (<2 mo old) or angina, or associated problems such as congestive heart failure, cardiomyopathy, significant valvular heart disease and left bundle branch block. SPECT studies were performed 48 hrs after withdrawal of β-adrenergic blocking agents

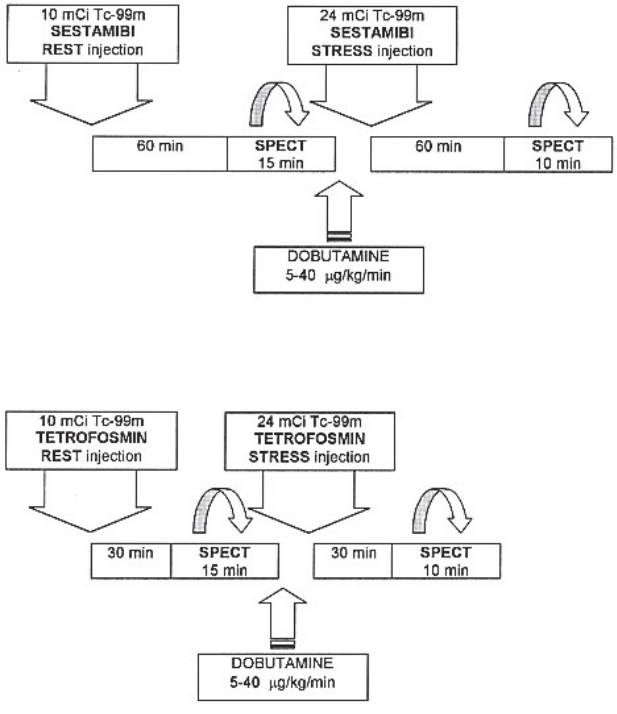

Fig. 1 Schematic representations of same day short rest-stress protocols for Tc-99m MIBI and TF studies.

Table 1 Clinical data and Tc-99m MIBI/TF-dobutamine stress test results

Pts. No.	Age (yrs)	Gender	MI	Aneurysm	Coronary angiography			Dobut. dose (μg/kg/min)		Dobut. time (min)		Peak double product (PDP)	
					LAD (%)	LCx (%)	RCA (%)	MIBI	TF	MIBI	TF	MIBI	TF
1	45	M	Ant	–	90	70	80	30	30	10	8	150.00	153.00
2	41	M	Ant	–	99	–	–	20	20	5	6	132.00	127.50
3	45	M	–	–	95	–	–	20	20	6	4	165.10	159.60
4	60	M	Ant	–	90	–	70	20	20	6	5	240.50	207.00
5	45	M	Ant	–	90	–	70	20	20	18	12	154.70	174.00
6	55	M	Ap, Ant	+	95	50	70	35	30	9	9	180.80	174.00
7	51	F	–	–	70	–	–	30	30	8	8	217.60	180.00
8	62	M	–	–	90	80	80	30	30	11	9	175.50	165.00
9	56	M	–	–	60	–	70	30	30	10	9	198.00	187.20
10	69	M	Ant	–	90	90	–	20	20	8	6	176.40	173.25
11	42	M	–	–	90	70	–	20	20	5	6	256.00	225.00
12	50	M	Ant	+	90	90	70	30	30	10	9	256.00	223.20
13	60	M	–	–	90	–	–	15	15	8	13	204.00	186.20
14	62	M	Inf	–	90	70	70	15	15	12	10	123.25	204.00
15	64	M	AS, Inf	–	70	99	99	10	10	10	8	168.00	178.35
16	54	M	Ant, Inf	–	90	–	99	15	15	15	15	144.00	136.95
17	53	M	–	–	–	–	–	10	10	12	14	133.00	145.00
18	52	M	–	–	–	–	–	10	10	8	5	120.00	132.00
19	56	F	–	–	–	–	–	10	15	6	14	133.90	153.00
Mean age: 53.8 ± 7.9 yrs				Lesion =	16	8	10	20.53 ± 8.15	20.53 ± 7.43	9.32 ± 3.37	8.95 ± 3.32	175.22 ± 43.33	172.85 ± 28.55

MI, myocardial infarction; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; Ant, anterior; Inf, inferior; AS, anteroseptal.

and calcium antagonists. Prior to the study, the physician explained the details to each patient individually. All patients gave informed consent before testing. This study protocol was based on the regulations of the hospital ethical committee.

Study Protocol: Studies were designed as a same day rest-stress protocol since the same day imaging protocol using a low dose rest study followed by a high dose stress study allows imaging with cationic complexes to be completed within a few hours.[1,3,8] MIBI SPECT imaging was performed first. Ten mCi (370 MBq) of MIBI was injected at rest condition, and 60 min after injection rest planar and SPECT images were acquired. After dobutamine infusion, 24 mCi (888 MBq) of MIBI was injected at the peak stress. Sixty min after injection stress planar and SPECT images were acquired. TF SPECT studies were performed one week after MIBI imaging in all patients. TF SPECT studies were performed using the same rest-stress radiotracer doses and dobutamine infusion doses as used for the MIBI studies. However, a 30 min waiting period was applied after the rest and stress injections before SPECT imaging for TF study. Total study time per patient was approximately 90 min for TF study, and approximately 150 min for MIBI study (Fig. 1).

Dobutamine Stress Protocol: Immediately after the rest SPECT imaging in both of the MIBI and TF studies, patients underwent dobutamine stress tests. Dobutamine was administered i.v. at incremental doses of 5, 10, 15, 20, 25, 30 and 40 μg/kg/min at 3 min intervals. Systolic and diastolic blood pressure, heart rate and 12 lead ECG were recorded during infusion and until the heart rate returned to <100 beats/min and all symptoms disappeared.[9,10–12] Criteria for termination of dobutamine infusion were: (1) angina or chest discomfort; (2) significant arrhythmia; (3) severe hypertension (systolic blood pressure ≥220 mmHg or diastolic blood pressure ≥110 mmHg or both); (4) decrease of the systolic blood pressure (20 mmHg or more); (5) heart rate of more than 85% of the predicted heart rate; (6) maximal dobutamine infusion dose rate (40 μg/kg/min); (7) significant ST segment depression on ECG (≥2 mm).[9,11–13] At the maximum tolerated dose of dobutamine, 24 mCi (888 MBq) of radiotracer was injected i.v., and dobutamine infusion was continued for an additional 1 min.

Image Acquisition, Processing and Analysis: SPECT imaging was performed using a dual head gamma camera (General Electric OPTIMA®, USA) equipped with low energy high-resolution parallel hole collimators and connected to a dedicated computer system (Starcam 4000i). SPECT images (64 projections) were obtained with a circular orbit over a 180° arc. Projections were acquired with a 64 × 64 matrix for 25 sec/projection for rest and 20 sec/projection for stress imaging. Tomographic reconstructions were obtained with filtered back projection and

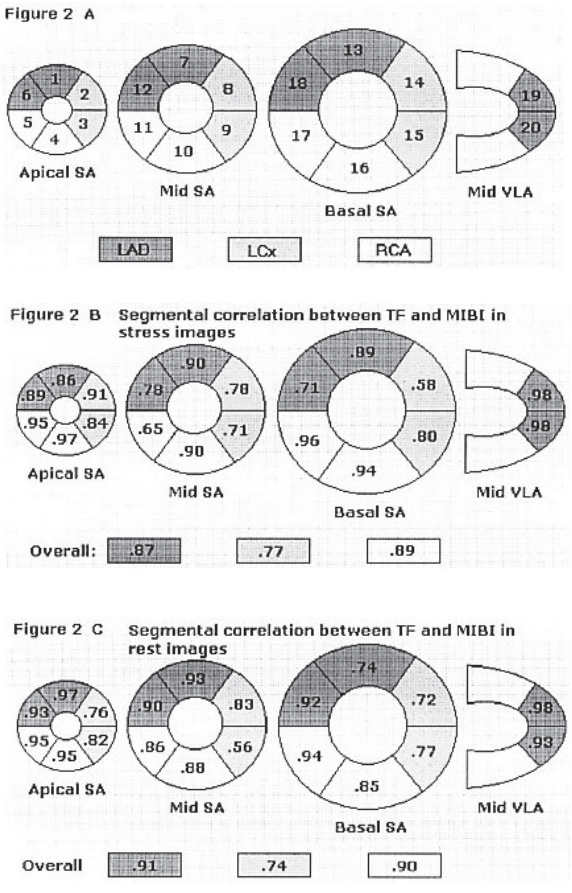

Fig. 2 A: Schematic representation of 20 segment-5 point scoring of apical-mid-basal short axis and vertical slices.[12,14–16] Segmental correlation between TF and MIBI in stress (B) and rest (C) images.

no attenuation correction. Images were processed using Ramp and Butterworth filters. Reconstructed tomographic slices were reoriented in the short, horizontal long and vertical long axes of the left ventricle for visual image interpretation.

To accurately calculate the heart-to-lung (H/Lu) and heart-to-liver (H/Li) activity ratios, and to compare with different imaging protocols, we used anterior planar images which included thorax and upper abdomen. These images were obtained for 5 minutes with a 256 × 256 matrix in all patients before SPECT imaging. The average counts per pixel of the box ROIs placed over liver and right lung and irregular ROIs placed over the left ventricle of the heart were used for calculating H/Lu and H/Li activity ratios. All ROI placements were done by the same physician.

Rest and stress tomographic slices were analyzed from apical-mid-basal short axis and apical vertical slices using 20 segments, 5-point scoring system (0 = normal uptake, 1 = mildly reduced, 2 = moderately reduced, 3 = severely reduced and 4 = absent uptake; 0–1 scores were considered normal, 2–4 scores were considered abnormal)[12,14–16] (Fig. 2A). Each segment on the stress slices was determined to be normal or abnormal according to its score. An abnormal segment was defined as reversible if there is an augmentation in segment activity at rest imaging. Regions were then interpreted as normal perfusion, stress induced perfusion defect, or fixed perfusion defect. An abnormal study was considered in the presence of a fixed or reversible perfusion defect. Data were interpreted by two experienced observers independently without prior knowledge of the clinical history or CA results of the patients. Any differences in interpretation were resolved by reaching consensus agreement in cases of contradictory segmental evaluation.

Statistical Analysis: The sensitivity, specificity and accuracy values of dobutamine stress MIBI and TF SPECT studies were obtained in the usual fashion. Hemodynamic data and H/Lu, H/Li activity ratios were presented as mean ± SD. Paired t-test and Pearson correlation analysis were used to analyze hemodynamic variables and H/Lu, H/Li activity ratios. H/Lu, H/Li activity ratios were also analyzed with Mann-Whitney U Test for CA positive and CA normal patients for stress and rest conditions. A p value <0.05 was considered statistically significant.

RESULTS

Significant increases in heart rate were detected for both studies during dobutamine infusion. The mean systolic blood pressure changed significantly in both MIBI and TF studies ($p < 0.001$, r: 0.80). There was no significant difference between post-infusion blood pressures in the two studies ($p > 0.5$). The mean diastolic blood pressure did not change significantly in MIBI study ($p > 0.05$), while a significant increase was detected in TF study ($p = 0.001$) (Table 2).

The hemodynamic responses to dobutamine infusions were similar in magnitude of cardiac stress for both studies. In this study group, after dobutamine infusions no significant differences were observed in levels of systolic blood pressures, diastolic blood pressures, peak double products, dobutamine doses, or infusion durations between MIBI and TF studies (Tables 1 and 2).

After dobutamine infusion, all side effects were mild, transient and reversed rapidly after termination of the infusion. The most frequent side effect was sense of palpitation during infusion, which resolved within several minutes after termination of the infusion [in 16 of 19 pts (84%)].

According to the statistical analysis of H/Lu and H/Li activity ratios, there was no significant difference between stress and rest H/Lu ratios for MIBI ($p > 0.05$) and TF ($p = 0.057$) studies, while a significant difference was found between stress and rest H/Li ratios for MIBI ($p = 0.02$) and TF ($p = 0.001$) studies. Additionally, there were no statistically significant differences in either H/Lu or H/Li ratios between MIBI and TF studies in stress and

Table 2 Hemodynamic changes during peak dobutamine stress

	MIBI		Tetrofosmin	
	Initial	Post-infusion	Initial	Post-infusion
Systolic blood pressure (mmHg)	142.11 ± 14.65 ($p < 0.001$,	157.63 ± 21.75* $r = 0.80$)	138.95 ± 14.68 ($p < 0.001$,	153.16 ± 11.69* $r = 0.80$) *$p > 0.1$
Diastolic blood pressure (mmHg)	87.11 ± 7.69 ($p > 0.05$)	90.79 ± 9.47**	85.26 ± 7.35 ($p = 0.001$)	90.79 ± 5.59** **$p > 0.5$
Mean dobutamine dose (μg/kg/min)	20.53 ± 8.15		20.53 ± 7.43 ($p = 1$, $r = 0.98$)	
Mean dobutamine infusion time (min)	9.32 ± 3.37		8.95 ± 3.32 ($p > 0.5$, $r = 0.60$)	
Peak double product (PDP)	175.22 ± 43.33		172.85 ± 28.55 ($p > 0.5$, $r = 0.80$)	

Table 3 Heart/Organ ratios

	MIBI (60 min post-injection)				Tetrofosmin (30 min post-injection)			
	Rest		Stress		Rest		Stress	
	H/Lung*	H/Liver**	H/Lung* +	H/Liver** #	H/Lung*	H/Liver**	H/Lung* +	H/Liver** #
Overall (Paired t-test)	2.34 ± 0.43 *$p > 0.1$	1.14 ± 0.41 **$p < 0.05$	2.26 ± 0.33	0.89 ± 0.26	2.26 ± 0.42 *$p > 0.05$	1.13 ± 0.35 **$p = 0.001$	2.12 ± 0.33 +$p > 0.05$	0.85 ± 0.26 #$p > 0.5$
CA positive pts.	2.27 ± 0.41	1.10 ± 0.41	2.26 ± 0.35	0.91 ± 0.28	2.20 ± 0.39	1.12 ± 0.37	2.10 ± 0.35	0.84 ± 0.28
CA negative pts. (Mann-Whitney U)	2.70 ± 0.44 ($p > 0.1$)	1.34 ± 0.41 ($p > 0.1$)	2.28 ± 0.21 ($p > 0.1$)	0.83 ± 0.19 ($p > 0.1$)	2.59 ± 0.55 ($p > 0.1$)	1.21 ± 0.18 ($p > 0.1$)	2.21 ± 0.29 ($p > 0.1$)	0.94 ± 0.16 ($p > 0.1$)

rest conditions ($p > 0.05$). There was no significant difference either in H/Lu or H/Li ratios for CA positive and CA normal patients for stress and rest conditions for both radiopharmaceuticals ($p > 0.1$) (Table 3). Although, the period between injection and imaging was shorter in TF study than MIBI, no significant difference could be found between H/Lu and H/Li ratios for the two radiopharmaceuticals.

High quality SPECT images were obtained for all patients in both studies. Totally 380 segments were analyzed from both stress and rest short axis and vertical long axis slices separately for each study. In TF study, stress perfusion defects were observed in 40.5% (segment score: 2–3–4) (154/380) while, normal perfusion was observed in 59.5% (segment score: 0–1) (226/380) of the investigated segments in stress images. Severe stress perfusion defects which had segment score: 3–4 were observed 23% (88/380) in stress images (Table 4A). In TF study, reversibility was seen in rest images in 59% (91/154) of segments which stress perfusion defect was observed (segment score: 2–3–4). Reversibility was seen in rest images in 55% (49/88) of segments which severe perfusion defects was observed at stress (segment score: 3–4). Partially reversibility was seen in 27% (42/154) of segments in which stress perfusion defect was observed (scores: 4→3, 4→2, 3→2), while 32% (49/154) of segments with stress perfusion defect (scores: 3→1, 2→1, 2→0) showed totally reversibility at rest images. Reverse perfusion pattern (scores: 0→1, 1→2, 2→3) was observed in 5% (21/380) of all segments in TF study (Table 4B). In MIBI study, stress perfusion defects were observed in 36.3% (segment score: 2–3–4) (138/380) while normal perfusion was observed in 63.7% (segment score: 0–1) (242/380) of the investigated segments in stress images. Severe stress perfusion defects which had segment score: 3–4 were observed 21% (80/380) in stress images (Table 4A). In MIBI study, reversibility was seen in rest images in 32% (44/138) of segments in which stress perfusion defect was observed (segment score: 2–3–4). Reversibility was seen in rest images in 25% (20/80) of segments in which severe perfusion defects were observed at stress (segment score: 3–4). Partially reversibility was seen in 12% (16/138) of segments in which stress perfusion defect was observed (scores: 4→3, 3→2), while 20% (28/138) of them showed totally reversibility (scores: 3→1, 2→1, 2→0) at rest images. Reverse perfusion pattern (scores: 0→1, 1→2, 2→3) was observed in 3% (11/380) of all segments in MIBI study (Table 4C).

A good correlation was found between segmental analyses for both studies. When we compared the segment

Table 4A

Segment scores	Tetrofosmin		MIBI	
	Stress	Rest	Stress	Rest
0	126	149	118	125
1	100	122	124	147
2	66	46	58	39
3	44	45	46	43
4	44	18	34	26
Total	380	380	380	380

Table 4B Reversibility at tetrofosmin

Stress segment scores	Rest segment scores				
	0	1	2	3	4
0		14			
1	23		4		
2	14	28		3	
3		7	16		
4			5	21	

Table 4C Reversibility at MIBI

Stress segment scores	Rest Segment Scores				
	0	1	2	3	4
0		7			
1	8		3		
2	2	22		1	
3		4	8		
4				8	

Table 4D

MIBI/Tetrofosmin	Matching segments at stress	Matching segments at rest
0/0	104 (89%)	121 (96.8%)
1/1	89 (71%)	110 (75.8%)
2/2	39 (63%)	26 (63%)
3/3	26 (57%)	31 (72%)
4/4	30 (88%)	16 (61.5%)
Total	288 (75.8%)	304 (80%)

scores in MIBI and TF studies for stress and rest; matching segments for all segment scores (0–4) were found as 75.8% (288/380) and 80% (304/380) in stress and rest images, respectively (Table 4D).

Overall sensitivity for the detection of CAD was calculated as 82%, specificity was 88%, and accuracy was 84% for MIBI study, while sensitivity, specificity and accuracy were calculated as 82%, 84% and 82% for TF study, respectively. Diagnostic accuracy results were similar for MIBI and TF studies.

There was a good correlation in segmental evaluation results in both studies. In MIBI and TF studies, when the same segments of all patients were compared, a good correlation was observed between stress images. When we evaluated this comparison according to coronary artery regions, in LAD region segmental correlation was found as r = 0.87. At the LAD region, the lowest correlation was found in segment number 18 (basal anteroseptal) (r = 0.71), and the highest correlation was found in segment number 19 (apical anterior) (r = 0.98). At the LCx region, segmental correlation was found as r = 0.77. In this region, the lowest correlation was found in segment number 14 (basal lateral) (r = 0.58), and the highest correlation was found in segment number 2 (apical lateral) (r = 0.91). At the RCA region, segmental correlation was found as r = 0.89. In this region, the lowest correlation was found in segment number 11 (mid inferoseptal) (r = 0.65), and the highest correlation was found in segment number 4 (apical inferior) (r = 0.97) (Fig. 2B).

There also was good segmental correlation between rest images in both of the studies. In rest images, in LAD region, segmental correlation was r = 0.91. In this region, the lowest correlation was found in segment number 13 (basal anterior) (r = 0.74), and the highest correlation was found in segment number 19 (apical anterior) (r = 0.98).

At the LCx region, segmental correlation was r = 0.74. In this region the lowest correlation was found in segment number 9 (mid lateral) (r = 0.56), and the highest correlation was found in segment number 8 (mid inferolateral) (r = 0.83). At the RCA region, the segmental correlation was r = 0.90. In this region, the lowest correlation was found in segment number 16 (basal inferior) (r = 0.85), and the highest correlation was found in segment number 4 (apical inferior) (r = 0.95) (Fig. 2C).

DISCUSSION

MIBI and TF lipophylic cationic tracers are currently the most widely used perfusion agents in clinical practice for the evaluation of CAD. The rest-stress protocol sequence was selected for this study because the same day imaging protocol using a low dose rest followed by a high dose stress allows imaging to be completed within a few hours.[3,8] Additionally, both real rest imaging on the rest and the imaging of the high dose on the stress give optimal imaging of stress-induced defects and is reported to improve detection of reversibility.[17,18]

We used same day rest-dobutamine stress protocols to be performed within 90 min for TF study and 150 min for MIBI study and evaluated their diagnostic accuracies (Fig. 1). Although TF study was completed in a shorter time than MIBI, this clinical study showed comparable diagnostic performance for the detection of CAD between

MIBI and TF. It should be noted that both MIBI and TF showed similar perfusion defects and good segmental correlation during dobutamine stress, but at rest, TF study showed better reversibility degree especially in segments with "severe" and "no uptake" perfusion defects than MIBI.

Dobutamine can be used safely as a valuable alternative agent to vasodilator agents in conjunction with myocardial perfusion SPECT imaging. In our study, we used dobutamine as a stress agent in patients with suspected or known CAD who had limitations to perform treadmill exercise or pharmacological vasodilator stress. In our study, because of the clinical characteristics of the patients (most of the patients had a history of MI) tolerable and safe dobutamine doses were applied. The dobutamine stress protocol was well tolerated by all patients, and no serious side effects were observed during or after either study.

We applied similar, even the same dobutamine doses and periods to patients to get identical stress levels in both of the studies. There was a very good correlation and no significant difference between the dobutamine doses applied to the patients ($r = 0.981$, $p = 1.0$), and also between dobutamine periods there was a good correlation and no significant difference ($r = 0.592$, $p = 0.60$). For head to head comparison of different radiopharmaceutical uptakes, identical stress levels are required, with good correlation and no significant difference found between peak double product (PDP) MIBI and PDP TF in our study ($r = 0.80$, $p = 0.70$). In MIBI and TF studies, statistically significant systolic blood pressure increment was found before and after dobutamine infusion ($p < 0.001$). And also between both studies, good correlation but no significant difference was found in systolic blood pressures after dobutamine infusion ($r = 0.806$, $p = 0.185$). According to these hemodynamic findings, it was agreed that appropriate and identical cardiac stress levels were applied to the patients during the two studies (Table 2).

In human studies, it has been reported that the myocardial uptake for MIBI is 1% of the injected dose after rest injection and 1.4% after exercise injection at 1 hr post injection[2,19] and approximately 1.2% of the administered dose of TF is taken up by the myocardium at rest as well as during exercise.[2,20]

Myocardial uptake of MIBI and TF is thought to be dependent on the cell and mitochondrial membrane potential and seems to be related to the Na^+-H^+ antiporter system.[7,21] Between 70–90% of MIBI is trapped within the mitochondria and only a small amount of the retained tracer remains in the cytosol. On the other hand, about 40% of the retained TF is accumulated in the mitochondria, and the rest remains in the cytosol.[7,21] Despite the difference in fractional mitochondrial retention for MIBI and TF, Schaefer et al. reported that the initial cellular uptake of these tracers should be the same.[7] Although it has been reported that both have similar properties, MIBI seems to be more suitable than TF for the detection of myocardial reversibility and viability since it accumulates mostly inside the mitochondria where the washout is much slower than the cytosol, this conflicts with our results. We think that this situation is related to the faster clearance of TF from the extra-cardiac organs, and application of rest study first with low dose for real rest imaging. This may also be related to the short waiting period between rest and stress acquisitions, which may reduce the undesirable high intestinal activity and prevent misinterpretations especially in evaluation of the inferior wall. For the imaging protocol in MIBI and TF studies, injection-SPECT acquisition periods could be equal but, because of TF's known rapid extra-cardiac clearance in combination with minimal myocardial washout, SPECT acquisitions were started 30 min after the injection. Additionally, no waiting period was applied between rest-stress studies in both studies. For these two reasons we thought that undesirable high intestinal activity could be reduced in images and misinterpretations could be prevented. Although different waiting periods were applied in both of the studies, Tc-99m MIBI and TF SPECT studies did not show any significant difference in diagnostic accuracy with the same day short rest-dobutamine stress protocol. However, we found that reversibility can be shown better with TF than MIBI according to our study protocol.

When compared, H/Lu and H/Li ratios obtained in a TF study done by Jain et al. on 20 patients with same day stress-rest protocol and 4 hrs waiting period, our ratios were similar[1] (Table 3).

This study has several noteworthy limitations. The number of patients included was relatively small. In addition to this, most of the patients in the study group were male and only two female, which have normal CA, could be included in the study [17 male (90%) and 2 female (10%)]. The possibility of undifferentiation of breast attenuation artifacts and real perfusion defects was minimized because of the limited number of female patients and lifting up their left breasts with tape during imaging. Because of this in our study we thought that there was no significant limitation by breast attenuation artifacts.

Further clinical studies with a larger number of patients are required for determination of the exact role of same day short rest-dobutamine stress myocardial perfusion SPECT with TF and MIBI in the myocardial perfusion abnormalities in patients with suspected or known CAD who had limitations to perform treadmill exercise or pharmacological vasodilator stress.

CONCLUSION

The same day short rest-dobutamine stress protocol is sensitive and effective in the diagnosis of CAD in patients who had limitations to perform treadmill exercise or pharmacological vasodilator stress for both radiopharmaceuticals. According to our results, rest-dobutamine

stress TF protocol provides a shorter study time (especially in nuclear cardiology departments with a high number of patients), similar accuracy as well as sensitivity and specificity for the identification of patients with CAD in defect detection, when compared to MIBI. When we take into consideration the high diagnostic accuracy of the study, we think that no waiting period is absolutely necessary between the rest-stress protocol studies where both radiopharmaceuticals were used. MIBI and TF have shown similar perfusion defects and good segmental correlation during dobutamine stress with same quality images. Both radiopharmaceuticals may be acceptable with this imaging protocol. Besides this, TF study showed better reversibility degree (55%) in a shorter time when compared to MIBI study (25%) in perfusion defects (especially in segments with severely decreased perfusion or no uptake).

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