Muscle Perfusion with Technetium-MIBI in Lower Extremity Peripheral Arterial Diseases

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There have been several methods utilized in the diagnosis or assessment of medical or surgical treatments of peripheral arterial diseases. In this study, the diagnostic value of a new tracer: ^{99m}Tc-methoxy-isobutyl-isonitrile (MIBI) has been demonstrated in patients with leg claudication. We successively performed muscle perfusion scans in 6 normals and 18 patients with claudication pain during rest and after exercise on the same day. Muscle perfusion abnormalities in all patients were consistent with the defects in the arteries of the affected limbs. The results show that this is a simple and accurate diagnostic procedure and superior to those that have been previously used.

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It is important to determine the healing potential of ischemic ulcers of the lower extremities in order to prevent premature amputation or unnecessarily prolonged hospitalization (*1*). Contrast angiography provides good anatomic information of the large arteries, but is not sufficient for the small vessels (*2*). The utility of digital subtraction angiography and magnetic resonance imaging is still under evaluation for these particular ischemic diseases.

Radionuclide studies, on the other hand, show perfusion in tissue. For this purpose, radiopharmaceuticals may be classified into two groups: particulates, such as macroaggregates labeled with ^{99m}Tc or ^{113m}In; and non-particulates, ^{99m}Tc-labeled serum albumin or red blood cells, ^{113m}In-transferrin, ^{99m}Tc-0$_4$, ^{99m}Tc-DTPA, ^{99m}Tc-PYP, and those radionuclides taken up by the muscles directly proportional to their perfusion, such as 43K, 24Na, 201T1 (*3–6*); and radiopharmaceuticals that show free diffusion and clearance from tissues according to the blood flow such as 133Xe, 131I-iodoantipyrene (*7–10*).

All the methods mentioned above have several major limitations; labeled particles require arterial injection, which is relatively invasive; and the principle radiations of 131I, 133Xe and 201T1 are not optimal for Anger camera imaging, and if more than one vascular territory is being investigated, ^{133}Xe requires multiple injections.

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A new product, ^{99m}Tc-MIBI (methoxy-isobutyl-isonitrile), which was developed primarily as a myocardial perfusion agent, has also proven valuable for skeletal muscle perfusion studies (*11,12*). Technetium has superior imaging and dosimetry characteristics in comparison to other radionuclides and is readily available in nuclear medicine labs to reconstitute with MIBI. This agent enters skeletal muscle tissue by passive diffusion and remains there for a prolonged period of time due to binding to intracellular protein and a relatively small amount of redistribution (*12*).

This study reports the patterns of perfusion in lower extremities recorded with MIBI in relation to the blood supply.

MATERIALS AND METHODS

Muscle perfusion of the lower extremities was examined in 24 patients. Six patients (mean age of 52.8 yr (43–59), 5 males, 1 female) referred for myocardial perfusion scintigraphy, with a low probability of coronary heart disease and negative ECG tests served as the control group. The control subjects had no physical signs or subjective complaints of peripheral arterial disease in the lower extremities. The remaining 18 patients (17 males, 1 female, mean age 56.5 yr) were symptomatic and seven described bilateral and 11 described unilateral claudication pain. Six of these patients had diabetes mellitus and 12 had Buerger's disease. Three patients had a history of lumbar sympathetic ganglionectomy operation. Contrast angiography supported the finding of peripheral arterial disease in seven patients.

For skeletal muscle scintigraphy, ^{99m}Tc-MIBI (Institute of Isotopes, Budapest, Hungary) was prepared according to the manufacturer's instructions and used after radiochemical purity was measured. Following intravenous injection of 259 MBq of ^{99m}Tc-MIBI during rest, the subjects were given 0.25 liters of fatty milk drink and recalled for imaging 45–60 min later.

A Siemens Basicam gamma camera (Siemens Medical Systems, Des Plaines, IL) detector, fitted with a low-energy, high-resolution collimator, positioned posteriorly, first over both thighs and then over both calves, was used to acquire word type images (300 sec, 64 × 64 matrix) onto a Microdelta computer (Siemens Medical Systems).

On the same day, treadmill exercise was performed up to 85% of maximal predicted heart rate due to age in normals or until the onset of symptoms in patients with arterial disease. Technetium-MIBI (999 MBq) was injected intravenously and exercise was terminated after 1 min. At this time, all subjects were given 0.25 liters of fatty milk drink and were imaged according to the criteria previously discussed.

TABLE 1
Results of Numeric Analysis for Normals

	LT/RT		LC/RC		$\frac{\sqrt{E^2 - I^2}}{E + I}$				$\frac{E - I}{E}$			
Patient	Rest	Stress	Rest	Stress	LT	RT	LC	RC	LT	RT	LC	RC
1	1.08	0.92	1.08	0.95	0.51	0.57	0.52	0.57	0.41	0.50	0.43	0.50
2	1.00	1.00	1.00	0.91	0.60	0.60	0.57	0.61	0.54	0.54	0.50	0.55
3	1.25	1.00	1.00	1.00	0.71	0.72	0.62	0.62	0.62	0.69	0.56	0.56
4	1.08	1.00	1.00	1.04	0.59	0.62	0.68	0.67	0.52	0.56	0.64	0.63
5	1.00	1.15	1.00	1.11	0.76	0.73	0.82	0.80	0.73	0.69	0.80	0.78
6	1.00	1.00	1.00	1.00	0.61	0.61	0.64	0.64	0.53	0.53	0.58	0.58

LT/RT = left thigh/right thigh; LC/RC = left calf/right calf; E = Exercise study average counts; and I = Initial rest study average counts.

All images were analyzed in a blinded fashion 1 wk later. Rest and stress studies of each subject were normalized to a constant (e.g., 255) and counts within the selected rectangular region of interests (ROIs) covering most of the muscle groups on each set of images of rest and stress studies, chosen symmetrically, then were calculated. Left-to-right ratios of counts for both thighs (LT/RT) and calves (LC/RC) during rest and stress were obtained (Tables 1 and 2). After checking to see if the count ratios approached unity, two equations were derived:

$$\frac{\sqrt{E^2 - I^2}}{E + I} \qquad \text{Eq. 1}$$

$$\frac{E - I}{E} \qquad \text{Eq. 2}$$

where E-average ROI counts of exercise and I-average ROI counts of initial rest studies were used to express the perfusion difference between rest and exercise states and to identify the magnitude of the hyperemic response to a physical activity.

Intraobserver variations were assessed by reanalyzing all data 1 wk later.

RESULTS

Visual assessment of the images showed the integrity of the blood supply to the leg muscles during rest and exercise. In normals, there was a symmetrical distribution of ^{99m}Tc-MIBI during both rest and after exercise (Fig. 1). The left-to-right count ratios in normals approached to unity as Siegel et al. (*5*) and Seder et al. (*6*) observed previously (Table 1), reflecting the symmetrical perfusion on both legs (mean ratio 1.02 ± 0.7).

On the other hand, in the patients with arterial disease,

TABLE 2
Results of Numeric Analysis for Patients

		LT/RT*		LC/RC*		$\frac{\sqrt{E^2 - I^2}}{E + I}$*				$\frac{E - I}{E}$*			
Patient no.	S	Rest	Stress	Rest	Stress	LT	RT	LC	RC	LT	RT	LC	RC
1	R, L	0.93	0.96	0.90	1.09	0.54	0.52	0.57	0.49	0.45	0.43	0.49	0.39
2	L	1.00	0.90	0.67	0.63	0.71	0.73	0.65	0.67	0.67	0.70	0.60	0.63
3	R	1.57	1.44	1.67	1.20	0.29	0.35	0.30	0.50	0.11	0.22	0.16	0.40
4	R	0.96	1.00	1.15	1.20	0.23	0.18	0.23	0.19	0.10	0.07	0.11	0.07
5	L	1.00	0.91	0.83	0.84	0.69	0.71	0.72	0.72	0.65	0.68	0.68	0.68
6	L	1.00	0.98	1.06	0.82	0.40	0.41	0.31	0.47	0.28	0.29	0.17	0.29
7	L	1.00	0.93	1.33	0.71	0.85	0.87	0.80	0.89	0.85	0.86	0.78	0.88
8	L	1.06	1.02	0.87	0.88	0.72	0.72	0.80	0.80	0.67	0.69	0.78	0.78
9	L	0.91	0.84	0.80	0.75	0.77	0.79	0.76	0.78	0.74	0.76	0.74	0.76
10	R	1.15	1.33	1.25	1.38	0.86	0.84	0.88	0.87	0.85	0.83	0.87	0.86
11	L, R	1.04	0.96	1.39	1.01	0.25	0.32	0.00	0.39	0.12	0.18	0.00	0.27
12	R	1.24	1.43	1.53	2.06	0.90	0.89	0.82	0.77	0.90	0.88	0.81	0.74
13	L, R	1.10	1.19	1.09	1.30	0.35	0.31	0.01	0.00	0.23	0.17	0.01	0.00
14	L, R	0.93	0.81	0.97	0.88	0.00	0.00	0.08	0.23	0.00	0.00	0.01	0.10
15	L	0.82	0.85	0.70	0.68	0.17	0.12	0.31	0.34	0.06	0.03	0.18	0.21
16	L, R	0.97	0.98	0.84	0.98	0.56	0.56	0.54	0.46	0.48	0.47	0.45	0.35
17	L, R	0.93	0.99	0.96	0.80	0.40	0.36	0.31	0.43	0.27	0.23	0.18	0.31
18	L, R	0.95	0.99	0.97	0.92	0.36	0.34	0.12	0.21	0.24	0.21	0.03	0.08

* See Table 1 for definitions. S = symptom's side.

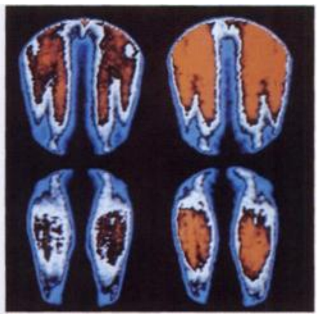

FIGURE 1. Rest (left) and stress (right) studies showing an even distribution of ^{99m}Tc-MIBI in lower extremity muscles of a normal case (Table 2, Patient 2).

FIGURE 3. Rest (left) and stress (right) studies of a patient with right-sided occlusive disease and contralateral circulation (Table 2, Patient 2).

it was easy to see the uptake difference between the two sides visually. These findings were subsequently supported by numerical analysis. In patients with bilateral disease, it was seen that this ratio approached unity, similar to results for normals (Table 2, Patients 1, 11, 14, 16, 17, 18). However, numerical analysis in these patients revealed a decrease in ^{99m}Tc-MIBI uptake in both legs.

The scintigraphic results of this study suggest three patterns of occlusive arterial disease:

1. In three patients, the rest study showed an increase in counts on the side of occlusion, probably due to maximal dilatation. Exercise did not increase perfusion on that side, but a significant increase in counts was seen on the other side (Table 2, Patients 6, 7, 11). These findings were interpreted as resting compensatory hyperemia (Fig. 2).

2. In certain patients with proven collateral circulation by contrast angiography (Table 2, Patient 3), while the counts on the same side with arterial occlusion were low during resting, they increased by exercise due to the collateral blood supply (Fig. 3).

3. Patients without any collaterals showed a perfusion difference between two lower extremities during rest, which increased after physical exercise (Fig. 4).

In normals, all data obtained from Equations 1 and 2 appeared to be symmetrical for both extremities, and the high and calf values were similar (Table 1).

In patients with occlusive arterial disease, the data were in accordance with the clinical findings. Also, it is worth noting that when there was an occlusion at the poplitea level, the calf values were abnormal, whereas the thigh values would be normal (e.g., Patient 8 in Table 2).

DISCUSSION

The main purpose of this study was to show the use of ^{99m}Tc-MIBI in skeletal muscle perfusion scintigraphy to identify arterial disease of the lower extremities. Because of favorable imaging characteristics, 140-keV peak energy, and availability in nuclear medicine departments, ^{99m}Tc-MIBI is superior to other radionuclide techniques.

Our results are in agreement with the results of Seder et al. and Dhekne et al. (*6,12*). The blood clearance half-time of this radiopharmaceutical is 2.18 min at rest and 2.13 min after exercise. This indicates a quick washout without a significant redistribution. The main routes of excretion are the hepatobiliary and renal systems (*12*). To facilitate high excretion rates, it is favorable to use any kind of fatty meal before imaging. Our study showed a stable uptake of radiopharmaceutical in the skeletal muscle even after 24 hr.

The small difference between the mean ages of the two groups studied eliminated the possibility of the dependence to age factors in the distribution of the radiopharmaceutical throughout the muscles.

FIGURE 2. Rest (left) and stress (right) studies of a patient with left-sided occlusive disease showing resting compensatory hyperemia on the left calf (Table 2, Patient 6).

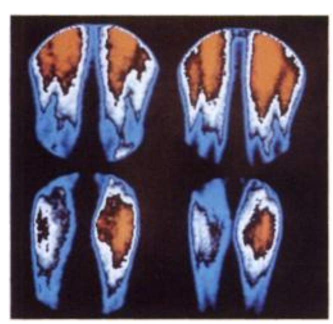

FIGURE 4. Rest (left) and stress (right) studies of a patient with a left-sided occlusive disease without any collateral circulation (Table 2, Patient 2).

It is known that claudication pain occurs in muscles without enough blood supply in accordance with increasing exercise. We assume that an asymmetrical distribution of ^{99m}Tc-MIBI seen as the lower uptake on the affected extremity is an indication of the lack of perfusion. On the other hand, in normal cases, the distribution of ^{99m}Tc-MIBI is symmetrical and its uptake increases in accordance with exercise.

Another advantage of this examination method is imaging of the myocardium without further preparation in the same setting, which is very useful since coronary and peripheral arterial diseases are frequently seen in the same patient.

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