Two-day stress-rest lower limbs perfusion scan in patients referred for myocardial perfusion imaging

Original Article

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ABSTRACT

Introduction: Peripheral Vascular Disease (PVD) is a major cause of morbidity and is associated with Coronary Artery Disease (CAD). We aimed to perform Lower Limb Perfusion Scan (LLPS) in patients referred for Myocardial Perfusion Imaging (MPI) and estimate prevalence of PVD in subgroups with normal and abnormal MPI results. We also compared quantitative indices of LLPS in patients with and without abnormal MPI results with semi-quantitative QPS indices.

Methods: 120 patients referred for MPI entered the study. Exercise or dipyridamole infusion was used as stress modality. After ^{99m}Tc-MIBI injection at peak stress, whole body posterior views and planar images from thighs and calves were obtained. Gated MPI was done subsequently. Rest phase was performed the following day. LLPS was analyzed visually and quantitatively.

Results: In patients with abnormal and normal MPI results, LLPS revealed 22.58% and 1.92% prevalence of PVD in exercise subgroup (P-Value=0.004) and 50.00% and 10.52% in dipyridamole subgroup (P-Value= 0.013), respectively. Both of these different prevalence were statistically significant. In exercise subgroup, mean ranks of Stress Index (I_s) for all lower limb regions were statistically significantly greater in patients with normal MPI result. Also, among patients who had ischemia in exercise-rest MPI, negative correlations were seen between Is and Rest Index (I_r) of all regions and QPS quantitative indices.

Conclusion: LLPS with ^{99m}Tc-MIBI, combined with MPI is a feasible method to detect lower limbs ischemia, especially in patients with abnormal MPI results. Correlating quantitative indices of LLPS with MPI-QPS also reflect coexistence of CAD and PVD.

Key words: Lower extremity; Myocardial perfusion imaging; ^{99m}Tc-MIBI

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INTRODUCTION

Peripheral Arterial Disease (PAD), which can be accompanied by intermittent claudication or rest pain, may necessitate revascularization procedures and seriously diminish health-related quality of life. Even when asymptomatic, PAD may decrease mobility and bone mineral density [1, 2, 4, 5] and is a strong predictor of subsequent cardiovascular disease (CVD) and mortality [3, 6, 7].

Peripheral Vascular Disease (PVD) affects approximately 8 million Americans [8] and an estimated 10% of the worldwide population [9], with increasing prevalence in older individuals [10].

Several techniques have been used for the evaluation and detection of PVD including ankle–brachial indices, duplex ultrasound, MR imaging, CT angiography, SPECT and PET imaging [11].

Although anatomical imaging provide anatomical information about large vessels, information about the hemodynamic significance of borderline lesions, small vessel disease or the adequacy of collateral flow is difficult to obtain [12]. Nuclear imaging approaches with SPECT and PET are the primary nuclear imaging modalities. The recent emergence of hybrid SPECT/CT and PET/CT systems has allowed the fusion of high-sensitivity SPECT and PET imaging with high-resolution anatomic imaging to optimally localize and quantify radiotracer uptake [13, 14].

Radionuclide studies show perfusion in tissue. For this purpose, different radiopharmaceuticals have been applied (particulates and non-particulates radiopharmaceuticals labeled with ^{99m}TcO4 or ^{111}In), radiotracers taken up by the muscles directly proportional to their perfusion, such as ^{43}K, ^{24}Na, ^{201}T1 [15-18] and radiopharmaceuticals that show free diffusion and clearance from tissues according to the blood flow such as ^{133}Xe and ^{131}I-iodoantipyrine [19-22].

All the radiopharmaceuticals mentioned above have several major limitations. Labeled particles require arterial injection, which is relatively invasive; and the principle radiations of ^{131}I, ^{l33}Xe and ^{20l} Tl are not optimal for Anger camera imaging, and if more than one vascular territory is being investigated, ^{133}Xe requires multiple injections. On the other hand, ^{99m}Tc-MIBI (hexakis-2-methoxy-isobutyl-isonitrile), which was developed primarily as a myocardial perfusion agent, has also proven valuable for skeletal muscle perfusion studies [23, 24]. Technetium has superior imaging and dosimetry characteristics in comparison to other radionuclides and is readily available in nuclear medicine labs to reconstitute with ^{99m}Tc-MIBI. This agent enters skeletal muscle tissue by passive diffusion and remains there for a prolonged period of time due to binding to intracellular proteins [24]. ^{99m}Tc-labeled compounds demonstrate little redistribution, allowing for injections during treadmill exercise and measurement of peak exercise perfusion at a delayed imaging time. Biodistribution and kinetics of the ^{99m}Tc-labeled compounds make them possible to perform lower extremity perfusion measurements in combination with MPI.

PAD has a meaningful association with CAD. After 38 years of follow-up, the Framingham Heart Study showed that the risk of developing intermittent claudication was increased by associated coronary heart disease and diabetes [25].

We hypothesized that in patients referred for cardiac scintigraphy as a means of CAD diagnosis or risk stratification, additional information might be obtained about presence, extent and severity of possible ischemia of the lower limbs if ^{99m}Tc-sestamibi studies were extended for investigation of perfusion in these regions. Actually, patients referred for MPI are good candidates for lower limb perfusion assessment. Hence, we aimed to perform lower limb scintigraphy in these patients and estimate prevalence of PVD in subgroups with normal and abnormal MPI results. We also aimed to compare quantitative indices of lower limb scan in patients with and without abnormal MPI results with semi-quantitative indices of MPI as provided by Cedars-Sinai QPS-QGS software programs.

METHODS

Study population

Scintigraphy of lower limbs perfusion was performed in 120 patients (56 men and 64 women), mean age of 59.24 ± 10.12 years, with intermediate pre-test probability of CAD according to Diamond-Forrester criteria [26] who were referred for MPI. Written informed consent for lower extremity perfusion scintigraphy was obtained from all participants.

Patient preparation

For myocardial perfusion imaging all patients were instructed to fast at least 4 hours before the study. Possible interfering medications with dipyridamole study mainly xanthine containing drugs were stopped 48 hours before the stress phase. Also caffeine containing foods and beverages were avoided for at least 24 hours. Patients were asked to discontinue long-acting nitrates for 12 hours and Ca-blockers and beta-blockers for 48-72 hours prior to exercise phase of the study.

Stress protocol

Exercise or dipyridamole infusion was used as the stress modality. For exercise protocol, all patients

performed symptom-limited treadmill exercise with cardiac monitoring. Patients exercised according to the Bruce protocol, or a low-level modification of the protocol. 740-1110MBq of ^{99m}Tc-MIBI were injected at peak exercise, and patients were asked to continue exercise for additional two minutes. For myocardial pharmacologic stress testing in patients who were not able to exercise, 0.56 mg/kg dipyridamole was infused within 4 min in the fasting state. 3-5 minutes later, ^{99m}Tc-MIBI was injected. The ECG was continuously monitored, and blood pressure was measured at 2-min intervals. Side-effects were recorded.

Image acquisition sequence

Immediately after exercise and 30 minutes after dipyridamole infusion, the patients were placed supine on the imaging table (Siemens, Symbia, T2 Series® Erlangen, Germany) and whole body posterior views were obtained with the scan speed of 40 cm/min. Then, planar images from 4 regions (right and left thighs and right and left calves) were obtained for 5 minutes from thighs and calves regions separately.

A low-energy high-resolution collimator equipped with large FOV gamma camera with a 20% energy window setting, centered at 140 keV and a 256×256 matrix were used for acquisition. After the completion of lower limbs scanning, gated MPI was done subsequently with SPECT-CT gamma camera. All patients imaged with the same rotating dual-head gamma camera for both the stress and rest phases. Two heads were placed in an L-Shaped configuration. AC and NAC acquisitions were obtained, using a low-energy high-resolution collimator in a 180-degree non-circular orbit from 45-degree right anterior oblique to 45-degree left posterior oblique in the step and shoot mode (32 projections, 25 seconds per projection) and gating at 8 frames/ cardiac cycle.

A 64×64 matrix was used for MPI acquisition. For the CT acquisition, tube current and voltage were 13mA and 130 kV, respectively. All patients were placed in the supine position with arms over their heads. CT acquisition was obtained first while the patient was asked to breathe normally. Images were processed with Iterative Reconstruction algorithm, using 6 iterations and 4 subsets. For the quantification of data, Quantitative Perfusion SPECT-Quantitative Gated SPECT (QPSQGS) (Cedars Sinai, Los Angeles, California) software program was used. Two expert nuclear medicine physicians interpreted both myocardial perfusion scans and lower limbs perfusion scintigraphies independently, without knowledge of patient's clinical data and results of the other study.

Analysis

Only the posterior views were used for analysis. Rectangular regions of interest of equal size were drawn around the whole body, buttocks, thighs, and calves.

No correction was made for background activity, which was negligible. Total counts in each region were determined by computer and expressed as a percentage of whole body activity.

Quantitative parameters [Stress Index (I_s), Rest Index (I_r), Symmetric Index (I_{sym}) and Perfusion Reserve (PR) for each four Regions of Interest (ROIs) were then calculated:

I_s = "Total counts in the thigh or calf in the stress phase" divided by "Total whole body stress counts".

I_r = "Total counts in the thigh or calf in the rest phase" divided by "Total whole body rest counts".

I_{sym} thighs = "Total counts in the right thigh in the stress phase" divided by "Total counts in the left thigh in the stress phase".

I_{sym} calves = "Total counts in the right calf in the stress phase" divided by "Total counts in the left calf in the stress phase".

Perfusion Reserve = "Total counts in the thigh or calf in the stress phase" minus "Total counts in the same region in the rest phase" divided by "Total calf in the same region in the rest phase".

Statistical analysis

All data were analyzed using a Statistical Package for Social Science (SPSS Inc. ver. 22). Kolmogorov-Smirnov test was performed to evaluate normal distribution of quantitative variables.

For comparison of mean values, Student's Independent Samples T-test was used for variables with normal distribution and Mann-Whitney U test was performed for variables with non-normal distributions.

Pearson's and Spearman's rho correlation coefficients were attributed to normally distributed and non-normally distributed variables, respectively. Chi-square test was performed for comparison of qualitative variables between two groups. Probability (P) values <0.05 were considered significant.

RESULTS

Demographic characteristics and clinical data in both exercise and dipyridamole subgroups are presented in Tables 1 and 2, respectively. As it can be inferred from tables, there were no statistically significant difference between age, sex, BMI, circumferences of 4 ROIs, claudication percentage, exercise Metabolic equivalents (METs) or dipyridamole complication percentage between two groups with normal and abnormal MPI results, neither for exercise nor for dipyridamole stress subgroups.

Tables 3 and 4 show results of visual assessment and quantitative indices of lower limbs perfusion scintigraphy in patients with two-day Exercise-Rest and Dipyridamole-Rest MPI protocols, respectively, calculated separately in subgroups with normal and abnormal MPI results.

Table 1: Demographic and exercise characteristics of patients underwent two—day Exercise-Rest MPI protocol, calculated separately in subgroups with normal and abnormal MPI results.

	Normal MPI Result	Abnormal MPI Result	P-Value
Number of Patients	52	31	
Age (Mean± SD)(years)	57.48 ± 10.61	60.81 ± 10.52	0.170
Sex (%Male)	44.23 %	64.51 %	0.111
BMI(Mean ± SD) (gr/cm^2)	27.22 ± 5.82	25.27 ± 4.16	0.122
Circumference Rt Th (Mean ± SD) (cm)	45.31 ± 9.71	45.97 ± 17.18	0.892
Circumference Lt Th (Mean ± SD) (cm)	45.12 ± 10.07	45.87 ± 17.69	0.881
Circumference Rt Cf (Mean ± SD) (cm)	35.48 ± 4.21	33.37 ± 5.33	0.194
Circumference Lt Cf (Mean ± SD) (cm)	35.41 ± 4.10	33.13 ± 5.60	0.177
METs (Mean Rank)	38.82	46.15	0.102
History of Claudication (%)	38.46 %	51.61 %	0.262

MPI: Myocardial Perfusion Imaging; SD: Standard Deviation; BMI: Body Mass Index; Rt Th: Right Thigh; Lt Th: Left Thigh; Rt Cf: Right Calf; Lt Cf: Left Calf; METs: Metabolic equivalents.

Table 2: Demographic characteristics of patients underwent two—day Dipyridamole-Rest MPI protocol, calculated separately in subgroups with normal and abnormal MPI results.

	Normal MPI Result	Abnormal MPI Result	P-Value
Number of Patients	19	18	
Age (Mean± SD)(years)	59.21 ± 7.55	61.67 ± 10.17	0.413
Sex (%Male)	31.58 %	38.89 %	0.737
BMI(Mean ± SD) (gr/cm^2)	30.92 ± 5.62	29.07 ± 5.82	0.331
Circumference Rt Th (Mean ± SD) (cm)	55.94 ± 15.20	45.27 ± 5.35	0.072
Circumference Lt Th (Mean ± SD) (cm)	55.11 ± 15.44	45.87 ± 5.22	0.116
Circumference Rt Cf (Mean ± SD) (cm)	35.67 ± 4.61	34.57 ± 4.60	0.579
Circumference Lt Cf (Mean ± SD) (cm)	34.44 ± 4.10	34.37 ± 4.03	0.964
Dipyridamole Complications (%)	61.11 %	70.59 %	0.725
History of Claudication (%)	62.50 %	93.33 %	0.083

MPI: Myocardial Perfusion Imaging; SD: Standard Deviation; BMI: Body Mass Index; Rt Th: Right Thigh; Lt Th: Left Thigh; Rt Cf: Right Calf; Lt Cf: Left Calf.

Table 3: Visual assessment and quantitative indices of lower limbs perfusion scintigraphy in patients with two-day Exercise-Rest MPI protocol, calculated separately in subgroups with normal and abnormal MPI results.

	Normal MPI Result	Abnormal MPI Result	P-Value
Lower limbs ischemia (%)	1.92 %	22.58 %	0.004
I_S Rt Th*	44.30	30.22	0.007
I_S Lt Th*	43.29	31.90	0.030
I_S Rt Cf*	43.33	30.67	0.015
I_S Lt Cf*	43.56	31.45	0.021
I_r Rt Th*	38.18	39.02	0.873
I_r Lt Th*	38.47	38.55	0.987
I_r Rt Cf*	37.27	40.50	0.535
I_r Lt Cf*	39.19	37.38	0.728
I_{sym} Thighs*	36.69	42.83	0.243
I_{syn} Calves*	38.68	38.21	0.928
PR Rt Th*	41.37	33.84	0.149
PR Lt Th*	40.57	35.14	0.297
PR Rt Cf#	0.703	0.505	0.151
PR Lt Cf#	0.702	0.537	0.273

* Mean Rank of Mann-Whitney U Test; # Mean values of Independent T-Test; MPI: Myocardial Perfusion Imaging; Rt Th: Right Thigh; Lt Th: Left Thigh; Rt Cf: Right Calf; Lt Cf: Left Calf; I_s=Stress Index; I_r= Rest Index; I_{sym}= Symmetric Index; PR=Perfusion Reserve.

Table 4: Visual assessment and quantitative indices of lower limbs perfusion scintigraphy in patients with two-day Dipyridamole-Rest MPI protocol, calculated separately in subgroups with normal and abnormal MPI results.

	Normal MPI Result	Abnormal MPI Result	P-Value
Lower limbs ischemia (%)	10.52 %	50.00 %	0.013
I_S Rt Th#	0.260	0.249	0.639
I_S Lt Th#	0.258	0.240	0.410
I_S Rt Cf#	0.114	0.110	0.822
I_S Lt Cf#	0.115	0.113	0.856
I_r Rt Th*	18.94	13.36	0.099
I_r Lt Th*	18.06	14.50	0.301
I_r Rt Cf*	19.06	13.21	0.084
I_r Lt Cf*	19.72	12.36	0.027
I_{sym} Thighs#	1.01	1.04	0.378
I_{syn} Calves#	0.985	0.986	0.994
PR Rt Th#	-0.105	0.021	0.232
PR Lt Th#	-0.097	-0.066	0.743
PR Rt Cf#	-0.218	-0.242	0.491
PR Lt Cf#	-0.208	.0.123	0.418

* Mean Rank of Mann-Whitney U Test; # Mean values of Independent T-Test; MPI: Myocardial Perfusion Imaging; Rt Th: Right Thigh; Lt Th: Left Thigh; Rt Cf: Right Calf; Lt Cf: Left Calf; I_s=Stress Index; I_r= Rest Index; I_{sym}= Symmetric Index; PR=Perfusion Reserve.

Table 5: Spearman's rho correlation coefficients between lower limbs perfusion indices Is and Ir with QPS attenuation-corrected semiquantitative indices in patients with abnormal exercise-rest MPI result.

	SSS (P-Value)	SRS (P-value)	SDS (P-Value)	TPDst (P-Value)	TPDrest (P-Value)
I_s Rt Th	- 0.162 (0.401)	- 0.217 (0.257)	- 0.089 (0.646)	- 0.132 (0.494)	- 0.380 (0.042)
I_s Lt Th	- 0.202 (0.292)	- 0.235 (0.220)	- 0.121 (0.533)	-0.197 (0.304)	- 0.446 (0.015)
I_s Rt Cf	- 0.211 (0.272)	-0.392 (0.036)	- 0.036 (0.854)	- 0.167 (0.386)	- 0.285 (0.133)
I_s Lt Cf	- 0.298 (0.116)	- 0.439 (0.017)	- 0.099 (0.610)	- 0.256 (0.180)	- 0.298 (0.117)
I_r Rt Th	- 0.192 (0.319)	- 0.156 (0.418)	- 0.072 (0.711)	- 0.216 (0.260)	- 0.196 (0.309)
I_r Lt Th	- 0.192 (0.319)	- 0.155 (0.423)	- 0.056 (0.775)	- 0.218 (0.256)	- 0.183 (0.343)
I_r Rt Cf	- 0.179 (0.352)	- 0.216 (0.260)	- 0.013 (0.948)	- 0.221 (0.249)	- 0.219 (0.255)
I_r Rt Cf	- 0.186 (0.334)	- 0.234 (0.221)	- 0.034 (0.859)	- 0.181 (0.346)	- 0.280 (0.141)

MPI= Myocardial Perfusion Imaging; Is= Stress Index; Ir= Rest Index; QPS= Quantitated Perfusion SPECT; SSS= Summed Stress Score; SRS=Summed Rest Score; SDS= Summed Difference Score; TPDst= Total Perfusion Deficit in stress phase; TPDrest= Total Perfusion Deficit in rest phase; Rt Th: Right Thigh; Lt Th: Left Thigh; Rt Cf: Right Calf; Lt Cf: Left Calf.

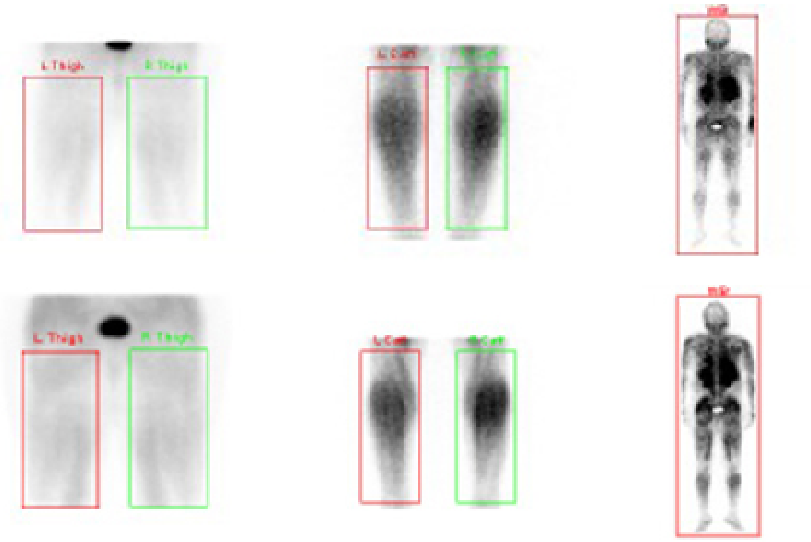

Fig 1. Normal LLPS. Rest phase images (posterior whole body scan, posterior spots from right and left thighs and calves) (Above) and stress phase images (same views) (Below) in a 47-year old man, with intermediate pretest probability of CAD, referred for MPI. Exercise-Rest MPI results were normal. Lower Limbs perfusion scans reveal normal increase in radiotracer uptake in all four ROIs in the stress phase as compared to the rest phase of the study. Quantitative indices of lower limbs perfusion scan also confirm the visual findings (CAD: Coronary Artery Disease; MPI: Myocardial Perfusion Imaging; LLPS: Lower Limbs Perfusion Scan; ROI: Region of Interest).

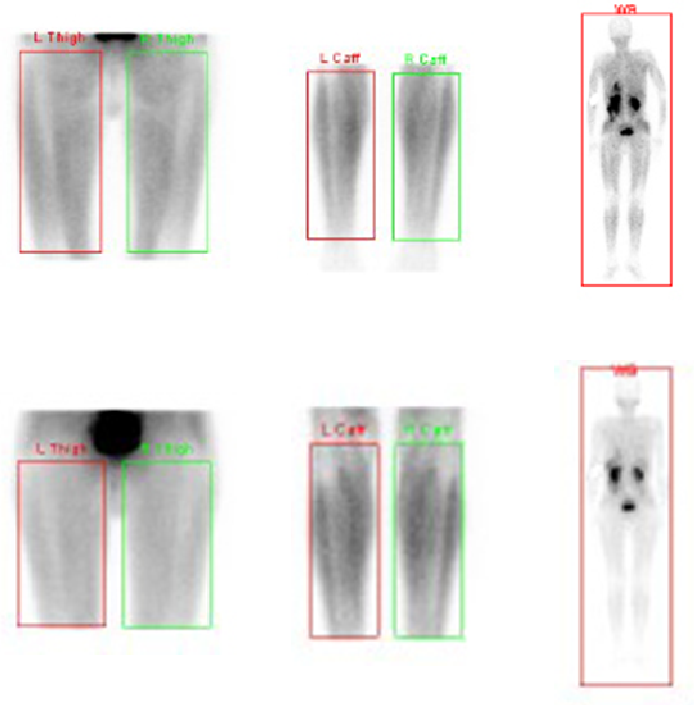

Fig 2. Abnormal LLPS. Stress phase images (posterior whole body scan, posterior calves and thighs spots) (Above) and rest phase images (the same views) (Below) in a 52 year-old man, with intermediate pretest probability of CAD, referred for MPI. Dipyridamole-Rest MPI results revealed ischemia in the apex, anterior and anteroseptal walls (SSS=14, SRS=0, SDS=14). Lower limbs perfusion scan showed no acceptable increase in radiotracer uptake in either of 4 ROIs. Calculated PRs of 4 ROIs confirm the visual findings. (PRs of Right Thigh, Left Thigh, Right Calf and Left Calf were 0.19, 0.25, 0.27 and 0.29 respectively) (CAD: Coronary Artery Disease; MPI: Myocardial Perfusion Imaging; ROI: Region Of Interest; LLPS: Lower Limbs Perfusion Scan; PR: Perfusion Reserve; SSS: Summed Stress Score; SRS: Summed Rest Score; SDS: Summed Difference Score.

First, visual assessment of the images was done regarding the integrity of the blood supply to the lower limbs muscles during stress and rest. In normal study, there is increased radiotracer uptake corresponding to increased blood supply to each ROI in the stress phase as compared to the rest phase; however, in ischemic region (thighs and/or calves), visual assessment reveals no such increase in radiotracer uptake in the stress phase or there is significant asymmetric uptake with decreased activity in the affected lower limb (Figures 1 & 2).

The scintigraphic results of this study suggest that in the exercise stress group (83 patients), abnormal lower limb perfusion was found in 22.58% of patients with abnormal MPI results and in 1.92% of the patients with normal MPI results (P-Value =0.004).

In the second group who had dipyridamole infusion as stress phase (37 patients), perfusion abnormality of the lower limbs was seen in 50.00% of patients with abnormal MPI results versus 10.52 % of patients with normal MPI results. (P-Value= 0.013). In both stress groups, differences in prevalence of lower limbs ischemia between patients with normal and abnormal MPI results were statistically significant.

In patients underwent exercise as stress modality, mean ranks of -Is- for all four ROIs were statistically significantly greater in subgroups with normal MPI result as compared to those with abnormal MPI result (all P-values <0.02). PRs of all 4 ROIS were also greater in normal MPI result subgroup, the difference was not significant though (P-Values > 0.05) (Table 3).

In patients underwent dipyridamole-rest protocol, no statistically significant differences were observed in lower limbs perfusion indices between subgroups with normal and abnormal MPI results (P-Values > 0.05) (Table 4).

Also, among patients who had ischemia in exercise-rest MPI, negative correlations were seen between Is and Ir of 4 lower limb regions and QPS quantitative values (attenuation corrected Summed Stress Score (SSS), Summed Rest Score (SRS) and Summed Difference Score (SDS), as well as stress and rest Total Perfusion Deficits (TPDs)) among which negative correlations between right thigh Is with rest TPD(r = - 0.380, P-Value = 0.042) and left thigh Is with rest TPD (r = - 0.446, P-Values = 0.015) and between right calf Is with SRS (r = - 0.392, P-Value = 0.036) and left calf Is with SRS (r = - 0.439, P-Value= 0.017) were statistically significant (Table 5).

DISCUSSION

Co-prevalences of CAD and PVD and complications of non-diagnosed or lately diagnosed PVD, suggest investigation of both diseases in patients with intermediate pre-test probability of CAD. Lower limbs perfusion scintigraphy is a valuable tool for assessment of lower limb perfusion at the microcirculation level. Several communications on its practical use in diagnosis of chronic hypoperfusion of lower limbs, hypoperfusion in asymptomatic patients and assessment of effectiveness of therapy are available [27-32].

A few methods of quantitative assessment of lower limbs perfusion have also been proposed [33-36]. As our study show, lower limbs perfusion scintigraphy in the stress and rest phases of MPI performed after ^{99m}Tc-MIBI injection and before each MPI phase is a non-invasive and logistically feasible method.

Due to difference in mechanism of stress modalities (exercise is based on increasing oxygen demand in tissues and secondary vasodilation of corresponding perfusing vessels while dipyridamole infusion is based upon direct vessel vasodilation, in both heterogeneity of myocardial blood flow in atherosclerotic and normal vessels provide visualization of presence, severity and extent of possible ischemia), we subdivided patients in two groups-exercise and dipyridamole stress groups. Interestingly, in both groups, those patients with abnormal MPI results, reveal statistically significantly more prevalences of lower limbs ischemia. Since all confounding variables of age, sex, previous history of claudication, amount of stress in terms of exercise METs or milligrams of infused dipyridamole, circumferences of thighs and calves were matched in both groups with normal and abnormal MPI results, these observed more prevalences of lower limb ischemia in abnormal MPI groups can be attributed to coexistence of PVD and CAD in these patients.

Amin et al [37] used ^{99m}Tc-MIBI lower extremity muscle perfusion scintigraphy as a screening tool for assessment of atherosclerosis in Rheumatoid Arthritis (RA) patients and compared PR in RA and control group. They used a leg-elevation exercise for calculation of PR and found significantly higher PRs in control group. Their patients did not follow Bruce or modified Bruce protocol and no MPI was performed. Other quantitative indices rather than PR were not calculated either.

Kusmierek et al [38] evaluated lower limb muscles perfusion in both stress and rest phases with ^{99m}Tc-MIBI in 47 male patients, referred for MPI. They divided patients in to two groups based on normal or abnormal ultrasonography result. They found statistically significantly lower mean values of Is and Ir of thighs and calves in the group with abnormal ultrasonographic result of lower limbs. They also found abnormal myocardial perfusion in 77% of

patients from ultrasonographically abnormal and in 28% of patients from ultrasonographically normal groups (p = 0.001).

Although their study design and results have some similarities with ours, their patients consist of only males, with no defined pretest probability of CAD and they did not perform dipyridamole stress in any of their patients.

In our study we evaluated all quantitative indices of lower limbs perfusion scan, separately for patients with exercise and dipyridamole stress modalities and for subgroups with normal and abnormal MPI results. Higher mean Is and PR in exercise-rest protocol that we found in patients with normal MPI results as compared to the patients with abnormal MPI results suggest using quantitative indices besides visual interpretation of lower limbs perfusion scans. Negative correlation coefficients between Is and Ir of thighs and calves and MPI-QPS indices (attenuation corrected SSS, SRS, SDS, TPD at stress and rest phases) reconfirm association between CAD and PVD in a quantitative scale.

Only some of these negative correlation coefficients were statistically significant. We assume that by increasing number of patients with abnormal MPI results, lower limbs perfusion quantitative indices reveal statistically significant negative correlation coefficients with MPI-QPS indices.

Based on our method and results, referring physicians can simultaneously ask for evaluating patients for CAD and PVD. Lower limbs perfusion scan can also be performed separately especially after an abnormal MPI results with abnormal QPS indices which warrant further evaluation of lower limbs perfusion, even if the patient is asymptomatic.

CONCLUSION

Lower limb perfusion scan with ^{99m}Tc-MIBI, combined with two-day stress/rest MPI protocol, is a feasible and non-invasive method to scintigraphically detect lower limbs ischemia, especially in patients with abnormal MPI results regardless of type of stress modalities applied, allowing referring physicians to further investigate these patients and avoid possible complications of lately/never diagnosed PVD. Comparison of quantitative indices of lower limb perfusion with MPI-QPS semi-quantitative parameters, also reflect this coexistence of CAD and PVD.

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