Molecular Perfusion Imaging with 99mTc-MIBI Lower Limb Muscle SPECT: In Diagnosis and Follow up of Peripheral Arterial Diseases (PAD)

Rashid Rasheed*
GINUM Cancer Hospital, Nizampur, Pakistan

Abstract

The study was conducted to evaluate the clinical utility of 99mTc-MIBI lower limb muscle perfusion single photon emission tomography (SPECT) for diagnosis and follow up of PAD.

Methods: The study was performed to develop normal values of lower limb muscle perfusion for normal local population (N=36) by using SPECT and planar scintigraphic techniques. Patients (N=44) with established PAD were compared with age matched data of normal population. Normal range developed for planar study (0.90-0.10 ± 2SD) was used as reference for planar study in patient population.

Results: In SPECT study visual analysis correlated extremely well with clinical features. Comparison of patient SPECT data with normal population showed significant hypoperfusion of lower limbs in terms of counts (P-value <0.001). Follow up of patients (N=12) showed significant improvement of muscle perfusion in nine patients while three patients showed no improvement. Comparison of follow up planar study values with baseline were not conclusive for any improvement in limb perfusion (p-value ~ 0.98). Comparison of SPECT study with other modalities showed higher sensitivity than Doppler ultrasound (P-value <0.05), ABI (p-value <0.001) and planar scan (p-value <0.001) for 99mTc-MIBI; 64%, 100%, 100%, 69% for ABI; 77%, 100%, 100%, 78.3% for Doppler ultrasound and 75%, 100%, 100%, 76.6% for Planar scan respectively.

Conclusion: 99mTc-MIBI lower limb muscle perfusion scan is an excellent tool for diagnosis and follow up in PAD and may be a baseline tool for assessment of patient response to treatment.

Keywords: 99mTc-MIBI; Lower limb muscle perfusion; Peripheral Arterial Diseases (PAD); SPECT

Introduction

Peripheral arterial disease (PAD) comprises those entities which result in obstruction to blood flow in the arteries, exclusive of the coronary and intracranial vessels. Peripheral vascular disease is a slow and progressive circulation disorder. It may involve any of the vessels outside the heart and is a disease of the arteries, veins and lymphatic vessels. However, the legs and feet are commonly affected thus the name peripheral vascular disease (PVD) [1]. The present study was undertaken to evaluate the potential of 99mTc-MIBI in Lower Limb Muscle Perfusion SPECT, its feasibility as a clinical tool for diagnosis and follow-up of peripheral arterial diseases (PAD) and to establish normal values of Lower Limb Muscle Perfusion SPECT for local population. 99mTc-MIBI SPECT gives excellent 3D analysis of perfusion in all muscular compartments. All SPECT slices give a refined perfusion status in objective manure starting from knee joint to ankle joint. 99mTc-MIBI is taken up in the mitochondria of muscles and stays inside the cells, therefore can be used for imaging perfusion when tagged with 99mTcO4.

Materials and Methods

This pilot study was approved by the local ethical and radiation committee of Multan Institute of Nuclear Medicine (MINAR), and Gujranwala Institute of Nuclear Medicine (GINUM), Pakistan. The entire human study was performed according to provisions of the Declaration of Helsinki of 1975, as revised in 2008 (5), regarding medical research involving human subjects. The study was carried out over a period of six months and conducted according to the national rules and following the international standards. Patients included in this study were referral cases from Outpatient Department (OPD), Nishat Hospital, Multan. Subjects selected in control group were non-diabetic, normotensive, nonsmokers, who were further screened by routine clinical investigations. All patients included in the study were true positive cases of Peripheral Arterial Diseases (PAD), because we were interested in such cases for evaluation and comparison of the diagnostic sensitivity of various diagnostic modalities related to peripheral arterial diseases. The clinical features due to apparent disease were used as gold standard. Doppler study and Ankle Brachial Index (ABI) were performed in all patients and all controls were screened for any underlying pathology. ABI was calculated as below:

\[
\text{ABI} = \frac{\text{Pa}}{\text{Pb}}
\]

\[
\text{Pa} = \text{Highest pressure obtained from the ankle vessels for that leg}
\]

\[
\text{Pb} = \text{Highest brachial pressure of two arms.}
\]

Patient selection

Thirty-six controls from normal population and forty-four patients (19 female and 25 male, mean ages, 33.9 y; range, 10–68 y) with suspected peripheral artery disease were selected for this study before starting any...
imaging procedure. No patient had a history of allergy. Each subject or a patient gave written consent after receiving a full explanation of the clinical procedure. As described earlier, patients with suspected peripheral artery disease of the bone or limbs were included in the study. However, patients with limb lesions were preferred because they could be compared with the healthy contralateral side. Pregnant or lactating women were excluded from this study. Candidates with known hepatic or renal insufficiency or a history of allergy were also excluded.

**99mTc-MIBI scintigraphy**

Preparation of **99mTc-MIBI**: Hexakis (2-methoxy-2-methylpropylisonitrile) - MIBI was obtained in a freeze-dried kit form from Pakistan Institute of Nuclear Science and Technology (PINSTECH). The kit was formulated as a five-patient vial which comprised 1.0 mg MIBI compound and 0.075 mg of SnCl₂·2H₂O. The kit was radiolabeled by adding 100-120 mCi of sodium pertechnetate from a freshly eluted technetium generator (PakGen; PINSTECH), shaking for about 20 sec and heating in boiling water for 10 min. Afterwards, the volume was raised to about 5.5 mL by addition of 0.5 mL of saline. The pH of the solution was in the desired range of 6–7. The entire vial content was mixed well and 1 mL out of it was injected intravenously to each patient.

**Quality control**: Radiochemical purity of the complex was determined by chromatographic techniques. Radiochemical purity of the **99mTc-MIBI** was studied by using two simple chromatographic techniques, e.g., Instant Thin Layer Chromatography (ITLC-SG strips; Gelman Sciences) and Paper Chromatography (PC) by using Whatman No. 3 chromatographic strips. The technique was employed to determine the percentage of hydrolyzed, (radionuclide bound to ligand) and free pertechnetate. Acetone was used as a mobile phase for paper chromatography and saline was used for ITLC. Small aliquots from the reconstituted kit were spotted on the respective strips. The strips, after elution, were cut in fractions of 1cm and counted for radioactivity in a well type scintillation gamma counter (Scaler Timer–ST7, Thorn EMI – Nuclear Enterprises, United Kingdom).

**Patient preparation**: Baseline investigations of all the subjects, including a complete blood examination (red blood cell count, total lymphocyte count, leucocyte count, erythrocyte sedimentation rate) and urea, creatinine, and liver function tests, were conducted. Urine samples were also collected beforehand for routine chemical and microscopic examination. A dose of 740–800 MBq (20 mCi) of **99mTc-MIBI** was injected intravenously as a bolus dose and flushed with 5 mL of 0.9% normal saline. Flexion and extension was continued 50 times after the injection. The dose in all patients and controls was strictly standardized to reduce the error in the counts. In all patients, imaging time was also standardized to avoid any statistical error in the count data due to decay of the radionuclide. All the patients were imaged after 20 ± 5 min and studied by following the same-day stress **99mTc-sestamibi** SPECT imaging protocol.

**Results**

**Quality control tests**: During labeling of MIBI with **99mTc** - besides the bound **99mTc** to MIBI complex, free pertechnetate (**99mTcO₄⁻**), reduced or hydrolyzed **99mTcO₂** were also formed as separated by PC and ITLC. In PC, **99mTcO₂** had an **Rf** of 0.9-1.0. The reduced or hydrolyzed fraction was separated from the other two fractions by using saline, in which case the **99mTc-MIBI** complex and the free **99mTcO₂** appeared at **Rf** =0.9-1.0. The overall labeling yield of the **99mTc-MIBI** complex as calculated by these methods was more than 98.6 ± 1.2%.

**Quantitative SPECT perfusion curves**: The leg can be divided in to 64 short axis slices. That is why SPECT offers a detailed compartmental and segmental analysis of the perfusion status of the leg, which is not possible in planar scan and in the Doppler study. As compared to the Doppler Ultrasound, the uptake of the tracer is directly proportional to the blood flow that is why SPECT scan reflects the exact status of the perfusion of the limbs. All controls and patients were analyzed in terms of standardized counts of both lower limbs. Initially, counts of each slice out of 12 slices of each normal subject (N=36) were calculated for both limbs. Perfusion curves were generated for each limb by using mean counts from each slice as shown in Figure 2a and 2b. The upper and lower limits were defined as ±15% of mean %age uptake counts of one particular slice for all 36 subjects. Afterwards, the counts of each slice from control group were compared with the counts of same slice from patient group to evaluate the significance of the difference. The **P** value was taken as <0.05 (Figure 1).

**Planar study**: The posterior static calf images show the major part of the leg muscles. The advantage of the posterior images when compared with images in anterior views is that there is no tibial bone attenuation. The rectangular Region of Interest (ROI) was drawn on one side and mirror method was used for the contralateral side as shown in Figure 2c.

**Case study**: Patient presented with history of pain and blackish discoloration of the liver, kidneys, and urinary bladder, and the percentage injected dose at 30, 120, and 240 min was calculated using the following formula: percentage injected dose in an organ=100 × organ count at particular time/total-body count at that time. Other subjects were not included in the biodistribution study, as the objective was to have an overview of the behavior of the kit in humans.

**Study protocol**: In our study, the stress to the lower limb muscles was created by performing exercise of feet. Exercise was performed with 100 times flexions and extensions of feet simultaneously on both sides. At peak stress (after 100 flexions and extensions), 20 mCi (740 MBq) of **99mTc-MIBI** was injected intravenously as a bolus dose and flushed with 5 mL of 0.9% normal saline. Flexion and extension was continued 50 times after the injection. The dose in all patients and controls was strictly standardized to reduce the error in the counts. In all patients, imaging time was also standardized to avoid any statistical error in the count data due to decay of the radionuclide. All the patients were imaged after 20 ± 5 min and studied by following the same-day stress **99mTc-sestamibi** SPECT imaging protocol.
of the right foot for last one month was treated locally with analgesics but no relief. On examination, all distal pulses were palpable except posterior tibial artery (PTA) on the right side. Ankle brachial index was calculated with values of 0.75 for right and 0.92 for left side.

SPECT data visual analysis

The reconstructed SPECT short axis slices of the perfusion scan showed perfusion defect in the posterior compartment of the right leg and there was normal perfusion in the anterior and lateral compartments of the right side. The visual inspection of the short axis SPECT slices helps to clearly differentiate between the different compartments, e.g., anterior lateral and posterior views. In this case, the short axis slices clearly showed perfusion in the decreased perfusion pattern on the left side. Moreover the SPECT study shows that the level of hypo-perfusion in the right limb starts from knee (Slice 1) to the ankle joint (Slice 12). This suggests that the level of obstruction is lying around the knee joint or above, thus we can predict the level of obstruction of artery easily. Follow up scan of same patient shows moderate improvement in the perfusion status of right limb as shown in Figure 3b.

Comparison of SPECT perfusion curves

The data plotted against the normal profile curves clearly demonstrate the difference from normal curves due to decreased perfusion in the posterior compartment of the right leg. It is clearly shown in the curves that the level of the perfusion defect is located at the knee joint (Figures 4a and 4b). As the anterior muscle compartment shows normal perfusion on the right side, this means that the obstruction lies at the origin of the posterior tibial artery (PTA) or proximal. Later on, Doppler study of both limbs was performed which also shows the thrombus at the origin of the PTA with dampened downstream flow, as shown in Figure 5a. Follow up study showed persistent thrombus in Figure 5b at origin of right PTA despite patient’s clinical symptoms had improved. The improvement of the perfusion of the limb was excellently manifested on 99mTc-MIBI SPECT perfusion scan and Doppler scan was unable to demonstrate the improvement.

Inter-comparison of diagnostic modalities

Doppler ultrasound is an investigation of choice in all the patients with peripheral arterial diseases. We performed color Doppler study in all 44 patients and results were compared with ABI, Planar scan, SPECT scan and clinical features. As all selected cases in this study were true positive, e.g., all patients had clinically established disease in one or both limbs so they served the basis for the evaluation and comparison of the diagnostic capability of all the techniques.

Sensitivity and specificity

Comparison of SPECT study with other modalities showed higher sensitivity than Doppler ultrasound (P-value<0.05), ABI (p-value<0.001) and planar scan (p-value<0.001). The sensitivity, specificity, positive predictive values and negative predictive values for 99mTc-MIBI are 93%, 100%, 92%, respectively, for ABI, these values are 64%, 100%, 100%, 69%; for Doppler ultrasound, these values are 77%, 100%, 100%, 78.3% and for planar scan, these are 75%, 100%, 100%, 76.6%, respectively.

Discussion

Peripheral arterial disease (PAD) is an important healthcare problem and is an indicator of widespread atherosclerosis in other vascular territories, such as the cerebral and coronary circulations [2]. Radiopharmaceuticals including 99mTc-transferrin, 99mTcO₄⁻, 99mTc-DTPA, 99mTc-pyrophosphate and K, 82Na, 81T1 etc., have been used to assess the perfusion for PAD [3,4] and radiopharmaceuticals that show free diffusion and clearance from tissues according to the blood flow such as 133Xe, 131I-iodoantipyrene were used as well [5,6]. 99mTc-MIBI (methoxy-isobutyl-isonitrile), which was developed primarily as a myocardial perfusion agent, has also proved valuable agent for skeletal muscle perfusion studies [7,8]. Technetium has superior imaging and dosimetry characteristics in comparison to other radionuclides [8]. For many years 99mTc-MIBI has been used in investigating peripheral arterial diseases using planar, whole body static and SPECT techniques. More emphasis was given to MIBI because of its uptake in the soft tissue. As MIBI is taken up in multiple areas of the body, there is potential diversity of usage of this tracer.

In the recent years, positron emission tomography (PET) imaging has also shown excellent results in the investigation of peripheral arterial diseases. But high cost, small half life of the isotopes and...
limited availability are the major limitations of this technique [9]. Though SPECT studies have been done in the past in investigation of peripheral arterial diseases but it has not been developed as a clinical tool for diagnosis and follow up. Owens et al. reported two cases in which he showed the usefulness of $^{99m}$Tc-MIBI in diagnosing chronic compartmental syndrome [10]. Oshima et al. quantified leg perfusion by using thallium-201 and showed that this technique is useful in investigating peripheral arterial diseases [11].

In our study, all patients were clinically diagnosed cases of peripheral arterial disease (true positive cases) because our aim was to evaluate the diagnostic sensitivity of different techniques e.g., Doppler vs. $^{99m}$Tc-MIBI scan, so we avoided the costly procedure of angiography. As there were no previous normal values of lower limb muscle perfusion developed for our local population, in the first part we developed our own normal values for local population. Arteriography shows only the morphologic occlusive features and does not reveal the compensatory capacity of the collaterals. In this study, we therefore, used $^{99m}$Tc-MIBI leg SPECT with single-headed gamma camera to quantify leg muscle perfusion. It takes 20 min to complete the study and reveals a three-
with normal blood flow indices [12]. Thus, analysis of 99mTc-MIBI hypoperfusion of the muscles in patients with diffuse atherosclerosis was able to demonstrate improvement of perfusion even in cases, in which no increase of the flow-rate in large arteries could be detected by means of Doppler ultrasound. Scintigraphy, which reflects limbs perfusion at the level of myocytes, has proved, therefore, to be objective method for evaluation of lower limb muscle perfusion.

This method of quantification of lower limb perfusion shows that there are many advantages of 99mTc-MIBI lower limb muscle perfusion SPECT over other diagnostic modalities. First of all, it shows the perfusion status of the limb at microvascular level or at the cellular level. Images of the 99mTc-MIBI lower limb muscle perfusion SPECT produced an excellent visual interpretation of the lower limb perfusion. We can easily identify the slice with abnormal perfusion. The three dimensional compartmental visual analysis is another additional advantage of this technique over other diagnostic modalities. All compartments, e.g., anterior, lateral and posterior fascial compartments can be seen in every slice at a glance and can be visually analyzed in terms of perfusion defect. These three dimensional images give further additional information about the vessel blockage, e.g., if the defect is in the posterior compartment then it means that posterior tibial artery may be blocked and if the defect is in the anterior or lateral compartments, then anterior tibial or peroneal artery, respectively, may be blocked. Another advantage of the 99mTc-MIBI lower limb muscle perfusion SPECT is that when the data are plotted in terms of quantification curves then one can easily analyze the point of drop of the perfusion curve at a particular level which indicates the level of blockage of the vessel in the leg. This finding could be of great help in deciding the level of amputation in the surgical aspect. We followed the patients through surgical wards and found high correlation of our results with the actual level of amputations performed by the surgeon.

Another advantage of 99mTc-MIBI lower limb muscle perfusion SPECT over Doppler was that it could be easily performed in those few cases as well where leg was partially covered by dressing applied over wounds which easily picked up the hypoperfusion from the tissues under the dressings in contrast to Doppler, and it was due to unique quality of gamma ray imaging. As compared to the other diagnostic modalities like computed tomographic angiography (CTA), catheter angiography and magnetic resonance angiography, theradioisotope modalities like computed tomographic angiography (CTA), catheter angiography and magnetic resonance angiography, theradioisotope technique by using MIBI is cost effective and widely available almost at every nuclear medicine center. Regarding radiation exposure, there was six times less dose than CTA or catheter angiography. Moreover, due to easy availability of 99mTc-MIBI, it can be used as a follow up tool to evaluate the response to treatment.

The findings of statistical analysis were very striking in our study. The chi-square test was applied to evaluate the significance of difference in multiple ways. In comparison of 99mTc-MIBI SPECT perfusion scan with ankle brachial index, there was a significant difference with p-value<0.001, thus showing a clear advantage of 99mTc-MIBI SPECT perfusion scan over ankle brachial index. The comparative difference of 99mTc-MIBI SPECT perfusion scan from planar scintigraphy was also taken to evaluate and compare the diagnostic capability of 99mTc-MIBI, it can be used as a follow up tool to evaluate the response to treatment.

which no increase of the flow-rate in large arteries could be detected by means of Doppler ultrasound. Scintigraphy, which reflects limbs perfusion at the level of myocytes, has proved, therefore, to be objective method for evaluation of lower limb muscle perfusion.

This method of quantification of lower limb perfusion shows that there are many advantages of 99mTc-MIBI lower limb muscle perfusion SPECT over other diagnostic modalities. First of all, it shows the perfusion status of the limb at microvascular level or at the cellular level. Images of the 99mTc-MIBI lower limb muscle perfusion SPECT produced an excellent visual interpretation of the lower limb perfusion. We can easily identify the slice with abnormal perfusion. The three dimensional compartmental visual analysis is another additional advantage of this technique over other diagnostic modalities. All compartments, e.g., anterior, lateral and posterior fascial compartments can be seen in every slice at a glance and can be visually analyzed in terms of perfusion defect. These three dimensional images give further additional information about the vessel blockage, e.g., if the defect is in the posterior compartment then it means that posterior tibial artery may be blocked and if the defect is in the anterior or lateral compartments, then anterior tibial or peroneal artery, respectively, may be blocked. Another advantage of the 99mTc-MIBI lower limb muscle perfusion SPECT is that when the data are plotted in terms of quantification curves then one can easily analyze the point of drop of the perfusion curve at a particular level which indicates the level of blockage of the vessel in the leg. This finding could be of great help in deciding the level of amputation in the surgical aspect. We followed the patients through surgical wards and found high correlation of our results with the actual level of amputations performed by the surgeon.

Another advantage of 99mTc-MIBI lower limb muscle perfusion SPECT over Doppler was that it could be easily performed in those few cases as well where leg was partially covered by dressing applied over wounds which easily picked up the hypoperfusion from the tissues under the dressings in contrast to Doppler, and it was due to unique quality of gamma ray imaging. As compared to the other diagnostic modalities like computed tomographic angiography (CTA), catheter angiography and magnetic resonance angiography, theradioisotope technique by using MIBI is cost effective and widely available almost at every nuclear medicine center. Regarding radiation exposure, there was six times less dose than CTA or catheter angiography. Moreover, due to easy availability of 99mTc-MIBI, it can be used as a follow up tool to evaluate the response to treatment.

The findings of statistical analysis were very striking in our study. The chi-square test was applied to evaluate the significance of difference in multiple ways. In comparison of 99mTc-MIBI SPECT perfusion scan with ankle brachial index, there was a significant difference with p-value<0.001, thus showing a clear advantage of 99mTc-MIBI SPECT perfusion scan over ankle brachial index. The comparative difference of 99mTc-MIBI SPECT perfusion scan from planar scintigraphy was also significant with p-value<0.001. The most striking finding of the study was the comparison of Doppler ultrasound with 99mTc-MIBI SPECT perfusion scan. The chi square test gave p-value<0.05 which means that there is a significant difference between the results of the two investigations. This proves the diagnostic advantage of 99mTc-MIBI SPECT perfusion scan over Doppler ultrasound. The reason of this finding was inability of the Doppler ultrasound to pick up the disease in those patients in which there was gangrene of the toes with normal indices of Doppler flow study. This was due to the reason that we did not take into account the diffuse atherosclerotic changes with normal blood flow as disease positive criteria for gangrenous patients because

dimensional image of leg muscle. Although 99mTc-MIBI leg SPECT images would be inferior for spatial resolution in terms of anatomic information to X-ray computed tomography, but it reflects local perfusion and also enables a transverse image of leg perfusion. In our study, 10/44 (22.7%) patients had normal Doppler flow but they were hypoperfused. This is also confirmed in the study of Dabrowski et al. in which he showed the significance of 99mTc-MIBI scan in picking up the hypoperfusion of the muscles in patients with diffuse atherosclerosis with normal blood flow indices [12]. Thus, analysis of 99mTc-MIBI SPECT can provide quantitative information and permit an objective, reproducible test, independent of observed bias in detecting ischemia of lower limb muscles. Local perfusion was also quantified by this method before and after treatment, e.g., in follow-up to assess for disease response to treatment.

Posterior static images of all normal subjects and patients were also taken to evaluate and compare the diagnostic capability of 99mTc-MIBI planar and 99mTc-MIBI SPECT scan. The results of planar scan were disappointing as it could only pick the disease in the unilateral and advanced cases. Secondly, all counts were diluted to whole length of the leg, not to the same area of defect, thus losing the diagnostic count difference. In SPECT study, the counts were normalized within the slice to maintain the diagnostic difference among the normal and diseased slices. Thirdly, there is no information about compartmental perfusion status in planar scans so we cannot evaluate which artery is blocked, e.g., anterior tibial artery or posterior tibial artery. Planar scan sensitivity reflective of improvement in lower limb muscle perfusion at follow up was also not significant (p-value=0.98). The qualitative-quantitative method of perfusion assessment, as applied in this study, seems sufficient for evaluation of the undertaken therapy and prognosis of peripheral arterial diseases. It seems important that both qualitative (visual) as well as quantitative analysis, when performed separately, demonstrated a high degree of concordance with the clinical evaluation. When juxtaposed with the Doppler ultrasound method, the scintigraphic perfusion method possessed higher diagnostic efficacy. It was able to demonstrate improvement of perfusion even in cases, in

Figure 5: Doppler ultrasound Results (A) Baseline Doppler study of patient showing a large thrombus at the origin of the Right PTA with dampened flow distal to the obstruction. (B) Follow up Study showed persistent thrombus at Origin of Right PTA. (C) Baseline (viewer’s left) and follow up planar study (Viewer’s right).

Another advantage of 99mTc-MIBI lower limb muscle perfusion SPECT over other diagnostic modalities. First of all, it shows the perfusion status of the limb at microvascular level or at the cellular level. Images of the 99mTc-MIBI lower limb muscle perfusion SPECT produced an excellent visual interpretation of the lower limb perfusion. We can easily identify the slice with abnormal perfusion. The three dimensional compartmental visual analysis is another additional advantage of this technique over other diagnostic modalities. All compartments, e.g., anterior, lateral and posterior fascial compartments can be seen in every slice at a glance and can be visually analyzed in terms of perfusion defect. These three dimensional images give further additional information about the vessel blockage, e.g., if the defect is in the posterior compartment then it means that posterior tibial artery may be blocked and if the defect is in the anterior or lateral compartments, then anterior tibial or peroneal artery, respectively, may be blocked. Another advantage of the 99mTc-MIBI lower limb muscle perfusion SPECT is that when the data are plotted in terms of quantification curves then one can easily analyze the point of drop of the perfusion curve at a particular level which indicates the level of blockage of the vessel in the leg. This finding could be of great help in deciding the level of amputation in the surgical aspect. We followed the patients through surgical wards and found high correlation of our results with the actual level of amputations performed by the surgeon.

Another advantage of 99mTc-MIBI lower limb muscle perfusion SPECT over Doppler was that it could be easily performed in those few cases as well where leg was partially covered by dressing applied over wounds which easily picked up the hypoperfusion from the tissues under the dressings in contrast to Doppler, and it was due to unique quality of gamma ray imaging. As compared to the other diagnostic modalities like computed tomographic angiography (CTA), catheter angiography and magnetic resonance angiography, theradioisotope technique by using MIBI is cost effective and widely available almost at every nuclear medicine center. Regarding radiation exposure, there was six times less dose than CTA or catheter angiography. Moreover, due to easy availability of 99mTc-MIBI, it can be used as a follow up tool to evaluate the response to treatment.
diffuse atherosclerosis changes were also seen in the patients without critical limb ischemia and without gangrene. These findings are supported by the study of Dabrowski et al., in which the $^{99m}$Tc-MIBI perfusion scan study picked up improvement of perfusion of lower limb muscles and Doppler ultrasound was non-conclusive after lumbar sympathectomy in chronic arteriosclerotic ischemia of lower limbs [13]. This basic limitation of Doppler ultrasound was observed in ten patients when compared to $^{99m}$Tc-MIBI SPECT perfusion scan. High values of specificity and positive predictive values are due to the design of study, e.g., due to selection of true positive cases for comparison of diagnostic modalities and secondly due to the fact that all subjects selected as control were normal adults with no previous history of disease. Keeping in view these parameters, there were technically no false positive cases in our study, which led to such high specificity and positive predictive values.

In our study, we tried to study maximum number of patients as follow up cases but it was possible in fourteen out of forty four patients, who showed willingness for follow up scan. Two patients with extensive gangrene of lower limb expired and remaining twelve patients were called for follow up scan after at least 2-6 months. Out of twelve patients called for follow up scans, nine patients showed improvements in the perfusion levels and three patients did not show any improvement even after three month of follow up (Table 1).

These results of follow up data were judged clinically on the basis of the improvement of symptoms, healing of wounds, improvement in the Doppler flow indices and scintigraphic SPECT curves. Overall slicewise comparison of baseline and follow up SPECT study showed that there was improvement of perfusion of both limbs on follow up (p-value<0.001). Planar study was non-conclusive for any improvement in lower limb muscle perfusion at follow up (P-value ~ 0.98). The present data confirmed observations made by Duet et al. [14] and Tellier et al. [13] concerning a potential usefulness of scintigraphy in the diagnosis of chronic hypoperfusion of lower limbs.

Acknowledgements

We acknowledge the valuable contribution of all technical staff at MINAR and Nishtar Hospital for their valuable contribution to the project. We also acknowledge the technical help of staff at GINUM Cancer Hospital for moral support to the project.

| Study                      | Chi-SQ | DF | P-Value |
|----------------------------|--------|----|---------|
| MIBI with Doppler ultrasound| 4.423  | 1  | <0.035  |
| MIBI with ABI               | 11.344 | 1  | <0.01   |
| MIBI with Planar Scan       | 5.436  | 1  | <0.02   |
| MIBI with True Positive     | 3.106  | 1  | 0.078   |

Table 1: Chi square values.

References

1. Wolfe JN (1986) Defining the outcome of critical ischaemia: a one year prospective study (seminar). Br J Surg 73: 321.
2. Remes L, Isoaho R, Vahlberg T, Hiekkanen H, Korhonen K, et al. (2008) Major lower extremity amputation in elderly patients with peripheral arterial disease: incidence and survival rates. Aging Clin Exp Res 20: 385-393.
3. Ohta T (1985) Noninvasive technique using thallium-201 for predicting ischaemic ulcer healing of the foot. Br J Surg 72: 892-995.
4. Seder JS, Botvinkin EH, Rahimtoola SH, Goldstone J, Price DC (1981) Detecting and localizing peripheral arterial disease: assessment of 201TI scintigraphy. AJR Am J Roentgenol 137: 373-380.
5. Harbert J, Da Rocha AFG (1984) Textbook of nuclear medicine, 2nd edition. New York: Lea Febriger.
6. Roon AT, Moore WS, Goldstone H (1977) Below-knee amputation: a modern approach. Am Surg 43: 153-154.
7. Christian Wi, Schiepers CA, Siegel ME (1988) Assessment of peripheral vascular perfusion of the lower extremities with MIBI (RP-30): a new noninvasive approach. Radiology 169: 336.
8. Dhekne RD, Moore WH, Ludwig EI, Long SE (1988) Skeletal muscle uptake of RP-30A in healthy individuals with stress and at rest. J Nucl Med 29: 775.
9. Ament W, Lubbers J, Rakhorst G, Vaalburg W, Verkerke GJ, et al. (1998) Skeletal muscle perfusion measured by positron emission tomography during exercise. Pflugers Arch 436: 653-658.
10. Owens S, Edwards P, Miles K, Jenner J, Allen M (1999) Chronic compartment syndrome affecting the lower limb: MIBI perfusion imaging as an alternative to pressure monitoring: two case reports. Br J Sports Med 33: 49-51.
11. Oshima M, Akanabe H, Sakuma S, Yano T, Nishikimi N, et al. (1989) Quantification of leg muscle perfusion using thallium-201 single photon emission computed tomography. J Nucl Med 30: 458-465.
12. Dabrowski J, Mikosiaski J, Kramierek J (2003) Scintigraphic and ultrasonographic assessment of the effect of lumbar sympathectomy upon chronic arteriosclerotic ischaemia of lower extremities. Nucl Med Rev Cent East Eur 6: 17-22.
13. Tellier P, Aquillanti S, Lecouffe P, Vasseur C (2000) Comparison between exercise whole body thallium imaging and ankle-brachial index in the detection of peripheral arterial disease. Int Angiol 19: 212-219.
14. Duet M, Virally M, Balliart O, Keverkian JP, Kedra AW, et al. (2001) Whole-body (201TI) scintigraphy can detect exercise lower limb perfusion abnormalities in asymptomatic diabetic patients with normal Doppler pressure indices. Nucl Med Commun 22: 949-954.

Submit your next manuscript and get advantages of OMICS

Group submissions

Unique features:
- User friendly/feasible website-translation of your paper to 50 world’s leading languages
- Audio Version of published paper
- Digital articles to share and explore

Special features:
- 400 Open Access Journals
- 30,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, IISSCC, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: www.editorialmanager.com/acrgroup