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Comparison of 18-FDG SUV Value with Bone Scintigraphy Findings in Diagnosed Cases of Malignancy with Sclerotic Bony Metastasis

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ABSTRACT

Objective: To determine the correlation of 18F-FDG SUV value with bone scintigraphy findings, i.e. uptake of Tc-99m in diagnosed cases of malignancy with sclerotic bone metastasis.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Armed Forces Institute of Radiology and Imaging, Rawalpindi Pakistan, from Sep 2020 to Mar 2021.

Methodology: This study included 30 patients of age 18 to 80 years who had sclerotic bone metastasis as confirmed in histopathology. All patients underwent whole-body PET/CT scanning to evaluate sclerotic bone metastasis and determined 18-FDG SUV after 5MBq/kg body weight of 18-FDG was injected. After two weeks of PET/CT scan, Tc-99m bone scintigraphy was carried out, and SUV of Tc-99m was determined after 20-25mCi technetium-99 methylene disphosphonate was injected, and the correlation was assessed between SUV of 18-FDG and Tc-99m.

Results: The mean 18-FDG SUVmax and mean Tc-99m SUVmax, were, 21.31±8.77g/ml and 15.29±6.49g/ml respectively. 21(70%) lesions on 18-FDG PET/CT and 8(26.7%) on Tc-99m bone scintigraphy were metastatic in bones. 18-FDG SUV on PET/CET and Tc-99m SUV on bone scintigraphy correlated positively with each other, and this correlation was found to be statistically significant (r=0.491, *p*=0.006).

Conclusion: 18-FDG SUV PET/CT significantly correlated with Tc-99m SUV on bone scintigraphy and helped detect metastatic lesions earlier and modulate treatment response.

Keywords: Bone metastasis, Bone scintigraphy, 18-FDG PET/CT, Tc-99m SUV.

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INTRODUCTION

The commonest site of distant malignant metastasis is the skeletal system.[1] It has been estimated that cumulative bone metastasis occurs in 2.9% of the patients.[1] For assessing such metastasis, the modality of choice is morphological imaging such as conventional radiographs, ultrasound, CT scan and MRI.[2] The newly introduced imaging techniques for such analysis are Bone scans and PET/CT.[3,4]

After introducing Technetium-99 methylenediphosphonate (Tc-99m), which was available readily, bone scintigraphy has become the commonest procedure that is carried out in the field of nuclear medicine for detecting involvement of skeletal tissue (metastasis) or at least detecting the extra-osseous uptake.[5]

PET/CT showed increased spatial resolution and higher sensitivity compared to the conventional gamma cameras, resulting in high-quality skeletal tissue imaging compared to bone scintigraphy.[6,7] Due to the increased availability of PET/CT, radiologists have started to have a growing interest in utilizing 18F-labeled-NaF as a radiotracer for imaging skeletal tissues since the previous limitations in terms of its usage daily due to technical and logistical restrictions are not present anymore.[8]

Despite its effectiveness in detecting skeletal tissue abnormalities, it is still being determined whether it is appropriate to shift from assessing malignant lesions anatomically to volumetric functional assessment with PET/CT9.[9,10] The study would help in highlighting the added value of metabolic imaging for evaluating the pathophysiological basis of sclerotic bony lesions that will be a valuable addition to the conventional assessment with imaging modality that is based solely on the morphology of tumours and thus can help in enhancing the diagnostic utility of various modalities by overcoming their limitations.

METHODOLOGY

This was a prospective longitudinal study, carried out at the Armed Forces Institute of Radiology and Imaging, Rawalpindi Pakistan, from September 2020 to

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March 2021. Approval for the study was taken from the Ethical Review Board. The sample size was calculated using the Raosoft sample size calculator, taking a 5% margin of error and the expected frequency of bone metastasis as 2.9%.[1] Non-probability consecutive sampling technique was used.

Inclusion Criteria: Patients aged 18 to 80 years, of either gender and with previously diagnosed primary malignancy and sclerotic bony metastasis as confirmed histologically by biopsy were included in the study.

Exclusion Criteria: Patients with benign bone lesions and osteoblastic metastasis, those with bony malignancy primarily, those who received radiotherapy in the last month and children were excluded from the study.

Demographical detail, clinical history and physical examination of all patients were carried out, and findings were noted in a predesigned proforma. All patients underwent whole-body PET/CT scanning to evaluate sclerotic bone metastasis. After two weeks of PET/CT scan, 99mTc-MDP bone scintigraphy was carried out. Before PET/CT, the patients were instructed to fast for 6 hours, except for water. They were further instructed to avoid extreme exercise for a minimum of 6 hours before the test was conducted to minimize uptake of 18-FDG in the muscles and reduce false positive results that were false positive. Blood glucose was monitored and was considered normal if it was <150mg/dl.[11] All patients were asked to void urine before the test, and then 5MBq/kg body weight of 18-FDG was injected into the patients. Data were acquired after 60-90 minutes of injecting 18-FDG. Instructions to the patients were given to stay laid down comfortably and avoid talking to avoid uptake of the tracer element false positive. The lesions were considered positive for uptake of 18-FDG on PET images if the foci were located away from the physiological areas (i.e. brain, myocardium, bowel, bladder and renal pelvis) which had high intake and the focus revealed higher FDG uptake, i.e. >19.5g/ml compared to the background and on CT scan it was confirmed that there was osteosclerotic lesion. If 18-FDG uptake was <19.5g/ml and was found in the joint or surface of bony tissue, that increased uptake was also labelled as negative. Further, CT data were used to attenuate PET images, and then the CT attenuation correction (CTAC) series was reconstructed. After 60 minutes of injecting the tracer element, a CT scan without contrast was carried out from the skull to mid-thigh. After scanning immediately with CT without IV iodinated contrast, PET data were gathered from the same locations anatomically. Consultants of the nuclear medicine and radiology department interpreted the results of the PET/CT. The lesion with the highest SUV was considered. SUVmax was defined as the maximum tissue FDG concentration ratio per millilitre of tissue to the activity injected per gram of the patient's body weight. The standardized uptake value (SUV) was calculated using the formula: SUV=ROIRC/(ID/BW)

Where, ROIRC=radioactivity concentration within the region of interest (in becquerels per millilitre), ID=injected dose of 18F-FDG (in becquerels), BW=body weight in grams.[12]

For bone scintigraphy, 20-25mCi Technetium-99 Methylene disphosphonate was injected into the patients, and after 2 to 4 hours of injection, images were taken. Images were taken from all bodies, both anteriorly and posteriorly (10-15cm/min speed of scan), and further projections, if required, were taken of the area of interest. Evaluation of the images was done visually as well as semi-quantitatively. To analyse semi-quantitatively, a region of interest (ROI) was drawn over the normal bone and bone lesion to have the maximum lesion-to-normal bone count ratio (ROImax), and Tc-99m SUV was calculated as well. Images of tumours on bone scintigraphy were classified positive (metastatic) depending upon the newly detected pathologically high Tc-99m uptake compared to the normal bone around the lesions. The value was above the cut-off. The cut-off value for labelling metastasis according to SUVmax on PET/CT and Bone scintigraphy was 19.5g/ml.[13] The 18-FDG PET/CT and bone scintigraphy findings were noted on the proforma and subjected to statistical analysis.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 25:00. Quantitative data were presented as mean and standard deviation. Qualitative data were presented as frequency and percentages. The Chi-square test and Pearson's correlation test were applied. The *p*-value of ≤0.05 was considered significant.

RESULTS

The mean 18-FDG SUVmax and mean Tc-99m SUVmax, were, 21.31±8.77g/ml and 15.29±6.49g/ml respectively. The location of the primary tumour was prostate in 13(43.3%), breast in 8(26.7%), thyroid in 4(13.3%), mucinous adenocarcinoma in 3(10.1%), transitional cell carcinoma in 1(3.3%) and lung carcinoid in 1(3.3%). On PET/CT, metastatic lesions were present in 21(70%) patients and on Bone scintigraphy, metastatic lesions were present in 8(26.7%) patients (Table-I).

Table-I: Descriptive Statistics of the Patients (n=30)

Parameters	Frequency (%)
Age Groups	
Young age (18 to 30 years)	3(10%)
Early middle age (31 to 45 years)	13(43.3%)
Late middle age (46 to 60 years)	5(16.7%)
Old age (61 to 80 years)	9(30%)
Location of primary tumor	
Male	1(70%)
Female	9(30%)
Location of primary tumor	
Prostate	13(43.3%)
Breast	8(26.7%)
Thyroid	4(13.3%)
Mucinous adenocarcinoma of colon	3(10.1%)
Transitional cell carcinoma	1(3.3%)
Lung carcinoid	1(3.3%)
Anatomical distribution of bony metastatic lesion	
Lumbar spine	7(23.3%)
Pelvis	4(13.3%)
Lower thoracic spine	4(13.3%)
Upper thoracic spine	2(6.7%)
Ribs and sternum	5(16.8%)
Cervical spine	1(3.3%)
Upper limb	3(10%)
Lower limb	1(3.3%)
Multiple areas	3(10%)
History of treatment	
Yes, chemotherapy alone	7(23.3%)
Yes, radiotherapy alone	11(36.7%)
Yes, combined chemotherapy and radiotherapy	4(13.3%)
No treatment	8(26.7%)
Lesions on PET/CT	
Positive	21(70%)
Negative	9(30%)
Metastatic lesions on Bone scintigraphy	
Yes	8(26.7%)
No	22(73.3%)

Metastatic lesions on PET/CT were identified in 3(10%) patients of young age,11 (36.7%) patients of early middle age, 2(6.7%) patients of late middle age and 5(16.7%) patients of old age. With respect to the location of metastasis, PET/CT revealed 10(33.3%) metastatic lesions in the prostate, 10(33.3%) in the breast, 3(10%) in the thyroid, 3(10%) in mucinous adenocarcinoma, 1(3.4%) in transitional cell carcinoma, however, the association was insignificant (p=0.315). In terms of the history of treatment, PET/CT revealed a metastatic lesion in 4(13.3%) patients with a history of chemotherapy, in 7(23.3%) patients with a history of radiotherapy and 2(6.7%) patients with a history of combined therapy, however, this association was also statistically insignificant (p=0.175) (Table-II).

In terms of the history of treatment, Bone scintigraphy revealed a metastatic lesion in 2(6.7%) patients with a history of chemotherapy, in 3(10%) patients with a history of radiotherapy and 3(10%) patients with a history of combined therapy and this association was statistically significant (p=0.05) (Table-III).

Table-II: Association of Study Parameters with 18-FDG PET/CT findings (n=30)

Parameters	18-FDG PET/CT Findings for Metastatic Lesion		*p*-value
	Negative (n=9)	Positive (n=21)	
Age Groups			
Young age (18 to 30 years)	0(0%)	3(10%)	0.130
Early middle age (31 to 45 years)	2(6.7%)	11(36.7%)	
Late middle age (46 to 60 years)	3(10%)	2(6.7%)	
Old age (61 to 80 years)	4(13.3%)	5(16.7%)	
Gender			
Male	5(16.7%)	16(53.3%)	0.258
Female	4(13.3%)	5(16.7%)	
Location of primary tumor			
Prostate	3(10%)	10(33.3%)	0.315
Breast	4(13.2%)	10(33.3%)	
Thyroid	1(3.4%)	3(10%)	
Mucinous adenocarcinoma of colon	0(0%)	3(10%)	
Transitional cell carcinoma	0(0%)	1(3.4%)	
Lung carcinoid	1(3.4%)	0(0%)	
History of Treatment			
Yes, chemotherapy alone	3(10%)	4(13.3%)	0.175
Yes, radiotherapy alone	4(13.3%)	7(23.3%)	
Yes, combined chemotherapy and radiotherapy	2(6.7%)	2(6.7%)	
No treatment	0(0%)	8(26.7%)	

Table-III: Association of Study Parameters with Bone Scintigraphy Findings (n=30)

Parameters	Bone scintigraphy Findings for Metastatic Lesion		*p*-value
	Negative (n=22)	Positive (n=8)	
Age Groups			
Young age (18 to 30 years)	1(3.3%)	2(6.7%)	0.097
Early middle age (31 to 45 years)	8(26.7%)	5(16.7%)	
Late middle age (46 to 60 years)	5(16.7%)	0(0%)	
Old age (61 to 80 years)	8(26.7%)	1(3.3%)	
Gender			
Male	16(53.3%)	5(16.7%)	0.589
Female	6(20%)	3(10%)	
Location of primary tumor			
Prostate	9(30%)	4(13.3%)	0.724
Breast	5(16.7%)	3(10.1%)	
Thyroid	4(13.3%)	0(0%)	
Mucinous adenocarcinoma of colon	2(6.7%)	1(3.3%)	
Transitional cell carcinoma	1(3.3%)	0(0%)	
Lung carcinoid	1(3.3%)	0(0%)	
History of treatment			
Yes, chemotherapy alone	5(16.7%)	2(6.7%)	0.05
Yes, radiotherapy alone	8(26.7%)	3(10%)	
Yes, combined chemotherapy and radiotherapy	1(3.3%)	3(10%)	
No treatment	8(26.7%)	0(0%)	

Correlation between mean 18-FDG SUVmax and Tc-99m SUVmax revealed significant positive correlations as was indicated by r of 0.491 and a *p*-value of 0.006 (Table-IV).

Table-IV: Correlation between 18-FDG SUVmax and Tc-99m SUVmax (n=30)

Parameters	Mean±Standard Deviation	Pearson correlation Coefficent "r"	*p*-value
18-FDG SUVmax	21.31±8.77	0.491	0.006
Tc-99m SUVmax	15.29±6.49		

DISCUSSION

The current study revealed that 18-FDG SUV on PET/CET and Tc-99m SUV on bone scintigraphy correlated positively with each other, and this correlation was found to be statistically significant (r=0.491, 0.006). This showed that a higher 18-FDG SUV on PET/CT was associated with a higher Tc-99m SUV on bone scintigraphy. Metastatic lesions confirmed initially by histopathology were more commonly detected by 18-FDG PET/CT compared to bone scintigraphy, i.e. 70% vs 26.7%. The results showed that bone scintigraphy findings were significantly associated with a previous history of treatment (*p*=0.05) and yielded more metastatic findings in those previously treated than those who did not receive any treatment. In comparison, PET/CT findings were not associated with previous treatment history. Other effect modifiers, such as age, gender and the primary tumour, had no significant association with metastatic findings on either PET/CT or bone scintigraphy.

In managing patients who have malignancies, imaging modalities such as bone scintigraphy and FDG PET/CT play a significant part.[11,12] Usually, bone scintigraphy images are visually assessed. There have been various studies that have used semi-quantitative analysis of bone scintigraphy.[13,14] The concentration of the tracer injected is measured by regional activity in certain areas as assessed on SPECT images. In the current study, to determine the osteosclerotic activity, the maximum uptake of the tracer element, i.e. SUVmax, was calculated by the ratio of maximum uptake by the metastatic lesion to surrounding normal bony tissue.[15]

In PET/CT, SUVmax is commonly determined for assessing the lesion's metabolic activity, and it can help differentiate benign lesions from malignant ones. Further, it can assess if the tumour is aggressive or not.[16] In a previous study conducted by Cook *et al*. it was revealed that sclerotic bony metastasis showed high uptake of 18-FDG in around 81% of the patients with osteolytic lesions, and 40% of those with sclerotic bony metastasis showed higher uptake on PET5. In the current study, around 70% of the patients with sclerotic bony metastasis showed increased 18-FDG uptake, which was more compared to the study done by Cook *et al*.[5] In a study by Ben-Haim, *et al*. it was revealed that sclerotic metastatic cells were comprised of less viable tumour cells and hence led to decreased uptake of tracer element in both 18-FDG PET/CT and Tc-99m bone scintigraphy.[2] The current study findings were in line with the findings in terms of low uptake of tracer elements on bone scintigraphy and PET/CT. However, 18-FDG PET/CT still showed a better detection rate and high value of 18-FDG SUV, thus, denoting that 18-FDG PET/CT was more helpful in detecting osteosclerotic bony metastasis compared to bone scintigraphy.[17,18]

The current study revealed that for assessing sclerotic bone metastasis, 18-FDG PET/CT could be very helpful in detecting such lesions earlier and modulating treatment response and thus overcoming the limitations of other diagnostic modalities such as bone scintigraphy, which often can miss the findings of a sclerotic metastatic lesion and may confuse it with a benign lesion, thus creating differences in the management of such patients. In addition, the study highlighted the added value of metabolic imaging for evaluating the pathophysiological basis of the sclerotic bony lesions, which can be a valuable addition to the conventional assessment with imaging modality that is based solely on the morphology of tumours and thus can help in enhancing the diagnostic utility of various modalities by overcoming their limitations.

LIMITATIONS OF STUDY

Only osteos-clerotic bony metastasis was assessed, and the SUV of 18-FDG on PET/CT and Tc-99m on bone scintigraphy were not assessed in osteoblastic and osteolytic metastasis, so the results cannot be justified for them.

CONCLUSION

18-FDG SUV PET/CT significantly correlated with Tc-99m SUV on bone scintigraphy and helped detect metastatic lesions earlier and modulate treatment response.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SW & TSS: Conception, study design, drafting the manuscript, approval of the final version to be published.

MM & HS: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

HS & KS: Critical review, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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