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Quantitative Analysis of ^{99m}Tc-MDP SPECT-CT Data in Diagnosing Bone Metastases in Breast Cancer Patients

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Abstract

Background: In patients with advanced breast cancer (BC), distant metastases happen mainly in the skeleton. This study aimed to investigate the role of ^{99m}Tc-MDP SPECT/CT in the differential diagnosis of malignant bone lesions from degenerative benign bone diseases in female BC patients.

Methods and Results: The study included 39 female BC patients who underwent a baseline ^{99m}Tc-MDP SPECT/CT bone scans. After lesion detection, a quantitative radiotracer uptake analysis was conducted, and the standardized uptake value (SUVmax) was identified in each patient, and the data were then statistically analyzed. SUVmax values were significantly higher in BC patients with malignant metastasis than in patients with degenerative changes (33.04±15.3 vs. 13.25±5.46 g/mL, $P<0.05$). The SUVmax cut-off value of 22.75 g/mL (25th percentile) obtained through box plot analysis can help to discriminate metastatic from degenerative lesions. The logistic regression analysis indicated that the SUVmax was a significant predictor of metastatic BL ($P<0.001$, OR = 159.90, B=5.07).

Conclusion: Our results suggested that quantitative analysis of the ^{99m}Tc-MDP SPECT-CT data can improve diagnostic accuracy in differentiating malignant metastatic bone lesions from degenerative bone lesions in high-risk BC patients.**(International Journal of Biomedicine. 2024;14(2):286-290.)**

Keywords: breast cancer • metastatic bone lesions • ^{99m}Tc-MDP • SPECT/CT • quantitative analysis

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Abbreviations

^{99m}Tc-MDP, ^{99m}Tc-labelled methylene diphosphonate; **BC**, breast cancer; **BL**, bone lesions; **DC**, degenerative changes; **SPECT/CT**, single photon emission computed tomography combined with computed tomography; **SUVmax**, standardized uptake value; **VOI**, volume of interest.

Introduction

Worldwide, BC is the most frequent tumor and occupies the first position in terms of incidence among women and the fifth position in terms of mortality.[1,2] For females, BC, colorectal cancer, and lung cancer account for 51% of all new diagnoses, with BC alone accounting for 32% of patients.[3] In Saudi Arabia, epidemiological studies reported that BC incidence was 19.8% of all tumor patients.[4,5]

In patients with advanced BC, distant metastases happen mainly in the skeleton. It was reported that 30%-85% of BC cases will develop bone metastases.[6,7] The thoracic spine, pelvis, and sternum are the most susceptible sites to metastases. However, some other bones are also involved in metastases, such as the femur, skull, and pelvis.[8-10] Bone metastases usually cause skeleton-related events such as hypercalcemia, pain, bone fractures, and spinal cord compression; thus, bone metastases in BC patients heavily affect patients' prognosis, life quality, and therapy procedure.[11] Consequently, skeletal metastasis response assessment and early diagnosis are even more important.[12,13] Moreover, sometimes, it is very difficult to make a differential diagnosis between degenerative benign and

malignant bone disease.[14] Despite planar bone scanning's, well-known limitations, such as poor specificity in response assessment and staging, it remains the main technique for detecting and staging skeleton lesions in cases of bone metastases risk.[7,15] Bone scanning accuracy is significantly improvable with the addition of single photon emission computed tomography combined with computed tomography (SPECT/CT).[16,17]

For visualizing skeletal lesions, bone scintigraphy using ^{99m}Tc-labelled methylene diphosphonate (^{99m}Tc-MDP) is the most frequent examination, including primarily either cancers or metastatic sites in other tumors, like BC.[7,13] To evaluate bone metastasis, whole-body bone scans using ^{99m}Tc-MDP are the most routine test.[18] The ^{99m}Tc-MDP biological distribution reveals high uptake in the urinary system and skeletal structure.[7]

This study aimed to investigate the role of ^{99m}Tc-MDP SPECT/CT in the differential diagnosis of malignant BL from degenerative benign bone diseases in female BC patients using an SUV (standardized uptake value) cut-off value.

Materials and Methods

Study design and patients' coherent and imaging protocol

Data were collected retrospectively, from January 2016 to March 2023. The information was gathered from two distinct database sources. The study included 39 female patients with BC. All patients underwent a baseline ^{99m}Tc-MDP SPECT/CT bone scan before their treatment, for staging purposes. However, any patients who had received therapy were excluded from the study.

The first database source was from Riyadh City Hospitals (Saudi Arabia). Patients had a baseline SPECT/CT. The dose was calculated using the patient's body weight, and an intravenous injection of 555-851 MBq equivalent to 15-23 mCi of ^{99m}Tc-MDP was administered. Images were taken 3 hours following the injection. A hybrid, SPECT/CT, dual-head gamma camera (GE Discovery D670) was used. Emission data were acquired using a parallel-hole, low-energy, high-resolution collimator with the patient in the supine position. The acquisition orbits were body contour orbits over 360° arcs, with 60 stops, each 6°. For 60 stops, emission data were acquired for 30 seconds per stop. The image acquisition matrix was 128×128, and the pixel size was 4.8 mm. Images were acquired on the 140 keV photo-peak with a 20% symmetrical window. SPECT was followed by CT examination with acquisition parameters of 130 kV, 100 mAs, Pitch-1, and 512×512 matrix using standard filters.

Additional secondary data were collected from an open-source platform, the Cancer Imaging Archive (TCIA), to improve the research analysis. TCIA is a service that provides a massive, publicly accessible archive of cancer-related medical images; it is financed by the Cancer Imaging Program. SPECT/CT data from University of Illinois Hospital was gathered from the second source. The patients had a bone scan for staging before they received their treatments, based on their body weight; (444–703 MBq), equivalent to 12–19 mCi of ^{99m}Tc-MDP intravenous injection, was administered, and a Siemens SPECT-CT camera was utilized to obtain the images after 3 hours of injection.

Image interpretation and quantitative assessment

The first database source images, from Riyadh City Hospital, were displayed on a workstation (GE Xeleris 4.0) for diagnosis by two experienced physicians, the initial qualitative examination was performed. As the physicians indicated, many regions with increased radiotracer activity were seen; out of the total number of patients, five were confirmed to have BC with bone metastases, with a mean age of 61±5 years. In contrast, four patients had confirmed BC but without bone metastases, with a mean age of 63±7 years. Next, Volumetrix GE Healthcare's Xeleris software was used to perform the quantitative SUV analysis using the following formula:[20]

$$SUV = \frac{C(T)}{[injected\ dose\ (Mbq)/patient\ weight(kg)]}\ ,$$

where C (T) reflects the radioactive concentration at a point in time.

The different SUVmax based on lean body mass for each patient was obtained. According to the vendor's recommendation, a volume of interest (VOI) was drawn using a multimodality computer platform, and then the SUVmax results were measured.

Regarding the second database, TCIA images revealed 13 patients with confirmed BC and bone metastasis with a mean age of 65±8 years, and 17 patients with confirmed BC and without bone metastasis with a mean age of 67±10 years. To obtain the quantitative analysis, we transferred the TCIA images to the 3D-slicer platform (version 4.10).[21] The SUVmax values were calculated from each segment using PET DICOM Extension installed on a 3D slicer.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). The normality of the distribution of continuous variables was tested by a one-sample Kolmogorov-Smirnov test. For comparisons between 2 independent groups, Student's t-test was applied. The boxplot was performed to define the cut-off value.[22] A logistic regression analysis was conducted to determine whether the SUV could predict the presence of degenerative or metastatic bone lesions. A probability value of $P<0.05$ was considered statistically significant.

Results

SUVmax values differentiated malignant lesions from degenerative bone changes

^{99m}Tc-MDP SPECT/CT (Figure 1) was performed for all patients, and the VOI was manually delineated for each image. We Collected the calculated SUVmax values for 39 patients with metastasis or degenerative changes (DC). In the normality test, SUVmax values of both metastasis (Figure 2A) and degenerative alterations (Figure 2B) were normally distributed. Quantitatively, SUVmax values were significantly higher in BC patients with malignant metastasis than in patients with DC (33.04±15.3 vs. 13.25±5.46 g/mL; P<0.05; Table 1). In the box plot, the cut-off was determined (25th percentile - 22.75 g/mL). The lower and upper quartiles and the median for metastasis (22.75, 45.11, and

30.27 g/mL, respectively) were higher than DC (9.50, 16.48, and 12.31 g/mL, respectively).

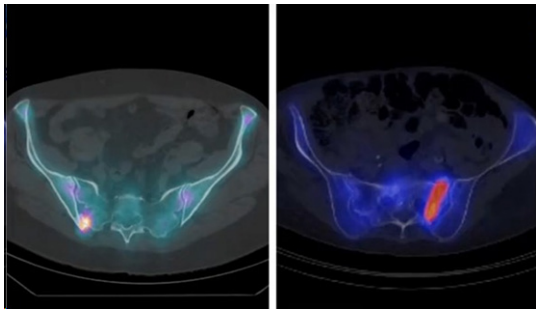

Fig. 1. *^{99m}Tc-MDP SPECT/CT bone scan of a 57-year-old female with a history of breast cancer who suffers from degenerative hip joints.*

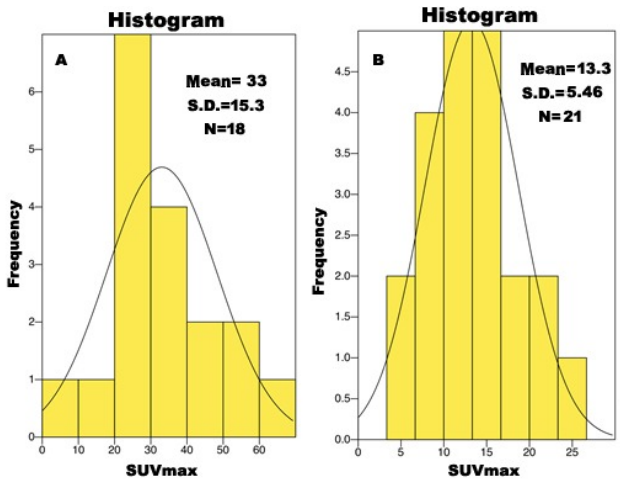

Fig. 2. *(A) SUVmax values for metastatic lesions and (B) degenerative alterations.*

Table 1.

Comparison of SUVmax values between BC patients with malignant bone metastasis and patients with benign degenerative changes.

Lesion type	Number	Minimum	Maximum	Mean	SD	t-test	*P*-value
Metastatic	18	7.44	65.8	33.04	15.3	5.21	<0.05
Degenerative	21	3.74	25.2	13.25	5.46		

Table 2.

Results of the logistic regression analysis.

Model Summary

-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
26.76	.50	.67

Classification Table

Observed			Predicted		
			Metastasis	DC	Percentage Correct
Step 1	Patient	Metastasis	15	3	83.33
		DC	3	18	85.71
	Overall percentage				84.62

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)	95% CI for Exp(B) Lower	Upper
Step 1	SUVmax	-.24	.08	10.33	1	.001	.78	.68	.91
	Constant	5.07	1.55	10.74	1	.001	159.90		

The logistic regression analysis indicated that the SUVmax was a significant predictor of metastatic BL (P<0.001, OR = 159.90, B=5.07; Table 2).

Discussion

BC represents one of the most frequently diagnosed tumors in female patients, with up to 75% of the patients with advanced stages of BC developing malignant metastatic BL.[23] In cancer patients, a planar whole-body bone scan is a sensitive and robust imaging technique to evaluate the presence of skeletal involvement. Unfortunately, this method suffers from low specificity and cannot differentiate benign skeletal lesions from malignant ones.[7,17] Thus, early detection of bone metastasis and differentiation from degenerative benign BL using molecular imaging modalities, such as SPECT-CT, is important for patient follow-up and therapeutic purposes.[24]

This study aimed to investigate the role of ^{99m}Tc-MDP SPECT/CT in the differential diagnosis of malignant BL from degenerative benign bone diseases in female BC patients using an SUVmax cut-off value. SUVmax values calculated from ^{99m}Tc-MDP SPECT/CT bone scan were normally distributed in both metastasis and degenerative alterations. SUVmax values were significantly (P<0.05) higher in BC patients with malignant metastasis (33.04±15.3 g/mL) than in patients with degenerative changes (13.25±5.46 g/mL). The box plot revealed a cut-off equal to 22.75 g/mL, and the logistic regression analysis indicated that SUVmax was a significant predictor of metastatic BL (P<0.001, OR= 159.90, B=5.07).

Skeletal structure uptake of radioactivity usually overlaps with radiopharmaceutical accumulation in several other benign disorders and situations, such as degenerative changes, trauma, and infection.[7,25] To a certain degree, SPECT-CT imaging resolves overlying activity superimposition, which causes a more accurate anatomical localization of skeletal lesions and helps differentiate malignant and benign lesions.[7,25]

Like our findings, other authors have reported that quantitative analysis of SPECT-CT data can enhance diagnostic accuracy in differentiating degenerative benign lesions from metastatic BL, leading to better follow-up and appropriate therapy in metastatic BC patients.[24] Arvola et al.[26] compared SUVmax between ^{18}F-NaF PET/CT and ^{99m}Tc-HDP SPECT/CT in bone metastases of BC and prostate cancer. They found that the measured SUVs very strongly correlated between PET and SPECT (R^2≥0.80, P<0.001), and this demonstrates that SPECT is an applicable tool for clinical quantification of bone metabolism in bone metastases in prostate cancer and BC patients. In metastatic BL, Gherghe et al.[24] reported that the SUVmax value of SPECT-CT was significantly greater than degenerative lesions. At a comparable cut-off value (16.6 g/mL) with our results, they found that SPECT-CT revealed a specificity of 93.3% and a sensitivity of 91.5%.[24] In prostate cancer patients, Rohani et al. evaluated bone scans with ^{99m}Tc-MDP SPECT/CT in differentiating patients with bone metastases from those with degenerative joint disease.[27] SUVmax was significantly greater in bone metastases than in normal vertebrae. SUVmax cut-off value ≥20 gave a specificity of 85.4% and a sensitivity of 73.8%

in differentiating bone metastases from degenerative joint disease.[27] Also, in patients with prostate cancer, Kuji et al.[28] evaluated the role of the skeletal SUVs by ^{99m}Tc-MDP SPECT/CT for differentiating active bone metastases from degenerative changes. They found that skeletal SUVmax may be helpful indices for bone metastatic prognostication, enhancing the discrimination of active bone osteoblastic metastases from frequently coexisting degenerative changes in patients with prostate cancer. Some studies revealed that SPECT/CT using different radiotracers significantly reduced equivocal findings in diagnosing bone metastases, which implies improved diagnostic confidence.[29-31]

In conclusion, our results suggested that quantitative analysis of the ^{99m}Tc-MDP SPECT-CT data can improve diagnostic accuracy in differentiating malignant metastatic BL from degenerative BL in high-risk BC patients. In BC patients, the SUVmax cut-off value of 22.75 g/mL obtained through box plot analysis can help to discriminate metastatic from degenerative lesions. Interpatient comparison, patient follow-up, and evaluation of treatment effectiveness may represent further benefits in performing ^{99m}Tc-MDP SPECT-CT SUVmax calculation. To use these findings in clinical practice, further extensive studies are required.

Ethical Considerations

The study protocol was reviewed and approved by the Ethics Committee at Princess Nourah bint Abdulrahman University.

Competing Interests

The authors declare that they have no competing interests.

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