ORIGINAL ARTICLE

BONY LESION ANALYSIS IN CARCINOMA PROSTATE: METHYLENE DIPHOSPHONATE BONE SCAN VS. GALLIUM-68 PSMA-11 PET/CT

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Background: Prostate cancer is the cause of the highest cancer-related death in males, 5-year survival is 31% in metastatic disease, and bone is a common site of metastases. Bone scintigraphy is a routinely used imaging modality for detecting skeletal metastases. It has variable sensitivity of 52–100%, whereas PSMA PET/CT scans have better sensitivity approaching 100%, so we determined the diagnostic accuracy, sensitivity, and specificity of planar M.D.P. (Methylene diphosphonate) bone scintigraphy. **Methods:** This analytical cross-sectional study was conducted at the N.M. & molecular imaging department of S.I.U.T. Karachi. Bone scans and PSMA-PET/CT scans of all patients who were visited from Janury-2018 to January 2023 were reviewed and interpreted by a nuclear physician& radiologist team. Inclusion criteria were histopathology-proven prostate cancer patients who had a bone scan and PSMA PET/CT scan within one month and had not received any treatment between scans. **Results:** Among 70 scans, 38 (54.2%) were positive for bone lesions. A total of 18 (47%) patients had positive bony lesions on both PSMA-PET/CT and Bone scintigraphy. Among 38 bone lesions positive patients, in eleven patients, bone lesions were detected only on PET/CT scans, whereas nine were positive only on Bone scans. The mean S.U.V. max of all bony lesions was 19.15 (range 3.2–57.5). The bone scan's sensitivity, specificity, and accuracy were 62.07%, 78.05%, and 62.87%, respectively. **Conclusion:** PSMA-PET/CT is better than bone Scintigraphy for detecting skeletal metastases. However, outcomes of bone scintigraphy may be improved when Tc-PSMA receptor bone scintigraphy is used.

Keywords: Prostate carcinoma; Bone metastases; PSMA-PET/CT; Bone scintigraphy

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INTRODUCTION

Prostate adenocarcinoma is one of the most typical cancers males may encounter and causes the highest number of cancer-related mortalities.[1] American Cancer Society estimates about 34,700 deaths from prostate cancer in the U.S. by 2023[2]. Cancer-related mortality calculates on the cancer stage at diagnosis as the five-year survival rate decreases from 100% in loco-regional to 31% in metastatic disease.[3] In Pakistan prevalence of prostate cancer ranged from 2–8% and the results age adjusted death rate is 5.99 per 100,000.[4,5] The stage of cancer also affects the management strategy.

Imaging modalities multipara metric M.R.I. (mpMRI), computed tomography (C.T.) scan, Bone scintigraphy (B.S.), and Prostate-specific membrane antigen (P.S.M.A.)-PET/CT scan is available for staging the carcinoma prostate. Osseous metastasis develops in more than 90% of prostate adenocarcinoma patients resulting in a reduction in survival.[6,7] The MDP-Bone scan is commonly advised due to having acceptable sensitivity and a relatively economical method for detecting bone metastases as part of staging workup.[8] The main shortcoming of B.S. in detecting skeletal metastases is that it depicts reactive osteoblastic activity rather than directly demonstrating the tumour, so early metastases and the osteolytic lesion may be missed, resulting in reduced sensitivity.[9] B.S. has limited specificity because many benign bone lesions and degenerative diseases are also detected as bone metastases, giving false positive results.[8]

Prostate-specific membrane antigen (P.S.M.A.) is a transmembrane receptor protein on the surface of prostate tissue and 1000 times over-expressed in prostate cancer cells.[10] In the current era of target-specific treatment and imaging, it is the area of interest for prostate cancer imaging and is under investigation with labelled with different radioisotopes. Ga-68 PSMA-11 PET CT is more sensitive and accurate than B.S. in determining bone marrow deposits and lytic lesions.[11] Both osteoblastic progressive metastases and bone healing after treatment show increased uptake in the lesion on B.S., and disease regression is nearly impossible to verify on follow-up scans.[12] PSMA-Ga-68 PET/CT scan solves this problem and can be assessed by measuring the change in the standard uptake value (S.U.V.).

H Gamma bone scintigraphy has inter-clinical reader variation in sensitivity range from 52–

100% in cancer patients.[13] We conducted this to see the sensitivity, specificity, and diagnostic accuracy of Tc-MDP bone scan keeping PSMA-Ga-68 PET/CT. We also compare the result of the Planar M.D.P. bone scan with the PSMA-PET/CT scan, as most previous studies compare the MDP-SPECT bone scan rather than the Planar M.D.P. bone scan.

MATERIAL AND METHODS

This analytical cross-sectional study was conducted at the N.M. & molecular imaging department of S.I.U.T. Karachi. Bone scans and PSMA-PET/CT scans of all patients visited from Janury-2018 to January 2023 were reviewed and interpreted by a team of nuclear physicians & radiologists. Inclusion criteria were histopathology-evident prostate adenocarcinoma patients who had a bone scan and PSMA PET/CT scan within one month and had not received any treatment between scans. Exclusion criteria were scan duration between PET/CT, and B.S. was more than one month, taking anticancer therapy between scans.

Approximately 20 milli curie of radiopharmaceutical (Tc99m-MDP) was injected in the peripheral vein for gamma MDP-bone scintigraphy. Planar images were acquired after 3 hours using a dual-head GE Infinia Gamma Camera with low energy high-resolution collimator. Scan parameters were a 10 cm/min scan speed, 128×128 matrices, and a zoom of 1.0.

For the 68Ga-PSMA PET/CT, 68Ga was extracted from the 68Ge/68Ga generator system and was labelled with PSMA-11 using a semi-automated module and good manufacturing practice-grade disposable cassettes and reagent kit (A.B.X. GmbH). Labelled PSMA-11-Ga-68 ligands were injected in the peripheral vein, and scans were acquired after 60 minutes. PET/CT scan was performed by Phillips Gemini PET-CT 64-slice scanner, and first plain C.T. scan followed by skull to knee P.E.T. scan was acquired. Scanning parameters for the C.T. scan were slice thickness 2 mm, 120 keV, and 50 mAs. All scans were interpreted by a team of nuclear physicians and radiologists using Phillips Fusion Viewer.

Results of 68Ga-PSMA PET-CT and B.S. were compared, and statistical analysis was done using MS Excel 2016 and Medcalc[12] online software.

RESULTS

Seventy patients fulfilled the inclusion criteria, and the mean age of included patients was 66.74 years. Among 70 scans, 38 (54.2%) were positive for bone lesions. PSMA-PET/CT detected bony lesions in 29 patients, and bone scans were positive in 27, as shown in Figure 1a. A total of 18 patients had positive bony lesions on both PSMA-PET/CT and MDP-Bone scintigraphy. A total of 11 PET/CT scans detected the osseous lesions, which were negative on the bone scan, whereas 09 patients were positive only on MDP-Bone scans, as shown in Figure-1b.

The mean S.U.V. max of all bony lesions was 19.15 (range 3.2-57.5). The detection of skeletal metastasis on bone scan and PSMA PET/CT scan images are shown in Figure 2. Figure 2.a) is PSMA-PET/CT image of a known prostate carcinoma patient with have a bone lesion in the left superior pubic ramus (thin arrow) and it is not appreciated on the bone scan of the same patient Figure 2.b). Fig 2.d is a bone scan of another prostate cancer patient that shows increased uptake in the left posterior rib (thin arrow) was absent on PET/CT scan image of the same patient Figure 2.c).

We also calculated the sensitivity, specificity, diagnostic accuracy, and positive and negative predictive value of Bone scintigraphy for detecting bone metastases keeping PSMA/PET CT scan as the gold standard, as shown in Table-1.

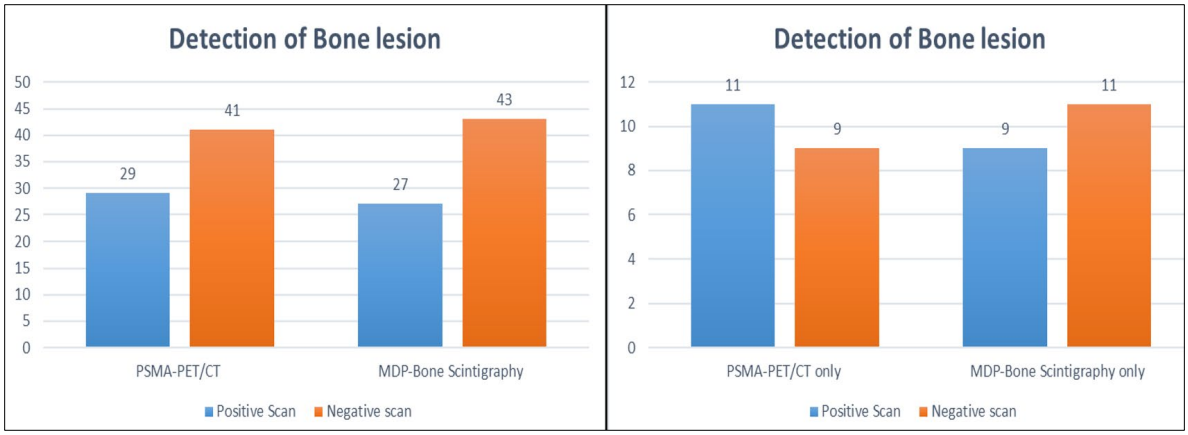

Figure-1: Detection of bone lesion on scan

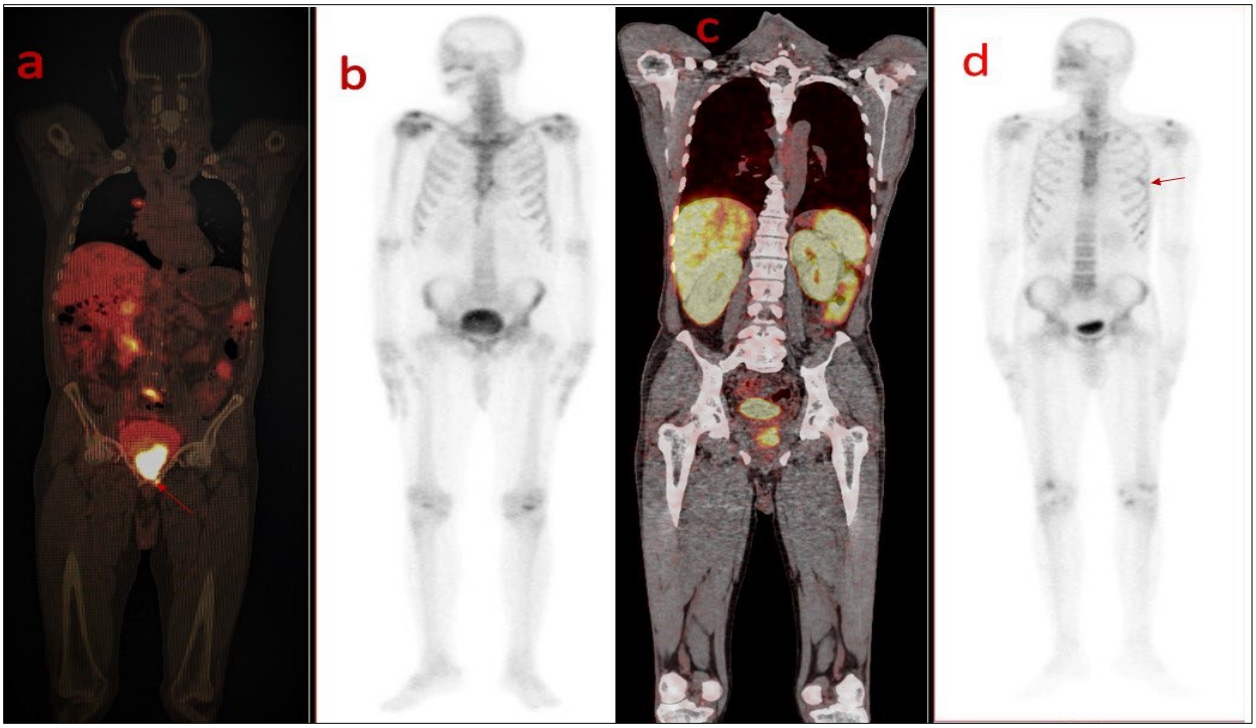

Figure-2: Bone lesion on PSMA-PET/CT & Bone Scan

Table-1: Diagnostic value of bone scan in detecting bone metastases

Statistic	Value
Sensitivity	62.07%
Specificity	78.05%
Positive Predictive Value	98.17%
Negative Predictive Value	9.77%
Accuracy	62.87%

DISCUSSION

Despite gamma, bone scintigraphy is easily accessible, and the cost-effective modality available for detecting bone metastasis has inter-clinical reader variation in sensitivity range from 52–100 cancer patients.[13–15] Gamma bone scintigraphy should be a part of staging workup in intermediate-high grade prostate adenocarcinoma patients but has a limited role in biochemically recurrent prostate cancer.[15–17] Compared with B.S., PSMA-PET-CT has better image quality, giving more information besides bone metastasis.[18]

PSMA-Ga-68 PET/CT scan has sensitivity and specificity of approximately 100% in searching for skeletal metastasis in the adenocarcinoma prostate group of patients.[19] We calculated the sensitivity and specificity of Tc-MDP bone scintigraphy for diagnosing osseous metastasis keeping PSMA-PET-CT findings as the gold standard. We found a sensitivity of 62.07% and a specificity of 78.05%. Thabo Lengana *et al*. conducted a study to analyze the PSMA-PET-CT scan and Tc-MDP-bone scintigraphy results in searching the skeletal metastasis. They found 36.7% of the bone scan were false positive and 8.4% false negative.[18] In our study, nine patients (33.3%) had false positives, and 11 (25.5%) bone scan were false negative results. False positive bone scan findings may be due to previous trauma, osteo degeneration, or other benign bone pathology. They also calculated the sensitivity and specificity of bone scans for searching osseous metastasis and found 73.1% and 84.1%, respectively. The mean SUVmax value of bony lesions in their study was 12.75, whereas, in our research, it is 19.15.

Our results are also comparable with Even-Sapir *et al*., who calculated sensitivity and specificity of planar bone scintigraphy were 70% and 57% in high-risk/metastatic prostate carcinoma, which were increased to 92% and 82% for bone SPECT.[12]

Zenus J Wilson *et al*. also compared the result of P.S.M.A. based PET/CT and Tc-MDP bone scintigraphy, and they noted 78% (71/91) concordance between PET/CT and bone scan findings. They found more concordance in results on bone metastases studies than positive scans, which were 81.7% (58/71) in negative studies and 18.3% (13/71) in positive studies.[20] In our research, concordance in scan findings was 71% (50/70), and concordance was also high in the bone lesion-negative scan, which was 64% (32/50).

We have some limitations in this study; there was no tissue diagnosis of the bony lesion, and we considered PSMA-PET/CT scan the gold standard. We have a small sample size and did not include the P.S.A. level/ Gleason Score to correlate with bony lesions. In the

future, study with large sample size and tissue diagnosis of bone lesions needs to be done.

CONCLUSION

We concluded that because of receptor specificity, Ga-68 PSMA-11 PET-CT has a decisive role in Prostate cancer management as it determines the appropriate disease status and is a superior imaging modality to M.D.P. bone Scan in the detection of skeletal metastasis. However, outcomes of bone scintigraphy may be improved when Technitium will label with PSMA peptide.

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Conflict of interest: None.

AUTHORS' CONTRIBUTION

HA: Data collection, data analysis, data interpretation, write-up. SRA: Proofreading, conceptualization of study design. AH: conceptualization of study design. NN: Scan interpretation and literature search.

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