https://doi.org/10.48047/AFJBS.6.2.2024.1472-1481

African Journal of Biological Sciences

ResearchPaper OpenAccess

Diagnostic value of ^{68}Ga-Labeled Prostate Specific Membrane Antigen ligand PET/CT in assessment and post therapeutic follow up in prostatic cancer

Manal Halim Wahba[1], Tamer Wahid Mahmoud Kassem[2], Alaa El-Din Wafik Meshref[3], Asmaa Sayed Eissa Farrag[4]

1 Professor of Radiodiagnosis, Faculty of Medicine, Cairo University.Email:manal_halim2002@yahoo.com
2 Professor of Radiodiagnosis, Faculty of Medicine, Cairo University. Email:tamerwahid@hotmail.com
3 Professor of Urology, Faculty of Medicine, Cairo University.Email:alaa.meshref@gmail.com
4 Radiodiagnosis specialist, Ministry of Health, Egypt.Email:asmaeissa87@gmail.com

Corresponding author: Asmaa Sayed Eissa Farragasmaeissa87@gmail.com
Mailing address: Hadaeq Al Qubbah, Cairo. Egypt.

Article History

Volume 6, Issue 2, April 2024

Received:3June 2024

Accepted: 2 July 2024

Published: 2 July 2024

doi:

10.48047/AFJBS.6.2.2024.1472-1481

Abstract:Background: The most widely studied type of PSMA based PET/CT is ^{68}Ga-labeled on the small molecular inhibitor PSMA-11 (also known as PSMAHBED-CC).**Objectives:** To assess the diagnostic value of ^{68}Ga-PSMAPET/CT in prostatic cancer patients referred for initial assessment and post therapeutic follow–up after prostatectomy+/- receiving adjuvant therapy. **Results:** 38 patients with PC performed ^{68}Ga-PSMA PET/CT scan for initial assessment of the disease; all of them (100%) showed prostatic activity, 26 (68.4%) showed nodal activity, 18 (47.4%) showed active osseous lesions and 7 (18.4%) showed active pulmonary nodules. In conventional CT,8(21%)showed prostatic disease, 18 (47.4%) showed metastatic lymphadenopathy, 24(63.2%) showed osseous lesionsand28 showed (73.7%) pulmonary nodules. Post-prostatectomy 24patients (+/-adjuvant therapy) presented by elevated serum PSA (ranging levels: 1-2ng/ml in 8patients &>2ng/ml in 16 patients. Operative bed recurrence was detected in 16 (100%) of patients with PSA level>2ng/mlandin62.5%(5)of patients with PSA level 1-2ng/ml. 18 patients performed complementary MRI for detection of prostatic lesions and that was compatible with the ^{68}Ga-PSMA PET/CT scan findings.**Conclusions:**^{68}Ga-PSMAPET/CT has higher sensitivity than CT conventional imaging for evaluation of the primary and metastatic disease. It gets near compatible findings with mpMRI in disease localization in the prostate. It can detect tiny metastatic lymph nodes beyond the resolution of CT scans. It can detect osseous metastasis with no underlying abnormality on conventional CT scans. The likelihood of a pathogenic^{68}Ga-PSMA PET/CT appears to be high in detection of disease recurrence with high PSA levels>2ng/ml and less at PSA levels<2ng/ml

Keywords:*prostatic cancer-68Ga-PSMA-PET/CT-PSA*

Introduction

The prostate specific membrane anti gene (PSMA) is a transmembrane protein with significantly elevated expression in PCcells compared to benign prostatic tissue **(1)**. The large transmembrane glycoprotein PSMA is composed of a significant extracellular component, a small intracellular component, and a transmembrane component **(2).**

PSMA overexpression has been discovered to be much higher in prostate cancer than in normal prostatic tissue, and it also increases with tumor grade and castrate resistance, making it one of the most attractive targets for PET imaging **(3).**

So far, several, mainly retrospective studies describe the value of ^{68}Ga-PSMA ligand PET/CT in different clinical scenarios **(1)**.All of them demonstrate a higher diagnostic efficacy of ^{68}Ga-PSMA ligand PET/CT compared to conventional imaging including PET with other tracers(e.g.,^{18}F-Choline,^{11}C-Choline) **(4)**.

Inparticular,^{68}Ga-PSMAligandPET/CTpromisesaccuratestagingofprimaryPCandre-stagingafterbiochemical recurrence. In a large study in primary intermediate to high-riskPC,^{68}Ga-PSMA-ligandimaginghasbeenreportedtoclearlyimprovedetection of lymph node metastases compared to morphological imaging thus potentially allowing for a more tailored therapeutic concept**(5)**. Similar encouraging results were obtained for patients with biochemical recurrence after radical prostatectomy **(4)**. Here, ^{68}Ga-PSMA ligand PET imaging has been shown to increase detection of metastatic sites even at low PSA-values in comparison to conventional imaging or PET examination with different tracers**(6)**.

The vast majority of PSMA-targeted PET radiotracers currently used in clinical practice 68Ga-labeled imaging agents **(7).**

Researchers found that 68Ga-PSMA PET/CT enabled the identification of one or more lesions in 83% of patients overall in a sizable study involving 319 individuals with biochemical recurrence, that even in patients with low PSA levels has great detection rates: 50% of cases were detected for individuals in the study with a serum PSA level of less than 0.5 ng/ml **(8).**

The aim of our study is to assess the diagnostic value of ^{68}Ga-PSMAPET/CT in prostatic cancer patients referred for initial assessment and post therapeutic follow–up after prostatectomy+/- receiving adjuvant therapy.

Patients and methods

The local ethical committee authorized the design of the study as prospective comparative study. Total 62 patients were studied. 38 individuals are pathologically proven to have prostate cancer (through TRUS-guided biopsies), were referred for initial assessment and metastatic work up. Other 24 individuals are post prostatectomy state presented by elevated serum PSA levels, were referred for follow-up to assess for the likelihood of recurrent illness. Their ages ranged 55:88 years (mean age 68.3years).

This study was carried out from January2019 to December2021.

The inclusion criteria include any patient with prostatic cancer detected by a TRUS guided biopsy for initial assessment. Also, patients who undergone prostatectomy +/- adjuvant therapy with a elevated serum PSA level for follow up.

Patients with impaired renal functions were excluded from receiving an iodinated IV contrast injection.

Imaging protocol: All exams were performed using Siemens BiographmCT20 Excel PET/CT. 18 individuals out of total 62 consented patients agreed to perform a complementary MRI for detection of prostatic lesions (to compare with the ^{68}Ga-PSMA PET/CT scan findings and for better anatomical details).

Patient preparation: Prior to the assessment, patients are requested to void and observe a 6-hour fast. All patients are asked to be well-hydrated before the study and during the uptake time (oral intake of 500mL of water during a 2-h period prior to acquisition).

Dosage administration: Intravenous bolus injection of 1.8–2.2 MBq/kg bodyweight (0.6 mCiper10 kilogram bodyweight) of ^{68} Ga. A 20-30 minutes interval before examination (Uptake time)**.** Examination time: Low

dose non-contrast CT scan done first, then attenuation correction of the whole body by ^{68}Ga-PSMA PET scan followed by a complete body enhanced CT scan. The entire study took approximately 20-35 minutes.

CT Technique: The contrast enhanced helical CT was performed following injection of 1- 2 ml/Kg of a low-osmolarity iodinated contrast medium at a rate of 4 ml/sec by using a power injector. For a typical whole body PET -CT study (neck, chest, abdomen, and pelvis), scanning began at the level of the skull base and extended caudally to the level of the mid thighs. Typical scanning parameters would be a collimator width of 5.0 mm, pitch of 1.5, gantry rotation time of 0.8 second, and field of view of 50cm. The helical data are retrospectively reconstructed at 1 mm intervals.

PET Technique: PET was performed following the CT study without moving the patient. Approximately six to seven bed positions are planned in the three- dimensional acquisition mode for scanning the entire patient with 3-5 minutes acquisition at each bed position.

PET/CT fusion: Hundreds of trans-axial PET and CT images were first reconstructed. These are then reformatted into coronal and sagittal images to facilitate image interpretation. For each of these sets of PET and CT images, corresponding "fusion" images, combining the two types of data, also were generated. The whole acquisition time for an integrated PET/ CT scan was approximately 25 min. PET image data sets were reconstructed using CT data for attenuation correction and co-registered images were displayed using special software.

Interpretation of the CT findings: Assessment of the prostatic volume and capsule for extra prostatic extensions. Detection of lymph nodes enlargement, osseous deposits, lungs and other soft-tissue lesions. Assessment of regional and distant lymph nodes regarding their size and morphology; they were considered malignant when measures more than 1.0 cm (short axis). The lymph nodes considered benign if calcified (like in mediastinal lymph nodes).Assessment of bone was done using bone window images for lytic, sclerotic lesions, extra osseous soft tissue component or pathological fractures. Pulmonary nodules were considered benign when measuring 4mm or less, calcified nodules, stable during the follow up. Lung nodules were considered malignant when newly developed or increasing in size or larger than 4 mm in diameter.

PET/CT interpretation: At multidisciplinary conference for reporting, all studies were evaluated by two nuclear medicine specialists and radiologists, as per institutional standards. Bone metastases and local recurrence were both characterized as the absence of morphological alterations. Because The CT detecting ability for these metastases is poor, increased localized tracer absorption in these areas was thought to be a sign of local recurrence or bone metastases even if there is no morphological relationship. The highest uptake plane for prostate lesions was used to place volumes of interest, and maximum standardized uptake values (SUVmax) were evaluated and reported. PSMA uptake was frequently observed but wasn't considered aberrant in the sacral, celiac, and stellate ganglia.

Statistical methods

Statistical analysis was done using IBM SPSS® Statistics version 26 (IBM® Corp., Armonk, NY, USA). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage.

Pearson's Chi-square test or Fisher's exact test was used to examine the relation between qualitative variables.

Evaluation of the Conventional CT and PET CT was done by calculating sensitivity, specificity, positive predictive values (PPV), negative predictive value (NPV).

Kappa test was used to evaluate agreement between two diagnostic methods (Conventional CT and PET CT). All tests were two-tailed. A p- value < 0.05 was considered significant.

Results

Total 62 patients were studied. Their ages ranged 55:88 years (meanage68.3years).1st group 38 individuals are pathologically proven to have prostate cancer (through TRUS-guided biopsies), were referred for initial assessment and metastatic work up. The ^{68}Ga-PSMA PET/CT findings in this group were compared with the

conventional CT findings. The 2nd group 24 individuals are posting prostatectomy state presented by elevated serum PSA levels, were referred for follow-up to assess for the likelihood of recurrent illness. 18 patients performed complementary MRI for detection of prostatic lesions and that was compatible with the ^{68}Ga-PSMA PET/CT scan findings.

In ^{68}Ga-PSMA PET/CT scan; all of the 1st group 38 patients (100%) showed prostatic activity, 26 (68.4%) showed nodal activity, 18 (47.4%) showed active osseous lesions and 7 (18.4%) showed active pulmonary nodules. In conventional CT, 8 (21%) showed prostatic disease, 18 (47.4%) showed metastatic lymphadenopathy, 24(63.2%) showed osseous lesionsand28 showed (73.7%) pulmonary nodules.

Sensitivity of ^{68}Ga-PSMA PET/CT in detection of cancer prostate was 100% and PPV=100%. Specificity or NPV could not be calculated since no negative cases by PET/CT were detected. Sensitivity of Conventional CT was 21%, PPV 100%.

According to **Fleiss et al. (2003)** in measure of agreement evaluation by Kappa value, ^{68}Ga-PSMA PET/CT study and conventional CT study showed fair agreement regarding the prostatic extra capsular extensions as well as nodal and osseous deposits with Kappa values=0.496, 0.587 & 0.689 respectively and p-value <0.001.

The 2nd group post-prostatectomy 24 patients (+/-adjuvant therapy) presented by elevated serum PSA (ranging levels:1-2ng/ml in 8 patients &>2ng/ml in 16patients.The rate of positive scans in evaluation of operative bed recurrence was 87.5%. The rate of positive scans was 20.8% for PSA levels 1-2 ng/mL and 66.6% for PSA levels >2ng/mL. It means that operative bed recurrence was detected in 16 (100%) of patients with PSA level>2ng/mlandin62.5%(5)of patients with PSA level 1-2ng/ml (P-value=0.028).No operative bed activity was detected in 3 individuals with PSA serum level 1-2ng/ml.

Cases

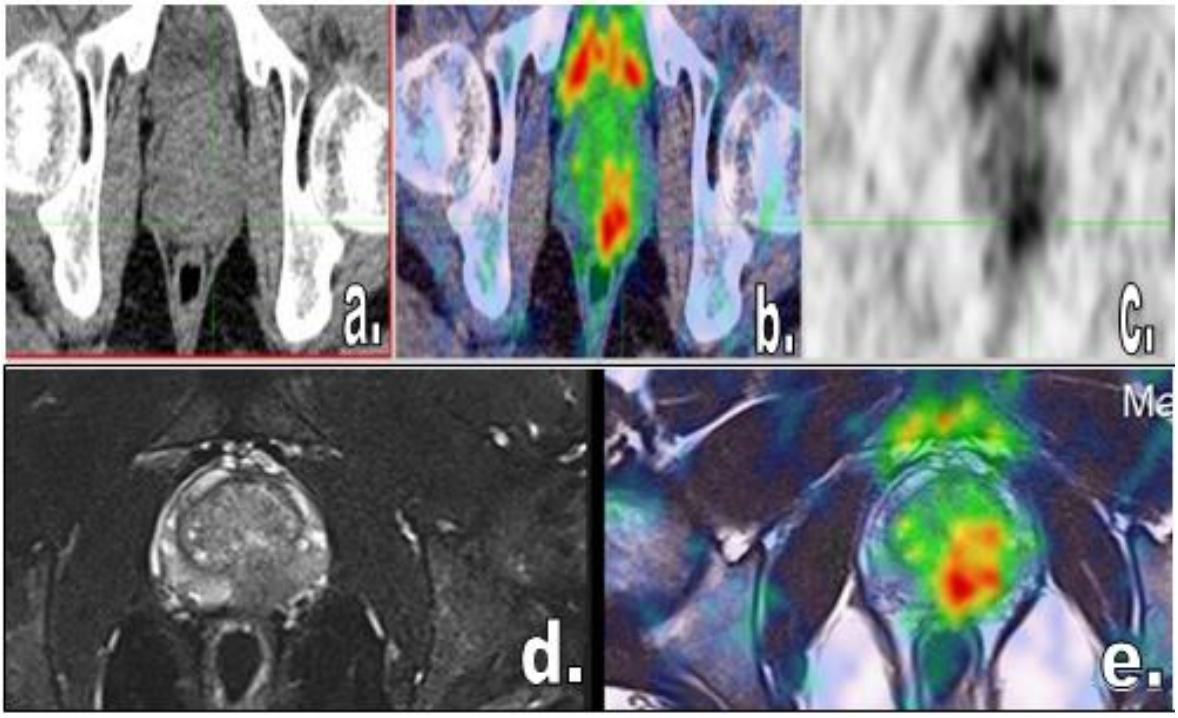


Figure 1: 63 years old patient presented by pathologically proven prostate cancer for 68Ga-PSMA PET/CT assessment and metastatic work up. **(a)** Axial conventional CT **(b)** axial fused PET/CT **(c)** axial MIP image **(d)** complementary axial STIR MR image (e) axial T2 MR Image with fusion show increased PSMA uptake within the left posterior peripheral zone (SUV max 5). Overlying left posterior capsular invasion and effaced recto-prostatic fat.

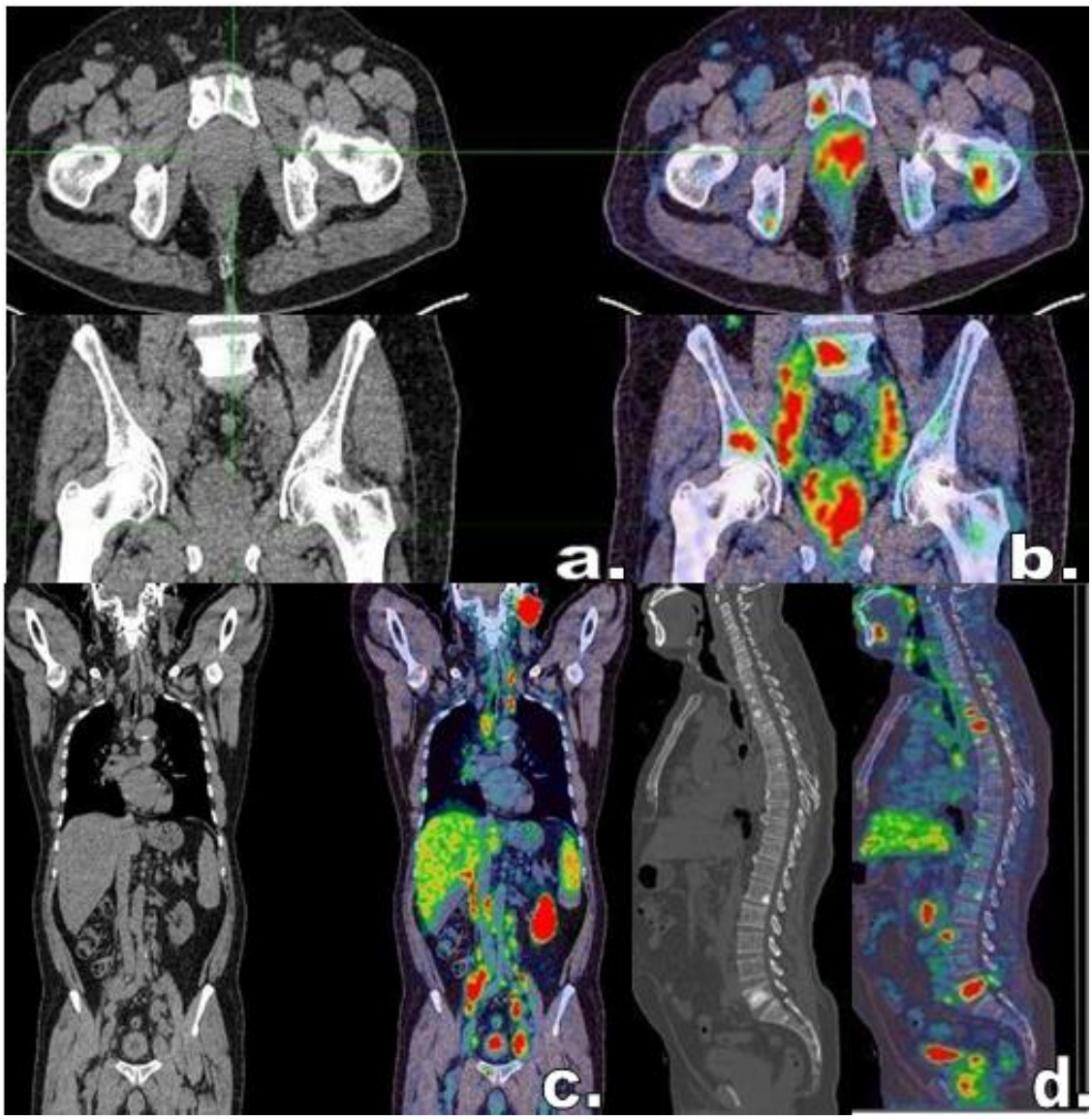
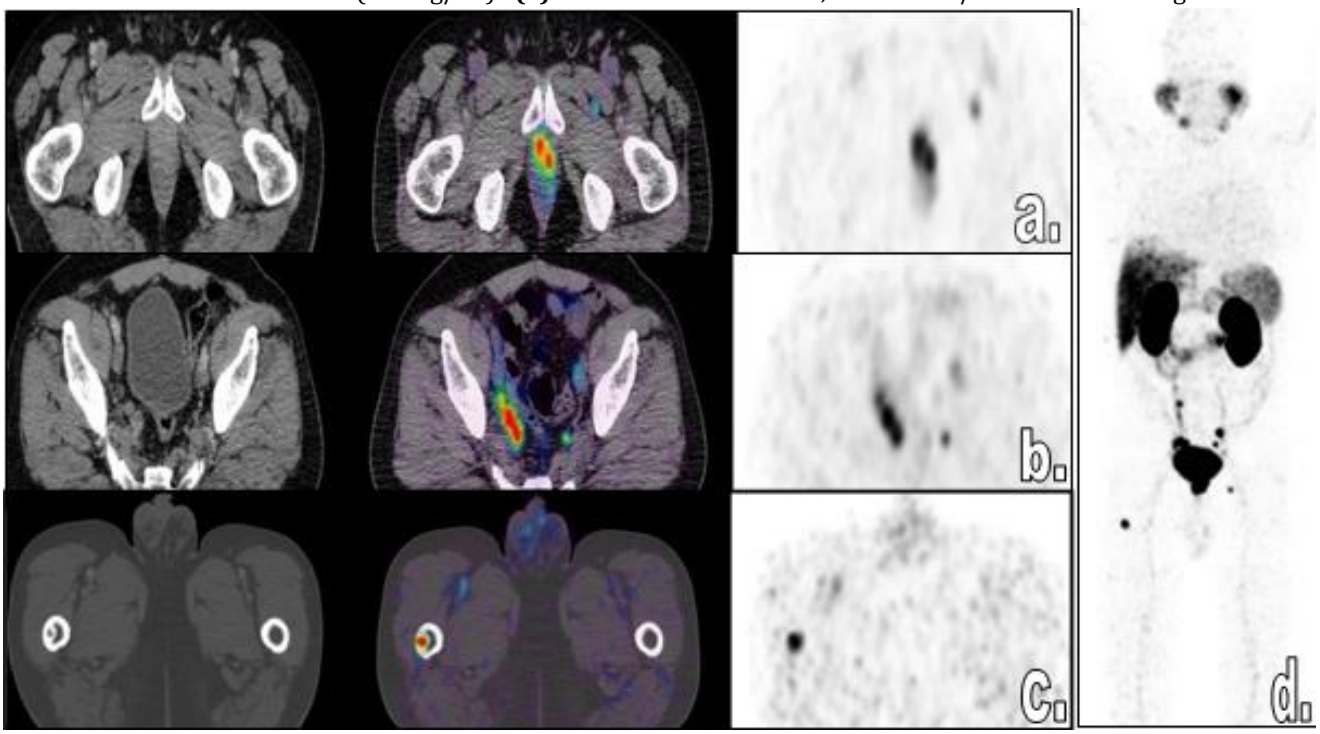


Figure 2: 53 years old patient presented by pathologically proven prostate cancer for ^{68}Ga-PSMA PET/CT assessment and metastatic work up. **(a)&(b)** axial and coronal conventional CT and fused PET/CT images of the prostate and pelvic bones show increased PSMA uptake by multiple confluent lesions within the gland (SUV max17.1) and the membranous urethra/external sphincter and sclerotic deposits within the right symphysis and left femur. **(C)** Coronal conventional CT and fused PET/CT images show PSMA active cervical, mediastinal and pelvi-abdominal lymphadenopathy (mot active is left external iliac (SUVmax 54). **(d)** Sagittal conventional CT bone window and fused PET/CT images show multiple spinal sclerotic deposits (SUVmax 18.1).

Figure 3: 68 years old patient underwent radical prostatectomy on hormonal treatment presented with elevated serum PSA level (11.5ng/ml). **(a)** axial conventional CT, fused PET/CT and MIP images show



operative bed recurrence (SUVmax35.1). **(b)** axial conventional CT, fused PET/CT and MIP images show right internal iliac nodal deposits (SUVmax34.3).**(C)** axial conventional CT bone widow, fused PET/CT and MIP images show right femur osseous deposit (SUVmax22.9). **(d)** Coronal MIP images of whole body show the operative bed recurrence, nodal deposits and right femoral osseous deposit.

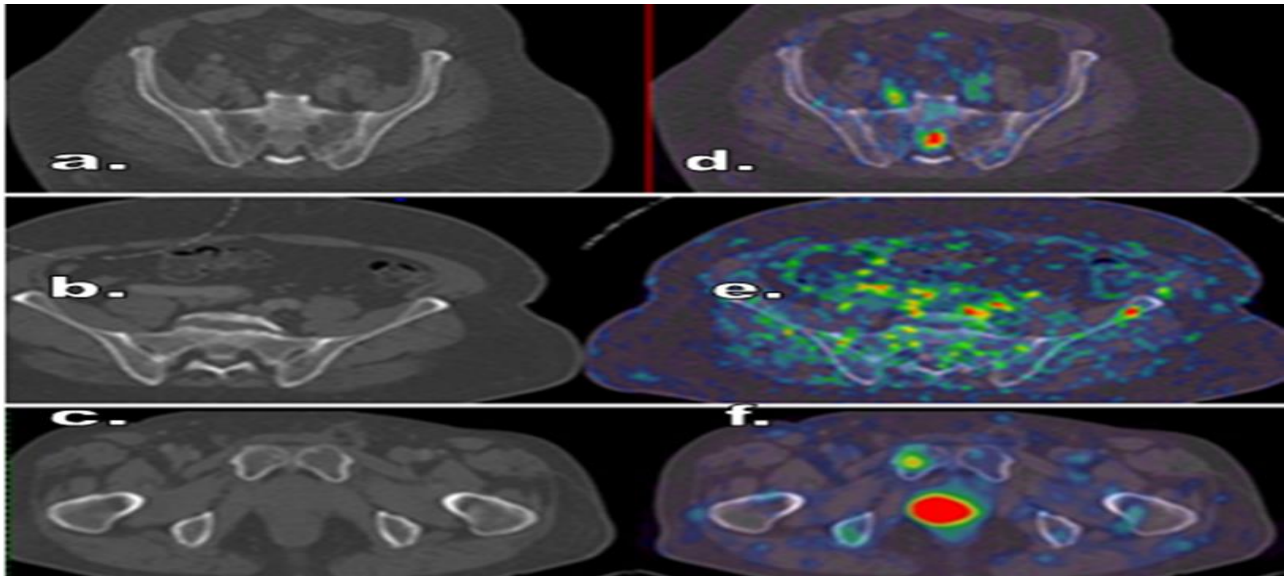


Figure 4:(a, b, c) axial conventional CT bone window of three different cancer prostate patients show no osseous abnormality **(d, e & f)** showosseous depositsin sacrum (SUVmax 20.3), left iliac bone (SUVmax 4.9), right pubic bone (SUVmax 3.1).

DISCUSSION

Conventional imaging techniques, such as Computed Tomography (CT) or multi-parametric magnetic resonance imaging (mpMRI), have been used to substantiate the diagnostic value. Given its poor sensitivity and specificity, anatomical diagnosis with CT of the prostate gland has been primarily used to stage the disease once diagnosis has been established. Computed tomography may reveal metastatic spread to pelvic lymph nodes, seminal vesicles, osseous metastases but is inherently based on changes in anatomy, particularly with regard to size. Thus, the failure to provide information pertaining to tumor metabolic activity limits its use to the early stage of disease **(9)**.

Gallium68-ligand-PSMA is a new radiotracer with great diagnostic potential in prostate cancer patients **(10)**.

The purpose of our study is to assess the diagnostic value of ^{68}Ga-PSMA PET/CT in prostatic cancer patients referred for initial assessment and post therapeutic assessment.

Total 62prostate cancer patients were studied.1st group 38 individuals were referred for initial assessment and metastatic work up. The ^{68}Ga-PSMA PET/CT findings in this group were compared with the conventional CT findings. The 2nd group 24 individuals are post prostatectomy state presented by elevated serum PSA levels, were referred for follow-up to assess for the likelihood of recurrent illness. 18 patients performed complementary MRI for detection of prostatic lesions and that was compatible with the ^{68}Ga-PSMA PET/CT scan findings.

Sensitivity of ^{68}Ga-PSMA PET/CT in detection of cancer prostate was 100% and PPV=100%. Sensitivity of Conventional CT was 21%, PPV 100%.^{68}Ga-PSMA PET/CT study and conventional CT study showed fair agreement regarding the prostatic extra capsular extensions as well as nodal and osseous deposits with Kappa values=0.496, 0.587 & 0.689 respectively and p-value <0.001.

Our results were matched with the systematic review and meta-analysis; conducted seven studies comprising 389 patients and published by **Satapathy et al., 2021 (11)**.in the American Journal of Roentgenology. The author reported that the pooled sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for the initial diagnosis of PCa using 68 Ga-PSMA were 0.97 (95% CI, 0.90–0.99), 0.66 (95% CI, 0.52–0.78), 2.86(95% CI, 1.95–4.20), and 0.05 (95% CI, 0.01–0.15), respectively.

Our results are near compatible with **Von Klot et al.,2017 (12)** study that included 21 patients and found that sensitivity, specificity, positive predictive value and negative predictive value were, respectively, 94.7%, 75.0%, 97.3% and 60.0% for intra prostatic tumor infiltration, 75.0%,100.0%, 100.0% and 97.4% for SVI, and 90.0%, 90.9%, 90.0% and 90.9%for ECE.

Our results appear compatible with **Maurer et al.,2016(13)** who compared^{68}Ga-PSM-PET/CT to conventional imaging (CT and MRI) for the detection of LNM for patients prior to RP and pelvic LND.^{68}Ga-PSMA-PET/CT resulted in a sensitivity and specificity of 65.9% and 98.9% on a per-patient level compared with 44.9% and 85.4% for conventional imaging.

Rauscher et al., 2016(14) also performed a comparison on ^{68}Ga-PSMA- PET/CT with traditional morphological imaging in detecting LNMs prior to salvage LND. From this, ^{68}Ga-PSMA-PET/CT had a resulting sensitivity and specificity of 78% and 97%. In comparison, morphological imaging [CT and magnetic resonance imaging (MRI)] had a sensitivity of 27% and specificity of 99%.

In 2016 Maurer and colleagues**(15)** retrospectively reviewed 130 patients with intermediate-to-high-risk PC who had undergone initial staging with both conventional (CT or MR) and ^{68}Ga-PSMA-11 PET imaging prior to radical prostatectomy (RP) with pelvic lymph node dissection (PLND). Thirty-one percent of patients had lymph node metastases at the time of surgery, and ^{68}Ga-PSMA-11 PET significantly outperformed conventional morphologic imaging with patient-based sensitivities of 65.9% versus 43.9%, and diagnostic accuracies of 88.5% versus 72.3%, respectively.

In a study performed for detection of false positive prostate cancer bone metastasis; **Abubakar et al., 2018(16)**reported a patient with high-risk prostate cancer with features consistent with skeletal metastases on MRI but negative for skeletal metastases on bone scan and ^{68}Ga PSMA PET CT. Histology confirmed the

absence of skeletal metastases. This can justify the conventional CT higher sensitivity in our study compared to PSMA PET/CT and confirms the high specificity of 68Ga-PSMA in diagnosis of bone metastasis.

The 2nd group post-prostatectomy 24patients (+/-adjuvant therapy) presented by elevated serum PSA. The rate of positive scans in evaluation of operative bed recurrence was 87.5%. The rate of positive scans was 20.8% for PSA levels 1-2 ng/mL and 66.6% for PSA levels >2ng/mL.In other words; the operative bed recurrence was detected in 100% of patients with PSA level>2ng/mlandin62.5%ofpatients with PSA level 1-2ng/ml (P-value=0.028).No operative bed activity was detected in 3 individuals with PSA serum level 1-2ng/ml.Our findings appear to be near comparable to findings from the two largest meta-analyses and a large prospective study **(17-20)**that reported the detection rate ranges from 74 to 81%, and that the pooled estimated rate of positive scans are correlated with the PSA level. It is also matched with study done by **Bois et al.,2020 (21)**where the rate of positive scans was 42- 57% for PSMA levels of 0.2-0.99 ng/mL, 58-84% for PSMA levels of 1.0-1.99 ng/mL, 76% for PSMA levels of 2.0-2.99 ng/mL, and 95% for PSMA levels above 2 ng/mL.

Study limitations

First, the lack of a histopathological gold standard of the metastatic nodal and osseous lesions to calculate the specificity of our imaging modality. Second, NPV could not be calculated since no negative cases detected by PET/CT in the group of initial staging. Third, lacking of including post prostatectomy patients with serum PSA level <0.5ng/mL to get more clinical value in detection of biochemical recurrence.

Conclusions

^{68}Ga-PSMAPET/CT is a superior modality of higher sensitivity than CT conventional imaging for evaluation of the primary and metastatic prostate cancer and near compatible with mpMRI in evaluation of the local disease. It can detect tiny metastatic lymph nodes beyond the resolution of CT scans. It can detect osseous metastasis with no underlying abnormality on conventional CT scans. The pathogenic likelihood of ^{68}Ga-PSMA PET/CT in the detection of disease recurrence appears to be higher in individuals with higher PSA levels.

List of abbreviations

PSA	Prostate specific antigen
PET/CT	Positron emission tomography/ Computed Tomography
PSMA	Prostaticspecific membrane antigen
^{68}Ga-PSMA	Gallium 68 prostaticspecific membrane antigen.
mpMRI	Multiplanar magnetic resonance imaging
LNM	Lymph node metastasis
LND	Lymph node dissection
ECE	Extracapsular extension
PCa	Prostate cancer
PC	Prostate cancer
IV	Intravenous.

SUV Standardized uptake value

References:

1. Rauscher I, Maurer T, Fendler WP, Sommer WH, Schwaiger M, Eiber M. 68 Ga-PSMA ligand PET/CT in patients with prostate cancer: how we review and report. Cancer Imaging. 2016 Dec; 16:1-0.
2. Wallitt KL, Khan SR, Dubash S, Tam HH, Khan S, Barwick TD. Clinical PET imaging in prostate cancer. Radiographics. 2017 Sep;37(5):1512-36.
3. Silver DA, Pellicer I, Fair WR, Heston WD, Cordon-Cardo C. Prostate-specific membrane antigen expression in normal and malignant human tissues. Clin Cancer Res. 1997;3:81-85.
4. Eiber M, Weirich G, Holzapfel K, Souvatzoglou M, Haller B, Rauscher I, Beer AJ, Wester HJ, Gschwend J, Schwaiger M, Maurer T. Simultaneous 68Ga-PSMA HBED-CC PET/MRI improves the localization of primary prostate cancer. European urology. 2016 Nov 1;70(5):829-36.
5. Maurer, T., Gschwend, J.E., Rauscher, I., Souvatzoglou, M., Haller, B., Weirich, G., Wester, H.J., Heck, M., Kübler, H., Beer, A.J. and Schwaiger, M., 2016. Diagnostic efficacy of 68gallium-PSMA positron emission tomography compared to conventional imaging for lymph node staging of 130 consecutive patients with intermediate to high risk prostate cancer. The Journal of urology, 195(5), pp.1436-1443.
6. Afshar-Oromieh A, Zechmann CM, Malcher A, Eder M, Eisenhut M, Linhart HG, Holland-Letz T, Hadaschik BA, Giesel FL, Debus J, Haberkorn U. Comparison of PET imaging with a 68 Ga-labelled PSMA ligand and 18 F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. European journal of nuclear medicine and molecular imaging. 2014 Jan;41: 11-20.
7. Lutje S, Heskamp S, Cornelissen AS, Poeppel TD, van den Broek SA, Rosenbaum-Krumme S, et al. PSMA Ligands for Radionuclide Imaging and Therapy of Prostate Cancer: Clinical Status. Theranostics. 2015; 5: 1388-401.
8. Afshar-Oromieh A, Avtzi E, Giesel FL, et al. The diagnostic value of PET/CT imaging with the 68Ga-labelled PSMA ligand HBED-CC in the diagnosis of recurrent prostate cancer. Eur J Nucl Med Mol Imaging 2015;42(2):197–209.
9. Sharma S. Imaging and intervention in prostate cancer: Current perspectives and future trends. Indian Journal of Radiology and Imaging. 2014 May;24(02):139-48.
10. Bural G, Torigian D, Alavi A. Gallium 68-ligand-PSMA PET/CT and PET/MRI in the diagnostic work-up of Prostate Cancer.The Journal of Nuclear Medicine, vol. 60 no. supplement2019; 1-1140.
11. Satapathy S, Singh H, Kumar R, Mittal BR. Diagnostic accuracy of 68Ga-PSMA PET/CT for initial detection in patients with suspected prostate cancer: a systematic review and meta-analysis. American Journal of Roentgenology. 2021 Mar 22;216(3):599-607.
12. Christoph A, MERSEBURGER AS, BÖKER A, SCHMUCK S, ROSS TL, BENGEL FM, KUCZYK MA, HENKENBERENS C, CHRISTIANSEN H, WESTER HJ, SOLASS W. ^{68}Ga-PSMA PET/CT Imaging Predicting Intraprostatic Tumor Extent, Extracapsular Extension and Seminal Vesicle Invasion Prior to Radical Prostatectomy in Patients with Prostate Cancer. Nuclear Medicine and Molecular Imaging. 2017:314-22.
13. Werner RA, Derlin T, Lapa C, Sheikbahaei S, Higuchi T, Giesel FL, Behr S, Drzezga A, Kimura H, Buck AK, Bengel FM. 18F-labeled, PSMA-targeted radiotracers: leveraging the advantages of radiofluorination for prostate cancer molecular imaging. Theranostics. 2020;10(1):1.
14. Rauscher I, Maurer T, Beer AJ, Graner FP, Haller B, Weirich G, Doherty A, Gschwend JE, Schwaiger M, Eiber M. Value of 68Ga-PSMA HBED-CC PET for the assessment of lymph node metastases in prostate cancer patients with biochemical recurrence: comparison with histopathology after salvage lymphadenectomy. Journal of Nuclear Medicine. 2016 Nov 1;57(11):1713-9.
15. de Kouchkovsky I, Aggarwal R, Hope TA. Prostate-specific membrane antigen (PSMA)-based imaging in localized and advanced prostate cancer: a narrative review. Translational andrology and urology. 2021 Jul;10(7):3130.
16. Abubakar S, Amoako Y, Tag N, Kotze T. False-positive prostate cancer bone metastases on magnetic resonance imaging correctly classified on gallium-68-prostate-specific membrane antigen positron emission tomography computed tomography. World Journal of Nuclear Medicine. 2018 Oct;17(04):305-7.
17. von Eyben FE, Picchio M, von Eyben R, Rhee H, Bauman G. 68Ga-labeled prostate-specific membrane antigen ligand positron emission tomography/computed tomography for prostate cancer: a systematic review and meta-analysis. European urology focus. 2018 Sep 1;4(5):686-93.
18. Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, Bolton D, Lawrentschuk N. Sensitivity, specificity, and predictors of positive 68Ga–prostate-specific membrane antigen positron emission tomography in advanced prostate cancer: a systematic review and meta-analysis. European urology. 2016 Dec 1;70(6):926-37.
19. Müller J, Ferraro DA, Muehlematter UJ, Garcia Schüler HI, Kedzia S, Eberli D, Guckenberger M, Kroeze SG, Sulser T, Schmid DM, Omlin A. Clinical impact of 68 Ga-PSMA-11 PET on patient management and outcome, including all patients referred for an increase in PSA level during the first year after its clinical introduction. European journal of nuclear medicine and molecular imaging. 2019 Apr 1;46:889-900.

20. Fendler WP, Calais J, Eiber M, Flavell RR, Mishoe A, Feng FY, Nguyen HG, Reiter RE, Rettig MB, Okamoto S, Emmett L. Assessment of 68Ga-PSMA-11 PET accuracy in localizing recurrent prostate cancer: a prospective single-arm clinical trial. JAMA oncology. 2019 Jun 1;5(6):856-63.
21. prostate cancer: a comprehensive review. American journal of nuclearmedicineandmolecularimaging,10(6),349–374.