Original Article

Comparison of Multiparametric Magnetic Resonance Imaging and Gallium-68 Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography for Detecting Carcinoma Prostate in Patients with Serum Prostate-Specific Antigen between 4 and 20 ng/ml

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Abstract

Introduction: We carried out this study to compare the diagnostic accuracy of multiparametric magnetic resonance imaging (mpMRI) and gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography (Ga-68 PSMA PET/CT) to detect prostatic carcinoma in patients with serum prostate-specific antigen (PSA) between 4 and 20 ng/ml in prebiopsy setting. **Materials and Methods:** This prospective study evaluated men with serum PSA values between 4 and 20 ng/ml. All patients underwent mpMRI and Ga-68 PSMA PET/CT, followed by 12-core transrectal ultrasonography (TRUS)-guided biopsy to detect prostatic carcinoma. The diagnostic accuracy of mpMRI and PSMA PET/CT scan was compared with histopathological findings. **Results:** There were thirty patients included in the study with a median age of 73 years (age range: 69–79 years). The median total serum PSA was 8.0 ng/ml (5.0–19.9 ng/ml). Of these, 18 had an identifiable lesion on imaging and had histopathological findings suggestive of carcinoma prostate. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of mpMRI were 100%, 92.30%, 94.73%, and 100%, respectively, and that of PSMA PET scan were 94.44%, 100%, 100%, and 92.31%, respectively. The diagnostic accuracy of both was 96.67%. **Conclusion:** PSMA PET scan showed higher PPV and specificity while mpMRI showed higher sensitivity and NPV. The accuracy in predicting presence of carcinoma was the same for both. PSMA PET showed higher specificity and PPV and predicted the subsequent need of biopsy. In our study, the NPV of PET, though good, was lower than mpMRI. Prospective trials with larger sample size are needed. In combination, PET/MRI may achieve greater accuracy and may serve as investigation of choice.

Keywords: *Carcinoma prostate, gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography, guided biopsy, multiparametric magnetic resonance imaging, prostate-specific antigen*

Introduction

Prostate carcinoma is one of the most common forms of cancer in men and has a documented increasing incidence. Transrectal ultrasonography (TRUS)-guided biopsy is considered the gold standard for the diagnosis; however, the false-negative rate is significant.[1] Men with a clinical suspicion of prostatic carcinoma on the basis of an elevated prostate-specific antigen (PSA) level or an abnormal digital rectal examination (DRE) are typically evaluated with standard TRUS-guided biopsy of the prostate during which 12 cores are obtained. This approach is associated with the underdetection of high-grade (clinically significant) prostate cancers and the overdetection of low-grade (clinically insignificant) cancers.[2] Moreover, TRUS-guided biopsy is an invasive procedure with complications.[3] Gallium-68 (^{68}Ga)-prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) is now popular in imaging of prostatic carcinoma, and recent guidelines on the use of ^{68}Ga-PSMA PET/CT in prostatic carcinoma imaging have been published.[4] In ^{68}Ga-PSMA PET-CT scan done for initial staging in patients with biopsy-proven prostate carcinoma, 98.5% showed an abnormal tracer concentration in the prostate gland

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suggestive of the primary site.[1] Multiparametric magnetic resonance imaging (mpMRI) has improved lesion detection in prostate cancer care by identifying suspicious lesions suitable for MRI-TRUS fusion biopsy. However, there is a considerable false-positive rate for mpMRI.[5] Furthermore, mpMRI is not disease specific, and many benign conditions such as acute and chronic prostatitis or postbiopsy changes can give false-positive results and thus may result in an unnecessary biopsy. Besides these, the field of evaluation is usually limited to the pelvis, and separate imaging is usually required to image for distant metastasis.[6,7] Ga-68 PSMA PET/CT has been introduced and is gradually establishing its place in the diagnostic algorithm of prostatic carcinoma. A distinct advantage of ^{68}Ga-PSMA PET scan is that PSMA is overexpressed by 100–1000 folds in prostatic malignancy as compared to benign tissue which theoretically makes PSMA PET scan relatively specific to malignant transformation as compared to mpMRI, which is not disease specific. However, the current utility of Ga-PSMA PET scan for detection of prostatic carcinoma in prebiopsy settings in patients with equivocal PSA values needs to be explored.[8] The aim of our study was to compare the diagnostic accuracy of mpMRI and Ga-68 PSMA PET/CT to detect carcinoma prostate lesion in patients with PSA between 4 and 20 ng/ml prior to biopsy.

Materials and Methods

This prospective study was carried out from June 2017 to the present date. All patients with age more than 50 years presenting with lower urinary tract symptoms (LUTS), with a serum PSA between 4 and 20 ng/ml and referred for suspected carcinoma prostate evaluation, were included in this study [Table 1]. All patients underwent mpMRI with sequences - T1 axial, T2 axial, short tau inversion recovery coronal, diffusion weighted imaging [DWI] with high b values [600 and 1000 s/mm2], apparent diffusion coefficient [ADC] map, magnetic resonance spectroscopy with or without dynamic contrast enhancement [DCE]) These are the sequences of MRI usually done for prostate cancer on a 1.5 Tesla MRI system (Achieva, Philips Medical System). Each mpMRI was evaluated by the radiologist. The Prostate Imaging Reporting and Data System (PI-RADS) score was calculated as per PI-RADS version 2 using T2, DCE, and DWI sequences as per recommendations of PI-RADS steering committee. Ga-68 PSMA PET scan was performed after Ga 68 PSMA HBED CC (name of PSMA molecule used) intravenous injection (2–3 mCi/patient), with imaging 60 min after injection, noncontrast PET/CT on Philips time-of-flight PET/CT. Reconstructions were conducted with row-action maximum likelihood algorithm. Attenuation correction was performed using the CT data. Maximum intensity projection, plain PET, plain CT, and fused PET/CT were then evaluated by a nuclear medicine physician. As per the Joint European Association of Nuclear Medicine and Society of Nuclear Medicine and Molecular Imaging procedure guidelines, any region of focal/abnormal PSMA ligand accumulation as compared to the background uptake was taken as suspicious of malignancy, and its size and location noted.[4] Semi-quantitative analysis was performed by drawing the region of interest around the area of focal tracer uptake calculating standard uptake values (maximum standardized uptake value [SUV_{max}]). The scans MRI and Ga-68 PSMA PET/CT were performed within 10 days of each other and with no intervention in between the scans. The MRI was read by an experienced radiologist of our department (with 12 years of experience in the field) and PET/CT was read by an experienced nuclear medicine physician (with 10 years of experience in the field). The MRI and PET/CT images were read separately, and no fusion was applied due to unavailability of the software for the same. The reader of MRI was blinded to the findings of the PET/CT and vice versa. Twelve-core systematic free-hand TRUS-guided prostate biopsies were performed for all the patients after obtaining informed consent due to high clinical suspicion as referred by the clinician. All TRUS-guided prostate biopsies were performed under periprostatic block using a Philips Affiniti 70 ultrasonography system with a transrectal probe in the end-firing mode. The biopsy was done after the imaging but within 10 days. The biopsy performer was not blinded for the imaging findings. Findings from mpMRI and Ga-68 PSMA PET/CT were assessed for concordance of lesion. This was done by noting the findings of the quadrants in the biopsy report and correlating with the MRI and PET/CT reports. The imaging modality was marked positive if the quadrant with carcinoma belonged to the positive findings reported at the same anatomical site. However, the images were not divided into 12 quadrants for analysis. The results reflect patient-based analysis. The index lesion with the highest PI-RADS score or highest SUV_{max} was considered for comparison. The biopsy report mentioned that the presence or absence of malignancy along with the Gleason score of each core was separately assessed. After comparing the results of mpMRI and Ga-68 PSMA PET/CT scan with biopsy results, the sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic accuracy for mpMRI and Ga-68 PSMA PET/CT were calculated. Various other statistical analyses for correlation between SUV_{max} and serum PSA level and correlation between SUV_{max} and Gleason's score were performed using SPSS software. Receiver operating characteristic curve (ROC curve) and area under curve (AUC) were derived for PSMA PET SUV_{max} [Tables 2-4].

Results

There were 30 patients included in the study with a median age of 73 years (age range: 69–79 years); all the patients presented with LUTS. The median total serum PSA was 8.0 ng/ml (5.0–19.9 ng/ml). All patients

underwent mpMRI as described. mpMRI identified a lesion in 15 of the 19 patients that was suggestive of malignancy (PI-RADS > II). Lesions with PI-RADS III score were re-evaluated. The most commonly reported PI-RADS score was III (11 patients), and four patients had PI-RADS IV and four had PI-RADS V lesion. The 11 patients with PI-RADS score III were re-evaluated. For peripheral zone lesions, the overall PI-RADS assessment was based on the DWI score, but a score of III was upgraded by the presence of dynamic contrast enhancement. For transition zone lesions with a T2-weighted score of II or III, a DWI score that is two higher (i.e. IV or V, respectively) was used to upgrade the overall PI-RADS assessment by one point (i.e. to III or IV, respectively). All these 11 patients' images were eventually reported as PI-RADS IV. The median maximum size of the lesion was 19 mm (14–29 mm). It correctly identified the suspicious lesions in all 18 patients in whom the biopsy was subsequently reported as malignancy. There was one false positive on MRI with serum PSA of 7.38 ng/ml; MRI findings revealed a well-defined nodule within left transitional zone of prostate with restricted diffusion (PI-RADS III upgraded to IV).Ga-68 PSMA PET scan was negative, and biopsy was reported as benign prostatic hyperplasia [Figure 1].

On Ga-68 PSMA PET scan, a focal increased tracer uptake in prostate could be visualized in 17 of the 18 patients with biopsy-proven carcinoma (median SUV_{max}: 18.35 [range: 5.36–27.41]). In the rest of the 13 patients, the scan did not show any abnormal focal tracer accumulation. There was one false negative on PSMA PET scan with serum PSA of 14 ng/ml; MRI revealed left peripheral zone lesion about 10 mm × 7 mm in size with restriction of diffusion and hyperintense lesion on DWI and hypointense on ADC and T2 weighted images. The biopsy was reported as adenocarcinoma, grade group II, Gleason's score 7 (3 + 4) [Figure 2].

Thus, by using the results of the MRI and PSMA PET/CT, lesion could be localized in all the 18 patients with biopsy-proven carcinoma. In 16 of these 18 patients, the lesion was seen at the same location on both MRI and Ga-PSMA PET scans [concordant lesion – Figure 3]. There were two patients with discordant lesion: one false negative on PSMA PET and one false positive on MRI. Twelve patients did not have an identifiable lesion either on the MRI or on Ga-68 PSMA PET scan. Therefore, there were 16 + 12 = 28 patients out of 30 (93.33%) showing concordant imaging findings. Of these 18 patients with biopsy-proven carcinoma, there was no seminal vesicle involvement seen, lymph node involvement was noted in 3 patients, and bone metastasis was noted in 3 patients (these were seen concordantly on both imaging modalities).

All patients underwent standard 12-core TRUS-guided prostate biopsy which was diagnostic of malignancy in 18 (60%) of the 30 patients. Seven of these 18 patients had a Gleason's score of >7 and 11 patients had Gleason's score ≤7. Twelve patients did not have an identifiable lesion either on the MRI or on Ga-68 PSMA PET scan, and all had no evidence of malignancy on biopsy. On comparing MRI with histopathology report, the scan was false positive in one patient, and there was no false negative. Similarly, on comparing Ga-68 PSMA PET scan results to histopathology results, the scan was false positive in none and false negative in one patient, respectively.

Statistical analysis

Patient characteristics were tabulated [Table 1]. The correlation between SUV_{max} and PSA and SUV_{max} and the Gleason score was calculated using Spearman's correlation coefficient. Correlation analysis showed a weak correlation between PSA and SUV_{max} (r_s = 0.42), and SUV_{max} values were significantly higher in prostate carcinoma with Gleason's score >7 than in those with Gleason's

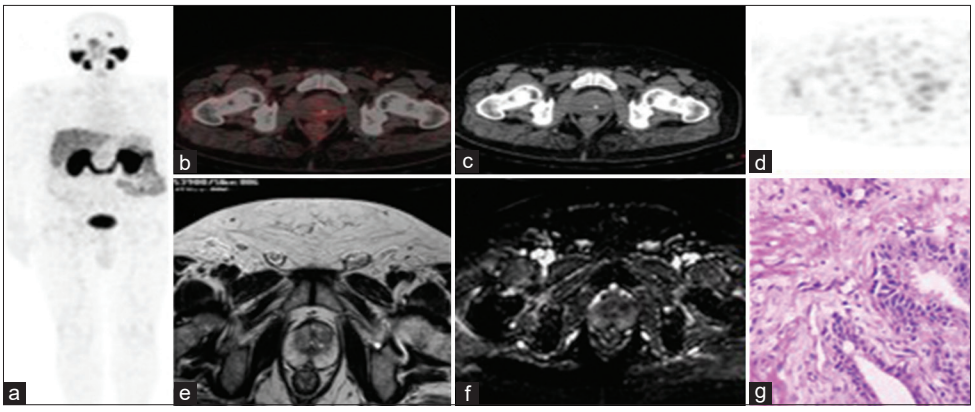

Figure 1: The images of patient 1.Gallium 68 PSMA PET/CT (maximum intensity projection) (a), axial fused PET/CT (b), axial CT (c) and axial PET (d) do not show any abnormal focal prostate-specific membrane antigen tracer uptake. Magnetic resonance imaging images (e and f) T2-weighted image showed hypointense lesions and diffusion-weighted image showing focal, marked hypointensity on apparent diffusion coefficient mapping in right transitional zone. Histopathology section (g) at ×40 showed benign gland with preserved basal layer in fibromuscular stroma suggestive of benign prostatic hyperplasia

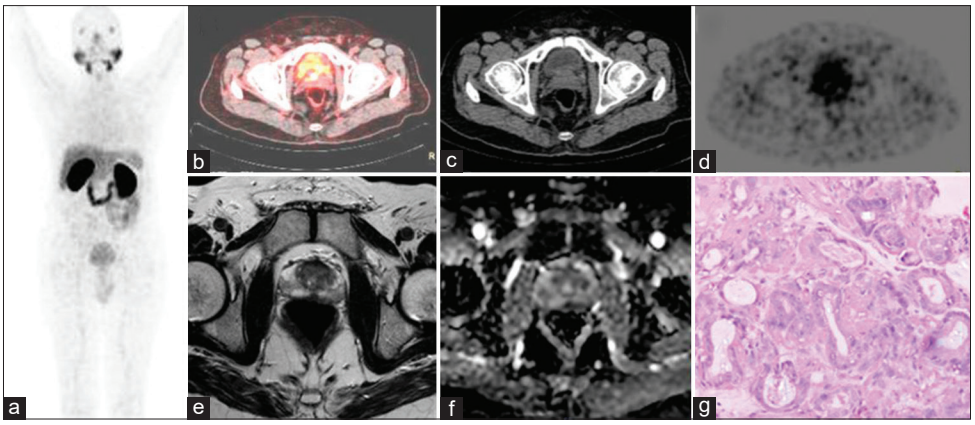

Figure 2: The images of patient 7. Gallium 68 PSMA PET/CT (maximum intensity projection) (a), axial fused PET/CT (b), axial CT (c) and axial PET (d) do not show any abnormal focal tracer uptake. MRI (e) T2 weighted image showed focal mild to moderate hypointense lesion in peripheral zone bilaterally and diffusion weighted image (f) showed subtle areas of restriction of diffusion in peripheral zone bilaterally. Histopathology (g) at × 40 showed show atypical cells arranged in glands and cribriform pattern, highly pleomorphic suggestive of adenocarcinoma

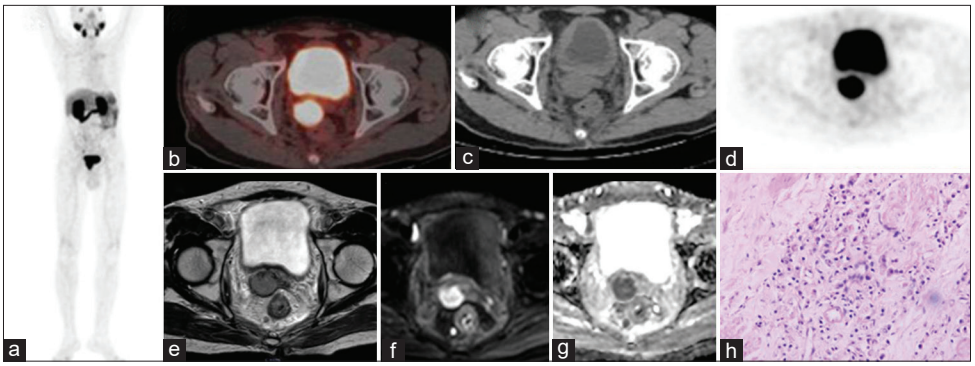

Figure 3: The images of patient 15. Gallium-68 PSMA PET/CT (maximum intensity projection) (a), axial fused PET/CT (b), axial CT (c) and axial PET (d) showed abnormal focal tracer uptake standardized uptake value 22.9 in right peripheral zone of enlarged prostate. MRI images (e) T2-weighted image showed discrete focal hypointense lesion in peripheral zone on right side causing mass effect on capsule and diffusion-weighted images (f and g) show restriction of diffusion in the lesion. Histopathology (h) at ×40 showed malignant cells suggestive of adenocarcinoma

score ≤7 ($P < 0.001$). On ROC analysis, the SUV_{max} cutoff value of 9.04 on PSMA PET/CT showed optimum sensitivity and specificity (AUC: 0.990, $P < 0.001$) [Table 3 and Figure 4]. The sensitivity, specificity, PPV, NPV, and diagnostic accuracy of mpMRI and Ga-PSMA PET scan as compared to the biopsy report as gold standard are given in Table 4.

Discussion

We evaluated the performance of Ga-68 PSMA PET/CT in detecting cancer prostate in patients with serum PSA between 4 and 20 ng/ml in prebiopsy settings. Ga-68 PSMA PET/CT was able to detect 17 out of 18 patients with carcinoma on biopsy and had no false positives and one false negative result each showing good sensitivity and specificity values. It was superior to mpMRI in predicting presence of malignancy. There is interest among treating oncologists regarding the utility of ^{68}Ga-PSMA PET/CT in suspected prostatic carcinoma due to limitations of existing modalities, namely, serum PSA levels, DRE,

Table 1: Patient characteristics

	***n* (%)**
Median age (IQR)	73 (69-79)
Median PSA (IQR)	8 (5.0-19.9 ng/ml)
Median SUV_{max} (IQR)	18.35 (5.36-27.41)
PI-RADS MRI	
PI-RADS 1	5 (16.7)
PI-RADS 2	6 (20.0)
PI-RADS 3	11 (36.7)
PI-RADS 4	4 (13.3)
PI-RADS 5	4 (13.3)
Biopsy	
Negative	12 (40.0)
Positive	18 (60.0)
Gleason score	
≤7	11 (61.1)
>7	7 (38.9)

IQR: Interquartile range, PSA: Prostate-specific antigen, SUVmax: Maximum standardized uptake value, PI-RADS: Prostate Imaging Reporting and Data System, MRI: Magnetic resonance imaging

Table 2: Correlation of prostate-specific antigen, prostate-specific membrane antigen maximum standardized uptake value and magnetic resonance imaging findings with biopsy

	Biopsy		*P*
	Positive (*n*=18), *n* (%)	Negative (*n*=12), *n* (%)	
Median PSA (IQR)	14.8 (5.5-18.77)	7.34 (6.72-8.7)	0.285
Median SUVmax (IQR)	22.65 (19.08-29.18)	3.9 (3.12-6.85)	<0.001
MRI PI-RADS			
Negative	0	11 (100)	<0.001
Positive	18 (94.7)	1 (5.3)	

IQR: Interquartile range, PSA: Prostate-specific antigen, SUV_{max}: Maximum standardized uptake value, PI-RADS: Prostate imaging reporting and data system, MRI: Magnetic resonance imaging

Table 3: Area under curve analysis of serum prostate-specific antigen and prostate-specific membrane antigen maximum standardized uptake value

Test result variable(s)	AUC	SE[a]	Asymptotic significant[b]	Asymptotic 95% CI (lower bound-upper bound)
PSA (ng/ml)	0.618	0.105	0.280	0.412-0.824
SUV_{max}	0.991	0.012	0.000	0.967-1.000

The test result variable(s): PSA ng/ml has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. [a]Under the nonparametric assumption, [b]Null hypothesis: True area=0.5. PSA: Prostate-specific antigen, SUV_{max}: Maximum standardized uptake value, SE: Standard error, CI: Confidence interval, AUC: Area under curve

Table 4: Statistics for prostate-specific membrane antigen positron emission tomography maximum standardized uptake value and multiparametric magnetic resonance imaging

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
Ga-68 PSMA PET/CT	94.44	100	100	92.31	96.67
mpMRI	100	92.30	94.73	100	96.67

PPV: Positive predictive value, NPV: Negative predictive value, mpMRI: Multiparametric magnetic resonance imaging, Ga-68 PSMA PET/CT: Gallium-68 prostate-specific membrane antigen positron emission tomography/computed tomography

transrectal ultrasonography (TRUS), TRUS-guided biopsy, and mpMRI.[9] A recent meta-analysis by Satapathy *et al*.[10] evaluated the diagnostic performance of Ga-68 PSMA PET/CT in the initial detection of prostate cancer in patients with clinical or biochemical suspicion. Ga-68 PSMA PET/CT showed excellent sensitivity and negative likelihood ratio to detect suspected prostate cancer and has potential utility as a "rule-out" test in this.[10] However, our study shows a good specificity also in addition to sensitivity and accuracy. Although, in our study, MRI showed a higher sensitivity as one case of carcinoma prostate was missed on PSMA PET/CT. Better resolution PET cameras with better technologies may be able to avoid these shortcomings. Larger prospective trials with a greater number of patients may be needed.

MpMRI is used to localize the primary tumor and local staging of cancer and to plan nerve-preserving radical prostatectomy. A meta-analysis showed that there is a wide variation in reported diagnostic accuracies (44%–87%) for MRI in the detection of clinically significant prostatic carcinomas.[11] A recent retrospective analysis evaluated patients with normal mpMRI and found that at a follow-up of 38 months, 12.8% of the biopsy-naive patients with normal mpMRI were detected to have cancer, of which 42.3% were clinically significant.[12]

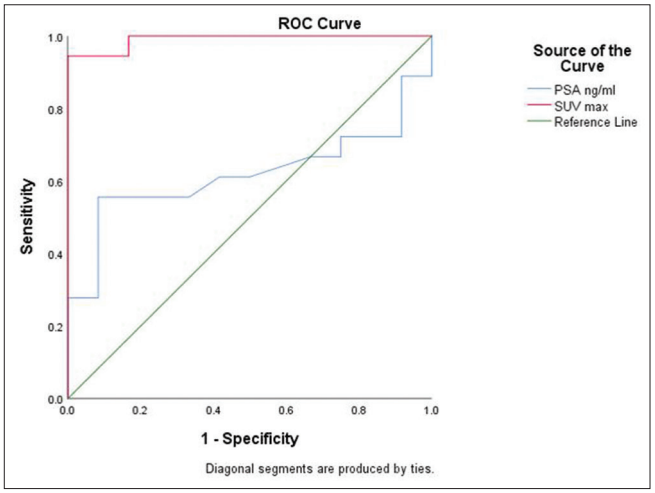

Figure 4: Receiver-operator characteristic curve of serum prostate-specific antigen and prostate-specific membrane antigen positron emission tomography standardized uptake value maximum for the prediction of prostate carcinoma

^{68}Ga-PSMA-11 PET/CT has been well documented for the early detection of biochemical recurrence of carcinoma prostate, even in patients with low PSA levels.[13] PSMA expression in the primary cancer, as seen by immunohistochemical staining, has been shown to correlate with SUV_{max} of Ga-68 PSMA PET scan,

thus enabling the detection of prostate cancer with high sensitivity.[14] Few authors have compared the accuracy of Ga-68 PSMA PET scan to mpMRI to detect and locate tumor foci within the prostate and found Ga-68 PSMA PET to have better accuracy and PPV.[15] In our study too, Ga-68 PSMA PET scan and MRI had the same accuracy while PSMA PET had better PPV. However, another recent study showed that Ga-PSMA PET scan has a higher NPV and accuracy than mpMRI in detecting tumor foci within the prostate.[16] There are reports where targeted biopsy using PSMA PET/CT is being explored with success.[17] This may be more beneficial in cases which are equivocal on serum PSA and mpMRI. A recent study by Zhang *et al*. showed that ^{68}Ga-PSMA PET/CT may serve as a triage tool for prostate biopsy.[18] Chandra *et al*. reported in a recent study that SUV_{max} cutoff value of 5.6 on PSMA PET/CT showed a sensitivity of 95% and a specificity of 90.9% and concluded that Ga-68 PSMA PET/CT can differentiate benign and malignant lesions of the prostate with very high accuracy and, when used alongside with ERSPC3 calculator and MRI, could potentially reduce painful and often unnecessary prostate biopsies.[19]

Our study has certain limitations. The number of patients was small. Furthermore, we did not rebiopsy patients who had an identifiable lesion on imaging, but the one biopsy was negative. However, they were on follow-up clinical evaluation. Despite these limitations, our data suggest that Ga-68 PSMA PET scan has a good diagnostic accuracy equal to mpMRI in detecting cancer prostate in patients with serum PSA of 4–20 ng/ml. It shows higher specificity and PPV and predicts the subsequent need of biopsy.

Conclusion

Ga-68 PSMA PET and mpMRI both have good diagnostic accuracy for diagnosing carcinoma prostate in men with PSA between 4 and 20 ng/ml. Ga-68 PSMA PET showed higher specificity and PPV and predicted the subsequent need of biopsy. In our study, the NPV, though good, was lower than mpMRI. However, larger prospective trials with larger sample size are needed to explore the possibilities. In combination, PET and MRI may achieve greater accuracy and PET/MRI may serve as investigation of choice when it is more widely available. Targeted biopsies in the setting of Ga-68 PSMA PET/MRI may open great avenues in diagnosis of carcinoma prostate.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sasikumar A, Joy A, Pillai AM, Oommen KE, Somarajan S, Raman VK, *et al.* Gallium 68-PSMA PET/CT for lesion characterization in suspected cases of prostate carcinoma. Nucl Med Commun 2018;39:1013-21.
2. Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, *et al.* MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767-77.
3. Bjurlin MA, Wysock JS, Taneja SS. Optimization of prostate biopsy: Review of technique and complications. Urol Clin North Am 2014;41:299-313.
4. Fendler WP, Eiber M, Beheshti M, Bomanji J, Ceci F, Cho S, *et al.* ^{68}Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: Version 1.0. Eur J Nucl Med Mol Imaging 2017;44:1014-24.
5. Turkbey B, Mena E, Lindenberg L, Adler S, Bednarova S, Berman R, *et al.* ^{18}F-DCFBC prostate-specific membrane antigen-targeted PET/CT imaging in localized prostate cancer: correlation with multiparametric MRI and histopathology. Clin Nucl Med 2017;42:735-40.
6. Gordetsky JB, Ullman D, Schultz L, Porter KK, Carmen D, Pena R, *et al.* Histologic findings associated with false-positive multiparametric magnetic resonance imaging performed for prostate cancer detection. Hum Pathol 2019;83:159-65.
7. Quon JS, Moosavi B, Khanna M, Flood TA, Lim CS, Schieda N. False positive and false negative diagnoses of prostate cancer at multi-parametric prostate MRI in active surveillance. Insights Imaging 2015;6:449-63.
8. Chakraborty PS, Kumar R, Tripathi M, Das CJ, Bal C. Detection of brain metastasis with ^{68}Ga-labeled PSMA ligand PET/CT: A novel radiotracer for imaging of prostate carcinoma. Clin Nucl Med 2015;40:328-9.
9. Singh H. Making the case for prostate-specific membrane antigen-targeted positron emission tomography/computed tomography in suspected prostate cancer. Indian J Nucl Med 2020;35:281-2.
10. Satapathy S, Singh H, Kumar R, Mittal BR. Diagnostic accuracy of 68GaPSMA PET/CT for initial detection in patients with suspected prostate cancer: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. 2021;216:599-607.
11. Fütterer JJ, Briganti A, De Visschere P, Emberton M, Giannarini G, Kirkham A, *et al.* Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015;68:10.
12. Panebianco V, Barchetti G, Simone G, Del Monte M, Ciardi A, Grompone MD, *et al.* Negative multiparametric magnetic resonance imaging for prostate cancer: What's next? Eur Urol 2018;74:48-54.
13. Perera M, Papa N, Roberts M, Williams M, Udovicich C, Vela I, *et al.* Gallium-68 prostate-specific membrane antigen positron emission tomography in advanced prostate cancer-updated diagnostic utility, sensitivity, specificity, and distribution of prostate-specific membrane antigen-avid lesions: A systematic review and meta-analysis. Eur Urol 2020;77:403-17.
14. Woythal N, Arsenic R, Kempkensteffen C, Miller K, Janssen JC, Huang K, *et al.* Immunohistochemical validation of PSMA expression measured by ^{68}Ga-PSMA PET/CT in Primary Prostate Cancer. J Nucl Med 2018;59:238-43.
15. Berger I, Annabattula C, Lewis J, Shetty DV, Kam J, Maclean F, *et al.* ^{68}Ga-PSMA PET/CT vs. mpMRI for locoregional prostate cancer staging: Correlation with final histopathology. Prostate Cancer Prostatic Dis 2018;21:204-11.
16. Kumar N, Yadav S, Kumar S, Saurav K, Prasad V, Vasudeva P. Comparison of percentage free PSA, MRI and GaPSMA PET

scan for diagnosing cancer prostate in men with PSA between 4 and 20 ng/ml. Indian J Urol 2019;35:202-7.
17. Simopoulos DN, Natarajan S, Jones TA, Fendler WP, Sisk AE Jr., Marks LS. Targeted prostate biopsy using ^{68}Gallium PSMA-PET/CT for image guidance. Urol Case Rep 2017;14:11-4.
18. Zhang LL, Li WC, Xu Z, Jiang N, Zang SM, Xu LW, *et al.* ^{68}Ga-PSMA PET/CT targeted biopsy for the diagnosis of clinically significant prostate cancer compared with transrectal ultrasound guided biopsy: A prospective randomized single-centre study. Eur J Nucl Med Mol Imaging 2021;48:483-92.
19. Chandra P, Rajaian S, Krishnamurthy K, Murugasen L, Chandran G, Kumar JS, *et al.* Diagnostic accuracy of prebiopsy Ga-68 PSMA PET/CT in detecting primary prostate carcinomas with prostate-specific antigen<50 ng/ml. Indian J Nucl Med 2020;35:283-90.