

# A comparison study of <sup>68</sup>Ga-PSMA PET-CT compared with mpMRI for locoregional staging of prostate cancer

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## Abstract

**Purpose:** Prostate cancer (PCa) is the most common malignancy in men aged 50 years and older and the second cause of cancer death among men. Accurate staging of PCa preoperatively is of high importance for treatment decisions and patient management. Conventional imaging modalities (ultrasound, computed tomography [CT], and magnetic resonance imaging) are inaccurate for the staging of PCa. Newer modality multiparametric magnetic resonance imaging (mpMRI) and prostate-specific membrane antigen (PSMA) positron emission tomography (PET) scan show promising results for the staging of PCa. Only fewer studies are available for comparison of these modalities with histopathology as reference. The objective of our study is to evaluate the diagnostic accuracy of independent <sup>68</sup>Ga-PSMA (<sup>68</sup>Ga-PSMA) PET-CT compared with mpMRI for preoperative staging of PCa, using histopathology as the reference standard.

**Materials and methods:** From August 2021 to December 2022, 30 patients of biopsy-proven PCa were prospectively enrolled as per eligibility criteria. Preoperatively, <sup>68</sup>Ga-PSMA PET scan and mpMRI were done in all the patients. Extracapsular extension (ECE), seminal vesicle invasion (SVI), and lymph node metastasis (LNM) were investigated separately. Subsequently, the patients underwent robotic-assisted radical prostatectomy with bilateral pelvic lymph node dissection.

**Results:** mpMRI prostate was more sensitive (66.66%) but less specific than PSMA PET-CT (55.55%) for ECE. mpMRI and PSMA PET-CT both had similar sensitivity (83.3%) and specificity (87.5%) for SVI. PSMA PET-CT was more sensitive (85.71%) and specific (95.6%) than mpMRI prostate (62.5% and 91.30%, respectively) for LNM.

**Conclusion:** PSMA PET-CT is more specific for the detection of ECE and more sensitive and specific for the detection of LNM than mpMRI, and similar for the detection of SVI. mpMRI provides only local staging, while PSMA PET-CT provides information about local, regional, and distal staging. Overall, PSMA PET-CT is superior to mpMRI for locoregional staging of PCa.

**Keywords:** <sup>68</sup>Ga-PSMA PET-CT, multiparametric MRI, prostate cancer, locoregional staging

## 1. Introduction

Prostate cancer (PCa) is the most common malignancy in men aged 50 years and older and has the second highest mortality rate among

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malignant carcinomas in men<sup>1</sup>. Accurate staging of PCa is important for treatment decisions and patient management<sup>2</sup>. The current European guidelines recommend magnetic resonance imaging (MRI) for local staging and computed tomography (CT) or bone scans to achieve accurate staging for those with distant metastases before the treatment of PCa<sup>3</sup>. However, these conventional imaging modalities have low sensitivity and specificity for identifying small lesions. Moreover, the misdiagnosis of benign lesions may lead to incorrect treatment or overtreatment in nonmetastatic patients with PCa. Novel imaging modalities, such as <sup>68</sup>Ga-PSMA PET-CT and multiparametric MRI (mpMRI) techniques, including diffusion-weighted imaging and dynamic contrast-enhanced T1-weighted imaging, have been developed for locoregional staging and treatment planning of patients with PCa<sup>3</sup>.

MRI plays an essential role in detecting suspicious lesions in patients with PCa, in guiding the biopsy procedure, and in staging in biopsy-proven patients with PCa. Recent advances in mpMRI have led to the detection of clinically significant

disease and have reduced the need for unnecessary biopsies and treatment<sup>4,8</sup>. mpMRI, including T1- and T2-weighted diffusion-weighted imaging and T1-weighted dynamic contrast-enhanced sequences, is used to increase the diagnostic accuracy of MRI in patients with PCa<sup>9-14</sup>. This modality is also widely used for active surveillance and guiding of repeat biopsies in these patients<sup>15</sup>.

PSMA is a type II transmembrane glycoprotein that is expressed in normal prostate gland epithelium and overexpressed on the surface of >80% of primary and metastatic PCa<sup>16</sup>. <sup>68</sup>Ga PSMA-11 binds to the receptor for transmembrane folate hydrolase and can be imaged using PET-CT scans<sup>17,18</sup>. Recently, <sup>68</sup>Ga-PSMA PET-CT has been used for the detection, diagnosis, and staging of PCa<sup>19,20</sup>.

However, few studies have compared the diagnostic accuracy of mpMRI and <sup>68</sup>Ga-PSMA PET-CT, and those were retrospective. Therefore, we conducted prospective studies to compare the diagnostic accuracy of <sup>68</sup>Ga-PSMA PET-CT and mpMRI for the staging of PCa, using histopathological findings as the gold standard.

## 2. Methods

From August 2021 to December 2022, 30 patients with biopsy-proven PCa were enrolled prospectively as per eligibility criteria.

### 2.1. Inclusion criteria

1. Patient aged between 45 and 80 years
2. Biopsy-proven PCa suitable for radical prostatectomy (RP) with pelvic lymph node dissection
3. Serum prostate-specific antigen (PSA) levels between 4 and 20 ng/mL
4. Eastern Cooperative Oncology Group performance status of patient 0 or 1
5. Patients who received no previous therapy and had no previous other malignancy.

### 2.2. Exclusion criteria

Exclusion criterion is patients on any other therapy (eg, hormonal therapy, radiotherapy, chemotherapy) at the time of their initial Outpatient Department presentation.

The study protocol was approved by the Poona Medical Research Foundation (approval no. RHC/Biopmrfiec/2020/316) and the study was conducted ethically at the Ruby Hall Clinic, Pune. Male patients who fulfilled the eligibility criteria were enrolled in this study.

PCa rarely causes symptoms at an early stage. Screening of suspected cases was conducted by performing a digital rectal examination and by measuring the serum PSA levels. Digital rectal examinations included determining the size of the prostate, its consistency, the surface, a rectal mucosa assessment, and tenderness.

Transabdominal ultrasound examinations were performed to assess the size of the prostate gland, the urinary bladder, and postvoid residual urine.

Transrectal ultrasound-guided biopsies were performed on all patients in the study. At least 12 prostate core biopsies were performed under local/spinal anesthesia under an adequate antibiotic cover. Additional targeted biopsies were performed at suspicious areas if required.

All patients had <sup>68</sup>Ga-PSMA PET-CT and mpMRI performed on their prostates to determine the local extent of the cancer

(extracapsular extension [ECE], seminal vesicle invasion [SVI]), and any regional lymph node metastasis (LNM).

Organ-confined PCa patients underwent robotic-assisted RP with bilateral pelvic lymph node dissection. Specimens were collected for histopathological examination.

The final histopathology report addressed the tumor grade, the presence of ECEs, SVI, and pelvic lymph node involvement. This report was compared with the PSMA PET scan report.

## 3. Results

In our study, data from 30 patients were analyzed (Figs. 1 and 2). Histopathologically, all cases were acinar adenocarcinomas of the prostate. The mean age of the patients was  $69.18 \pm 7.04$  years (range: 55–79). The mean serum PSA level was  $11.43 \pm 5.19$  ng/mL (range: 4.3–20). Among the 30 patients, ECE, SVI, and LNM were present in 19 (63.33%), 6 (20%), and 7 (23.33%) of the cases, respectively (Table 1).

Preoperative Gleason scores were upgraded in the final histopathology report in approximately 20% of the patients. Most of the patients (86.66%) included in the study had Prostate Imaging Reporting and Data System (PIRADS) 4 and 5 lesions by mpMRI. The mean SUVmax value was  $16.78 \pm 11.63$  (range: 3.8–49.4) by PSMA PET-CT.

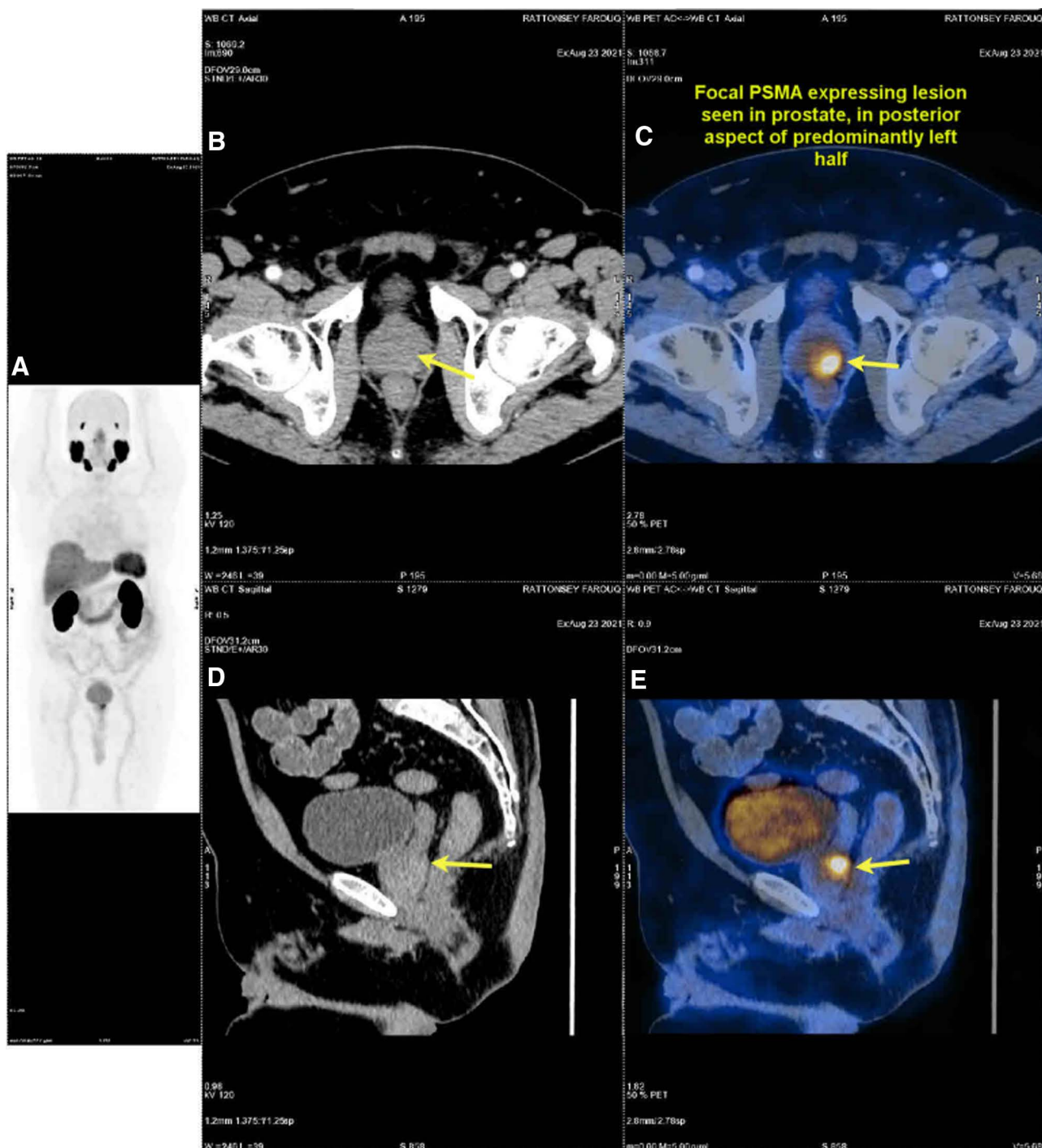
Postoperative patients with higher Gleason scores (4+5) also had higher PIRADS scores by mpMRI and a higher SUVmax value by PSMA PET-CT. However, Gleason scores of 3+4 and 4+3 were not significantly different from the PIRADS scores and SUVmax values (Table 2).

Prostatic mpMRI were more sensitive (66.66%) than PSMA PET-CT (55.55%) for identifying ECE. mpMRI and PSMA PET-CT both had similar sensitivities (83.3%) and specificities (87.5%) for identifying SVI. PSMA PET-CT were more sensitive (85.71%) and had better specificity (95.6%) than prostatic mpMRI for identifying LNM (Table 3).

## 4. Discussion

An accurate test for patients with suspected PCa must provide valuable information about the initial evaluation, diagnosis, and staging of the disease. The most valuable imaging technique for the diagnosis and staging is controversial for patients with PCa. Unfortunately, the most frequently used conventional imaging test has limited specificity and sensitivity for providing a preoperative assessment<sup>21,22</sup>. Novel imaging modalities, such as <sup>68</sup>Ga-PSMA PET-CT and mpMRI, have produced promising results for the staging of preoperative PCa. However, few studies have been conducted that compare mpMRI and <sup>68</sup>Ga-PSMA PET-CT for locoregional staging of PCa. Despite the small number of patients, to the best of our knowledge, this is the first prospective study to compare both <sup>68</sup>Ga-PSMA PET-CT and mpMRI for locoregional staging of PCa to histological findings from RP specimens.

An accurate preoperative assessment of lymph node involvement, SVI, and ECE status is critical in treating intermediate to high-risk patients with PCa. Our results demonstrate that mpMRI of the prostate was more sensitive (66.66%) but less specific than PSMA PET-CT (55.55%) for identifying ECE. mpMRI and PSMA PET-CT had similar sensitivities (83.3%) and specificities (87.5%) for the identification of SVI. PSMA PET-CT was more sensitive (85.71%) and more specific (95.6%) than mpMRI of the prostate (62.5% and 91.30%, respectively) for identifying LNM.

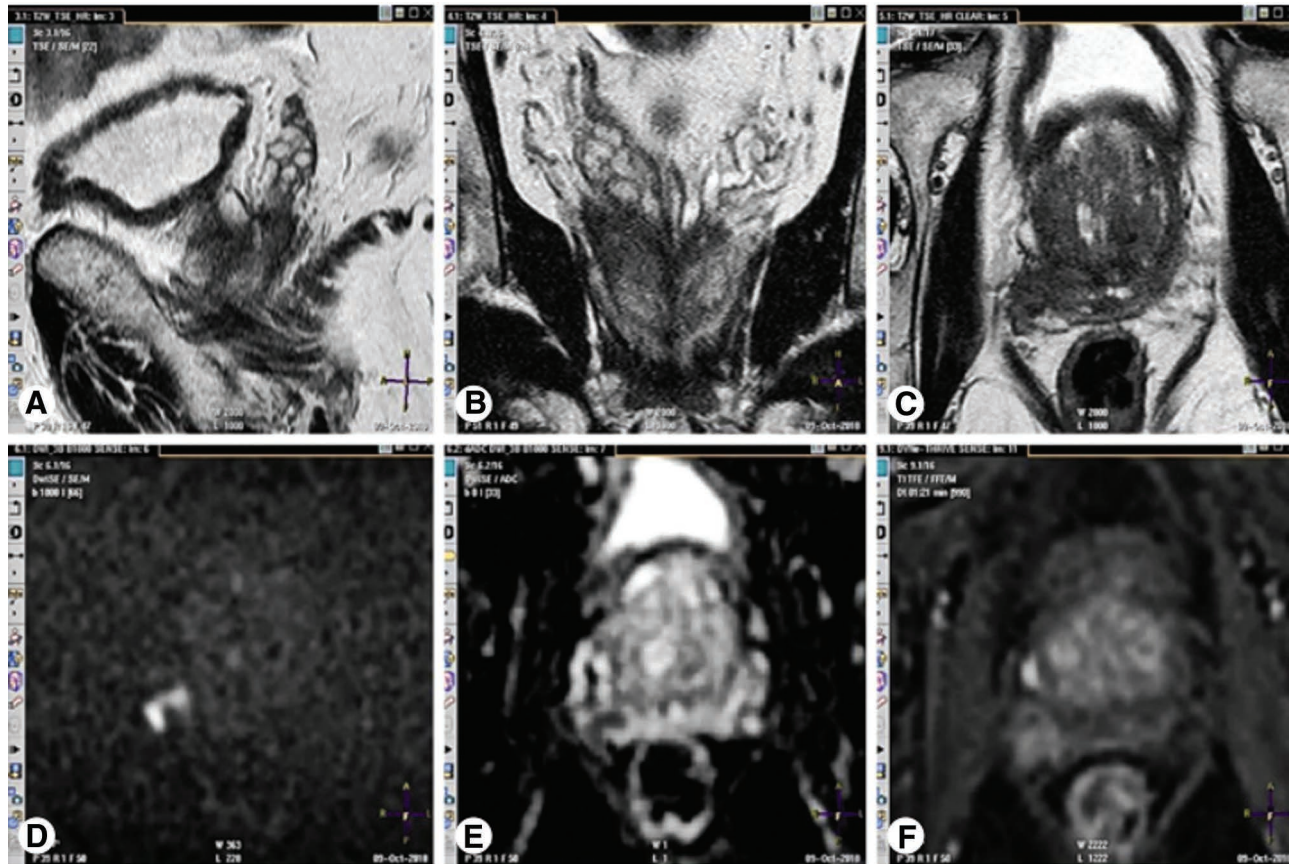


**Figure 1.** <sup>68</sup>Gallium-prostate-specific membrane antigen positron emission tomography-computed tomography (PET-CT) of a 74-year-old patient with prostate cancer (Gleason score 4 + 3 = 7 and preoperative prostate-specific antigen 4.3 ng/mL). (A) Maximum intensity projection image of pretreatment. (B, C) Transaxial fused PET-CT and computed tomography (CT) images with a gross tumoral lesion at the left posterior aspect (yellow arrows). (D, E) Sagittal fused PET-CT and CT images establishing seminal vesicle invasion.

Evaluation of SVI and ECE in PCa is critical for determining the correct therapeutic approach because SVI or ECE invasions are crucial prognostic factors for recurrence after RP. Patients with an advanced local disease with ECE and SVI have a worse prognosis because the risk of a positive surgical margin and the incidence of LNM are increased<sup>23</sup>.

SVI assessment before RP is important for planning a surgical modality. Assessment of SVI may alter surgery time, morbidity, and even mortality. Accurate knowledge of the SVI status may

completely alter the treatment modality<sup>23</sup>. Berger et al<sup>24</sup> reported that the specificity of both PSMA PET-CT and mpMRI was similar for diagnosing SVI (92.7 vs 95.0%;  $P = 0.39$ ). Yilmaz et al<sup>25</sup> demonstrated that mpMRI had a higher sensitivity (100% vs 75%) and a similar specificity (90%) compared with <sup>68</sup>Ga-PSMA PET-CT for the detection of SVI. These studies were retrospective studies, and they had their own limitations. In our study, we found that <sup>68</sup>Ga-PSMA PET-CT and mpMRI had similar sensitivities (83.3%) and similar specificities (87.5%) for the detection of SVI.



**Figure 2.** Prostate multiparametric magnetic resonance imaging (MRI) of a 72-year-old patient with a prostate-specific antigen value of 16.16ng/mL and a Gleason score of 4+3 prostate cancer. The sagittal (A), coronal (B), and axial (C) T2-weighted, high b value (1800s/mm<sup>2</sup>) diffusion-weighted (D), apparent diffusion coefficient map (E), and dynamic contrast-enhanced (F) MRI images reveal a PIRADS score of 5 lesions in the right peripheral zone, with extraprostatic extension and right seminal vesicle invasion.

**Table 1**  
**Clinical and pathological data of the patients.**

Derivatives	Value
Age, y	69.18 ± 7.04 (55–79)
PSA, ng/dL	11.43 ± 5.19 (4.3–20)
Prostate size, cc	45.10 ± 16.76 (12–80)
Preoperative Gleason score	
3+3	8 (26.66%)
3+4	9 (30%)
4+3	10 (33.33%)
4+4	2 (6.66%)
4+5	1 (3.33%)
mpMRI PIRADS score	
PIRADS 3	4 (13.33%)
PIRADS 4	11 (36.66%)
PIRADS 5	15 (50%)
PSMA PET-CT SUVmax	16.78 ± 11.63 (3.8–49.4)
Postoperative Gleason score	
3+3	3 (10%)
3+4	12 (40%)
4+3	12 (40%)
4+5	3 (10%)
ECE	19 (63.33%)
SVI	6 (20%)
LNM	7 (23.33%)

Abbreviations: ECE, extracapsular extension; LNM, lymph node metastasis; mpMRI, multiparametric magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; PIRADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; SVI, seminal vesicle invasion; SUVmax, maximum standardized uptake value.

**Table 2**  
**Relations between postoperative Gleason score and imaging findings.**

Postoperative Gleason score	mpMRI, PIRADS	<sup>68</sup> Ga-PSMA PET-CT, SUVmax
3+3 (n = 3)	PIRADS 3 = 2	4.76 ± 1.26
	PIRADS 4 = 1	
3+4 (n = 12)	PIRADS 4 = 4	15.11 ± 9.38
	PIRADS 5 = 8	
	PIRADS 3 = 2	
4+3 (n = 12)	PIRADS 4 = 6	17.54 ± 12.50
	PIRADS 5 = 4	
4+5 (n = 3)	PIRADS 5 = 3	32.5 ± 2.64

Abbreviations: mpMRI, multiparametric magnetic resonance imaging techniques; PET-CT, positron emission tomography-computed tomography; PIRADS, Prostate Imaging Reporting and Data System; PSMA, prostate-specific membrane antigen. Postoperative patients with higher Gleason scores (4+5) also had higher PIRAD scores by mpMRI and a higher SUVmax value by PSMA PET-CT. However, Gleason scores of 3+4 and 4+3 were not significantly different from the PIRAD scores and SUVmax values.

The presence of ECE is a poor prognostic factor and is known to increase the risk of PCa-related mortality<sup>26</sup>. Furthermore, nonnerve-sparing surgery should be performed to avoid positive surgical margins at the high-risk area of ECE<sup>3</sup>. Yilmaz et al<sup>25</sup> reported that mpMRI had higher sensitivity than PSMA PET-CT (90% vs 30%), but <sup>68</sup>Ga-PSMA PET-CT had higher specificity (92.6% vs 85.7%) for the detection of ECE. In this study, we also found that mpMRI had higher sensitivity compared with

**Table 3****Diagnostic accuracy of mpMRI and <sup>68</sup>Ga-PSMA PET-CT for the staging of prostate cancer.**

	Sensitivity, %	Specificity, %	PPV, %	NPV, %	P value
Extracapsular extensio					
mpMRI	66.66	75	80	60	0.573
PSMA PET scan	55.55	91.6	90.9	57.8	0.476
Seminal vesicle invasion					
mpMRI	83.3	87.5	62.5	95	0.058
PSMA PET scan	83.3	87.5	62.5	95	0.058
Lymph node metastasis					
mpMRI	62.5	91.30	71.4	87.5	0.654
PSMA PET scan	85.71	95.6	85.71	95.6	0.038

Abbreviations: mpMRI, multiparametric magnetic resonance imaging techniques; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; PPV, positive predictive value; NPV, negative predictive value

PSMA PET-CT (66.66% vs 55.55%), but PSMA PET-CT had higher specificity (91.6% vs 75%) for the detection of ECE.

Histological identification of LNM is a robust negative predictor of survival<sup>27</sup>. Therefore, an evaluation of lymph nodes should be performed optimally before treatment decisions are made. The accurate assessment of locoregional lymph nodes was shown to be more sensitive with <sup>68</sup>Ga-PSMA PET-CT than with mpMRI<sup>28</sup>. Furthermore, <sup>68</sup>Ga-PSMA PET-CT can detect LNM of diameter 3 to 4 mm, whereas MRI can generally only identify pathological lymph node when they exhibit significant anatomical changes, such as nonoval shape, destruction of intimal architecture, and a short-axis diameter of >1 cm<sup>28</sup>. In general, the sensitivity of <sup>68</sup>Ga-PSMA PET-CT was 66% in most trials at the patient level. Moreover, <sup>68</sup>Ga-PSMA PET-CT have a high specificity (98.9%) and high accuracy (88.5%)<sup>29</sup>. Berger et al<sup>24</sup> suggested that <sup>68</sup>Ga-PSMA PET-CT provide superior detection of pelvic nodal disease over mpMRI alone. Çelen et al<sup>30</sup> reported that PSMA PET-CT had higher sensitivity (100%) and specificity (47.62%) for the detection of LNM. In the present study, we also found that PSMA PET-CT had higher sensitivity (85.71%) and specificity (95.6%) for the detection of LNM.

We are aware that mpMRI PSMA PET is now available and may eventually become a better procedure for locoregional staging of PCa, as mpMRI of the prostate has better soft-tissue differentiation than CT scans. However, no prospective studies have been performed on this.

We recognize several limitations to the present study, including the single-institution study design and small sample size. There are no randomization and no crossover. Another limitation is the potential influence of interobserver variability in image interpretation.

## 5. Conclusion

A PSMA PET-CT is more specific than mpMRI for the detection of ECE, more sensitive and specific for the detection of LNM, and is similar for the detection of SVI. An mpMRI can provide local staging only, while a PSMA PET-CT can provide information about local, regional as well distal staging. Overall, a PSMA PET-CT is superior to mpMRI for locoregional staging of PCa.

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## Author contributions

KSP and RC contributed to the conception and design of the study. KSP performed the literature searches and did the initial sorting of eligible papers. SS helped in data collection. KSP extracted data and drafted the manuscript. All authors critically revised the manuscript and approved the final version of the manuscript.

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