



# Comparing the diagnostic value of <sup>68</sup>Ga-prostate-specific membrane antigen PET/CT and multiparametric MRI in pelvic lymph node metastasis of locally advanced prostate cancer

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**Background:** Multiparametric magnetic resonance imaging (mpMRI) is a commonly used method to diagnose pelvic lymph node metastasis (PLNM) in prostate cancer (PCa) patients, but there are few comparative studies on mpMRI and <sup>68</sup>Ga-prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) in locally advanced PCa (LAPC) patients. Therefore, we designed a retrospective study to compare the diagnostic value of <sup>68</sup>Ga-PSMA PET/CT and mpMRI for PLNM of LAPC.

**Methods:** A retrospective study was performed on 50 patients with LAPC who underwent radical prostatectomy (RP) in Tongji Hospital from 2021 to 2023. All patients underwent PET/CT and mpMRI examination, and were diagnosed as LAPC before surgery, followed by robot-assisted laparoscopic prostatectomy or laparoscopic RP and extended pelvic lymph node dissection (ePLND). Routine postoperative pathological examination was performed. According to the results, the sensitivity, specificity, positive predictive value, and negative predictive value of <sup>68</sup>Ga-PSMA PET/CT and mpMRI for the diagnosis of PLNM of LAPC were compared.

**Results:** Among the 50 patients, the mean age was 65.5±10.3 years, the preoperative total serum prostate-specific antigen (PSA) was 30.7±12.3 ng/mL, and the Gleason score was 7 [7, 8]. The difference in diagnostic efficacy between <sup>68</sup>Ga-PSMA PET/CT and mpMRI in the preoperative diagnosis of PLNM of PCa was determined by postoperative pathological results. Based on the number of patients who developed PLNM, the sensitivity, specificity, positive predictive value, and negative predictive value of <sup>68</sup>Ga-PSMA PET/CT were as follows: 93.75%, 100.00%, 100.00%, 97.14%, and 68.75%, 97.06%, 91.67%, 86.84% for mpMRI, respectively. Based on the number of pelvic metastatic lymph nodes, the sensitivity, specificity, positive predictive value, and negative predictive value of <sup>68</sup>Ga-PSMA PET/CT were 95.24%, 100.00%, 100.00%, 99.48%, and 65.08%, 99.13%, 89.13%, 96.30% for mpMRI, respectively. It turned out that PET/CT was more sensitive than mpMRI in detecting PLNM of PCa, and the difference was statistically significant.

**Conclusions:** <sup>68</sup>Ga-PSMA PET/CT is more sensitive than mpMRI in the detection of PLNM in patients with LAPC. It is a promising method in the diagnosis and preoperative assessment of PLNM in LAPC.

**Keywords:**  $^{68}\text{Ga}$ -prostate-specific membrane antigen positron emission tomography/computed tomography ( $^{68}\text{Ga}$ -PSMA PET/CT); multiparametric magnetic resonance imaging (mpMRI); locally advanced prostate cancer (LAPC); lymph node metastasis (LNM)

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## Introduction

Prostate cancer (PCa) is the most common malignant tumor of male urinary and reproductive system (1), which is one of the main causes of cancer-related death in elderly men. PCa is prone to lymph node or bone metastasis (2). Patients with locally advanced PCa (LAPC) is generally defined as those who have regional lymph node metastasis (LNM) or clinical stage T<sub>3</sub>–T<sub>4</sub> without systemic metastasis, regardless of the level of prostate-specific antigen (PSA) or Gleason score (3,4). According to the clinical guidelines of the European Association of Urology (EAU), if the risk of nodal involvement calculated by nomogram is more than

7%, the patient is suspected LNM (5). For these patients, pelvic lymph node dissection (PLND) is considered as the “gold standard” for determining LNM of PCa. PLND can not only provide accurate lymph node pathological staging, but also remove potential LNM (6). Radical prostatectomy (RP) and PLND are commonly performed in patients with LAPC, especially those diagnosed with PLND before surgery. However, relevant studies have shown that PLND may increase the incidence of complications (such as organ damage, lymphatic fistula, etc.) (7), which increases the economic burden on patients. Therefore, it is crucial to find a non-invasive method for preoperative pelvic lymph node evaluation.

Computed tomography (CT), magnetic resonance imaging (MRI), and other imaging examinations take the size of lymph nodes as the diagnostic criteria for identifying metastatic lymph nodes. Multiparametric MRI (mpMRI) is a comprehensive evaluation of the lesions by multiparameter and multi-sequence MRI, and has become a commonly used imaging method for the preoperative evaluation of PCa, which can well display the condition of the prostate capsule, to check whether PCa encroaches on the surrounding tissues and organs, and the metastasis of pelvic lymph nodes (8). However, the accuracy of mpMRI for the detection of pelvic lymph nodes is limited, not only small metastatic lymph nodes may be missed, but also false positive result may occur in the case of lymph node hyperplasia, which affects the treatment of PCa patients.

Prostate-specific membrane antigen (PSMA) is a transmembrane glycoprotein composed of 751 amino acids in the form of monomer or dimer, which contains prostate extracellular segment, transmembrane segment, and intracellular segment. Its expression in PCa tissues is significantly higher than that in normal prostate tissues (9), and is positively correlated with Gleason score, PSA level, and other factors (10). It is a good target molecule related to PCa (11-13).  $^{68}\text{Ga}$ -PSMA positron emission tomography (PET)/CT is a new imaging examination method based on  $^{68}\text{Ga}$  nuclide labeled PSMA, which can accurately locate

### Highlight box

#### Key findings

- $^{68}\text{Ga}$ -prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/computed tomography (CT) is more sensitive than multiparametric magnetic resonance imaging (mpMRI) in the diagnosis of locally advanced prostate cancer (LAPC) pelvic lymph node metastasis (PLNM), which can play a guiding role in determining whether LAPC patients need to undergo pelvic lymph node dissection in clinical practice, and provide a method for realizing individualized and accurate treatment for LAPC patients.

#### What is known and what is new?

- Both  $^{68}\text{Ga}$ -PSMA PET/CT and mpMRI can play a role in the diagnosis of PLNM in prostate cancer.
- Through a retrospective analysis of the two examination modalities in LAPC patients, we found that  $^{68}\text{Ga}$ -PSMA PET/CT was more sensitive than mpMRI in the diagnosis of PLNM in LAPC patients.

#### What is the implication, and what should change now?

- Based on our analysis, we found that it was a more effective method to decide whether to conduct intraoperative lymph node dissection for LAPC patients by  $^{68}\text{Ga}$ -PSMA PET/CT, and different imaging measures help to improve the selection of whether LAPC patients need lymph node dissection by selecting different imaging measures, finally achieving individual precise treatment and reducing unnecessary medical measures.

PCa tissues, and has become a hot spot in PCa diagnosis and treatment research (14).

This retrospective study analyzed 50 patients with LAPC who underwent preoperative  $^{68}\text{Ga}$ -PSMA PET/CT and mpMRI examinations. The study aimed to compare the diagnostic value of the two methods in detecting pelvic LNM (PLNM) in PCa. We present this article in accordance with the TRIPOD reporting checklist (available at <https://tau.amegroups.com/article/view/10.21037/tau-24-15/rc>).

## Methods

### General information

We included 257 patients with PCa and performed post-surgical histopathological analysis to determine whether the patient was in the locally advanced stage of PCa. Ultimately, clinical data of 50 patients diagnosed with LAPC before surgery were retrospectively collected in Tongji Hospital from 2021-2023. The mean age of the patients was  $65.5 \pm 10.3$  years old, the total PSA (tPSA) before surgery was  $30.7 \pm 12.3$  ng/mL, and the Gleason score was 7 [7, 8]. All patients underwent  $^{68}\text{Ga}$ -PSMA PET/CT and mpMRI before surgery. All the 50 patients underwent laparoscopic/robot-assisted laparoscopic RP and extended PLND (ePLND), the excision area of lymph node dissection included the ureter across the iliac vessel and was performed bilaterally. Lymph nodes adjacent to the external iliac artery, obturator artery, and internal iliac artery were respectively removed. Dissection of anterior sacral lymph nodes was not performed routinely. The boundaries of lymph node dissection were as follows: upper to the ureter across the iliac vessel, lower to the start of abdominal wall arteriovenous, outer to genitofemoral nerve, inner to internal iliac artery. The exclusion criteria were (I) pathologically confirmed non-LAPC; (II) patients who did not perform  $^{68}\text{Ga}$ -PSMA PET/CT or mpMRI before surgery; and (III) patients who did not receive PLND during the operation. After operation, the patients were divided into clinical lymph node positive (cN+) and clinical lymph node negative (cN0) groups according to the results of pathological examination of lymph node. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (No. 2019CR101) and individual

consent for this retrospective analysis was waived.

### $^{68}\text{Ga}$ -PSMA PET/CT examination and image analysis

$^{68}\text{Ga}$ -PSMA-617 was synthesized by automated labeling module of ITM (Munich, Germany). The radiochemical purity of the synthesized product was higher than 95%. Patients receiving  $^{68}\text{Ga}$ -PSMA PET/CT were intravenously injected with  $^{68}\text{Ga}$ -PSMA-617 at 1.8–2.2 MBq per kg of body weight, followed by PET/CT imaging for 1 to 1.5 hours, which were produced by General Electronic Healthcare located in Chicago, IL, USA.

The scanning adopted 120 kV voltage, 120 mA current, and 3.8 mm layer thickness. The scans covered the pelvis and prostate, and each bed was scanned for two minutes. The PET image after attenuation correction of CT data was reconstructed by the sequential subset maximum expected value selection method, and the multi-directional fusion image of CT, PET, and PET-CT was obtained. LNM of PCa is considered to occur when maximum standardized uptake value (SUVmax)  $>2.5$  or the short diameter of the lymph node is more than 1.0 cm on  $^{68}\text{Ga}$ -PSMA PET/CT.

### mpMRI examination

The Avanto 1.5-T superconducting resonator of Siemens was used for magnetic resonance examination of the patients. Before the examination, the patient was given 15 mL glumine gadolinium penate intravenously with a syringe. The first scan was performed 20 seconds after the injection, and the scan lasted for 12–15 sessions. Before enhanced scanning, scanning was performed in four directions of prostate sagittal position, cross section, longitudinal relaxation position, and relaxation coronal plane, then localization scanning was performed in four directions, and magnetic resonance spectroscopy (MRS) was performed in these directions to scan the whole prostate. The scan sequences included transverse, coronal, and sagittal T2-weighted imaging (T2WI), transverse T1-weighted imaging (T1WI), adipose suppression T2WI, and diffusion-weighted imaging (DWI). Repetition time of scanning was 700 ms, echo time was 120 ms, excitation times were 6, reverse angle was  $90^\circ$ , layer thickness was 50 mm, and the total scanning time was 12 minutes. LNM of PCa is considered to occur when the short diameter of the lymph node is more than 1.0 cm on mpMRI.

**Table 1** Patient baseline data (n=50)

Basic information of patients	Values
Preoperative TNM staging	
T <sub>2</sub> N <sub>1</sub> M <sub>0</sub>	2 [4]
T <sub>3</sub> N <sub>0</sub> M <sub>0</sub>	29 [58]
T <sub>3</sub> N <sub>1</sub> M <sub>0</sub>	9 [18]
T <sub>4</sub> N <sub>0</sub> M <sub>0</sub>	6 [12]
T <sub>4</sub> N <sub>1</sub> M <sub>0</sub>	4 [8]
Age (years)	65.5±10.3 [57, 74.5]
Gleason score	7 [7, 8]
PSA (ng/mL)	30.7±12.3 [23, 39]
Intraoperative blood loss (mL)	90.1±36.3 [62.5, 110]
Operation time (min)	116.3±29.3 [95.1, 146.5]
Post-operative hospital stay (days)	7.1±1.9 [6, 8]
Complication	
Fever	5 [10]
Urine leakage	2 [4]
Lymphatic leakage	5 [10]
ISUP grading	
I	3 [6]
II	8 [16]
III	19 [38]
IV	8 [16]
V	12 [24]
Number of removed nodes per patient	12.82±3.71 [10.3, 14]
Number of positive nodes per patient	3.93±2.19 [5, 7]

Data are presented as n [%] or mean ± SD [range]. TNM, tumor, node, metastasis; PSA, prostate-specific antigen; ISUP, International Society of Urological Pathology.

### Image analysis

<sup>68</sup>Ga-PSMA PET/CT and mpMRI examination results were evaluated by two professional and senior nuclear medicine or imaging doctors without knowing the pathological diagnosis of patients, with visual analysis and semi-quantitative method. For those image results which were difficult to judge or with different opinions, a third experienced evaluator was invited to participate, and the final decision was made by combining opinions. mpMRI showed metastatic lymph nodes which were defined

as locally enhanced or diminished abnormal signals. If there is LNM, the signal is bright and high on DWI and significantly low on apparent diffusion coefficient (ADC).

### Statistical methods

Statistical analysis was conducted with SPSS (24.0) software. Statistical data conformed to normal distribution were described with mean ± standard deviation (SD), and inter-group comparison was conducted with *t*-test of two independent samples. For measurement data that did not conform to normal distribution, M (Q1, Q3) was used to describe them, and rank sum test was used for comparison between groups. Continuity check (Kappa test) was used to compare the consistency of the two imaging findings and postoperative pathological findings. Based on the number of patients who had lymphatic metastasis and the number of pelvic metastatic lymph nodes, chi-squared test was used to compare the sensitivity and specificity of local metastases detected by the two tests. The sensitivity and specificity of the two tests for the detection of local metastases were compared by chi-squared test. *P*<0.05 meant the difference was statistically significant.

### Results

In this study, 50 patients underwent <sup>68</sup>Ga-PSMA PET/CT and mpMRI examinations, followed by laparoscopic/robot-assisted laparoscopic RP and ePLND, and none was converted to open surgery during the operation. The operation time was 116.3±29.3 min. The intraoperative blood loss was 90.1±36.3 mL, and the hospital stay was 7.1±1.9 days after the operation. Postoperative complications occurred in 12 cases, including postoperative fever in five cases, urine leakage in two cases, and lymphatic leakage in five cases, which were relieved after anti-infection, urethral catheter pulling, and drainage catheter indentation time extension (see *Table 1* for details).

Postoperative pathological examination revealed that LNM was found in 16 patients, a total of 641 lymph nodes were dissected, including 63 metastatic lymph nodes. Fifteen patients were diagnosed with LNM with PSMA-PET, and 60 positive lymph nodes were detected. mpMRI diagnosed 11 patients with LNM and detected 41 positive lymph nodes. The number of removed nodes per patient was 12.82±3.71, and the number of removed nodes per patient was 3.93±2.19. In the diagnosis of PLNM of PCa, the detailed results of <sup>68</sup>Ga-PSMA PET/CT and mpMRI

**Table 2** Comparison of the number of LAPC pelvic lymph node and the number of positive PLNMs diagnosed by the two kinds of imaging examination

Test characteristics	PSMA-PET CT		mpMRI	
	Patient analysis	LN analysis	Patient analysis	LN analysis
Number of true-positive cases	15	60	11	41
Number of true-negative cases	34	578	33	573
Number of false-negative cases	1	3	5	22
Number of false-positive cases	0	0	1	5
Sensitivity, n/N (%)	15/16 (93.75)	60/63 (95.24)	11/16 (68.75)	41/63 (65.08)
Specificity, n/N (%)	34/34 (100.00)	578/578 (100.00)	33/34 (97.06)	573/578 (99.13)
PPV, n/N (%)	15/15 (100.00)	60/60 (100.00)	11/12 (91.67)	41/46 (89.13)
NPV, n/N (%)	34/35 (97.14)	578/581 (99.48)	33/38 (86.84)	573/595 (96.30)

LAPC, locally advanced prostate cancer; PLNM, pelvic lymph node metastasis; PSMA, prostate-specific membrane antigen; PET, positron emission tomography; CT, computed tomography; mpMRI, multiparametric magnetic resonance imaging; LN, lymph node; PPV, positive predictive value; NPV, negative predictive value.

are shown in *Table 2*. The sensitivity, specificity, positive predictive value, and negative predictive value of  $^{68}\text{Ga}$ -PSMA PET/CT diagnosis were as follows: 93.75%, 100.00%, 100.00%, 97.14%. The counterparts of mpMRI diagnosis were: 68.75%, 97.06%, 91.67%, 86.84%, both in sensitivity and negative predictive value,  $P < 0.05$ , the difference was statistically significant, compared with both in specificity and positive predictive value.

According to the number of LNMs, the diagnostic efficacy of  $^{68}\text{Ga}$ -PSMA PET/CT and mpMRI for PLNMs of PCa was analyzed, and the results are shown in *Table 2*. The sensitivity, specificity, positive predictive value, and negative predictive value of  $^{68}\text{Ga}$ -PSMA PET/CT were: 95.24%, 100.00%, 100.00%, 99.48%; the sensitivity, specificity, positive predictive value, and negative predictive value of mpMRI were 65.08%, 99.13%, 89.13%, and 96.30%, respectively. Comparing the sensitivity of the two methods,  $P < 0.05$  meant that the difference was statistically significant. Conversely, for specificity, positive predictive value, and negative predictive value,  $P$  value  $> 0.05$  indicated that the difference was not statistically significant.

As is shown in *Figure 1*, a typical case showed that  $^{68}\text{Ga}$ -PSMA PET/CT was significantly more sensitive than mpMRI in finding metastatic lymph nodes. The patient was a 68-year-old male with preoperative PSA 7.41 ng/mL and Gleason score of 4+5=9. *Figure 1A, 1B* show  $^{68}\text{Ga}$ -PSMA PET/CT detected right PLNM (arrow), while *Figure 1C* shows mpMRI did not detect PLNM. Postoperative

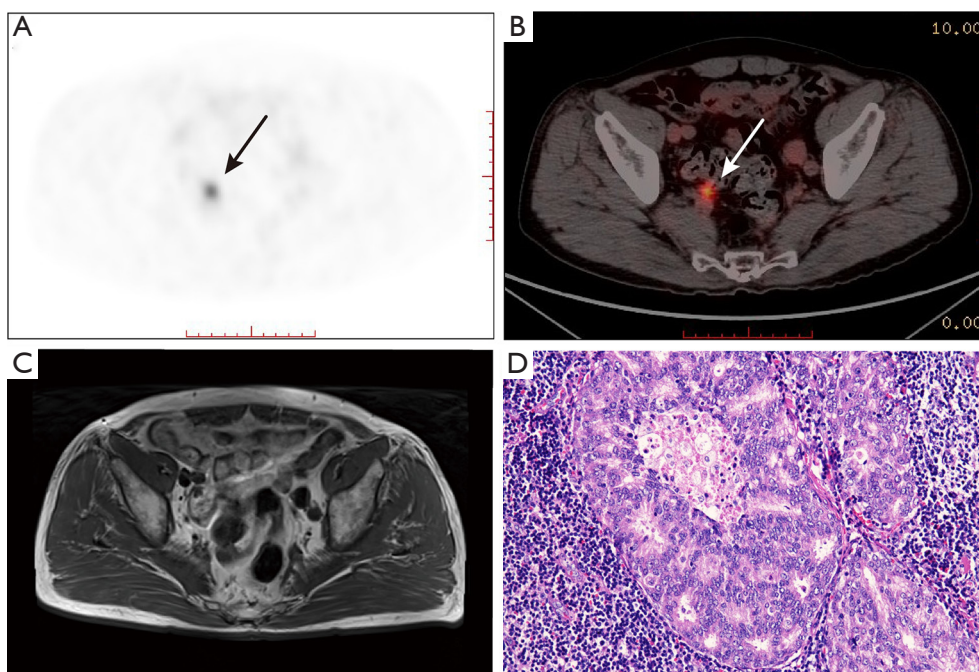
pathological report showed PCa metastasis in right pelvic lymph nodes (3/3). *Figure 1D* shows the hematoxylin-eosin (HE) staining image of the lymph node detected by  $^{68}\text{Ga}$ -PSMA-PET but omitted by mpMRI ( $\times 20$ ).

## Discussion

PCa is a kind of solid malignant tumor with the highest incidence in males, and the incidence of PCa is increasing rapidly in China (11,15). Approximately 30–40% of newly diagnosed PCa patients in China are LAPC, which is characterized by poor prognosis and prone to recurrence and metastasis (LNM), and once a patient develops LNMs, the prognosis is usually poor. For LAPC patients, the choice of treatment plan is often controversial. Surgical treatment has certain advantages in the treatment of LAPC, and RP can be used as one of the options.

A variety of predictive models have been proposed for preoperative assessment of the risk of LNM in PCa. For example, 588 patients with localized PCa who underwent RP and ePLND were enrolled in a scientific research (6). Based on PSA, clinical stage, Gleason score and the proportion of positive needle number in prostatic puncture, the risk of LNM was predicted by a Briganti nomogram (6). The sensitivity, specificity, and negative predictive value of LNM were 87.8%, 70.3%, and 98.4%, respectively. The AUC value was 87.6%. ePLND is recommended for patients with a risk of LNM more than 5%, which plays a major role in





**Figure 1** Comparison of  $^{68}\text{Ga}$ -PSMA PET/CT and mpMRI in detecting PLNM of PCa. (A)  $^{68}\text{Ga}$ -PSMA PET image reveals one focally increased tracer uptake (black arrow) in the right pelvic region. (B)  $^{68}\text{Ga}$ -PSMA PET/CT fusion image shows positive lymph node (SUVmax 7.3; white arrow) in the right pelvic region. (C) mpMRI image of the pelvic region is unremarkable. (D) The pathological result (HE staining,  $\times 20$ ) after PLND demonstrated PLNM in the right pelvic. PSMA, prostate-specific membrane antigen; PET, positron emission tomography; CT, computed tomography; mpMRI, multiparametric magnetic resonance imaging; PLNM, pelvic lymph node metastasis; PCa, prostate cancer; SUVmax, maximum standardized uptake value; HE, hematoxylin-eosin.

guiding the selection of surgical methods for PCa patients. However, the predictive effect of this model needs further clinical verification.

mpMRI is the most commonly used imaging examination method for judging the tumor, node, metastasis (TNM) staging of PCa at present, which can well display the prostate capsule, to check whether cancer lesion encroaches on the surrounding tissues and organs, and the metastatic situation of pelvic lymph nodes. However, mpMRI mainly identify metastatic lymph nodes by lymph node size. Previous studies have shown that mpMRI has the disadvantage of insufficient sensitivity, which makes it easy to miss PLNM before surgery (16,17), and up to 30% of patients have no suspicious LNMs in preoperative CT or mpMRI. However, LNM was found in the ePLND (18). Meanwhile, mpMRI is often difficult to distinguish inflammatory lymph nodes and reactive hyperplasia lymph nodes from tumor metastases (19).

Therefore, finding an accurate way to identify and diagnose PLNM is of great significance for the selection of treatment

methods and prediction of postoperative prognosis (20). In recent years, with the rapid development of nuclear medicine technology,  $^{68}\text{Ga}$ -PSMA-PET has been increasingly used in the early diagnosis of PCa and the detection of postoperative metastases (LNM, bone metastasis, visceral metastasis), showing good sensitivity and specificity. PSMA is a type II transmembrane glycoprotein (21), and it has the characteristics of tissue specificity, and is a promising target molecule for therapy of PCa (11). It has the following advantages:

- (I) PSMA is physiologically expressed in some human organs (such as prostate, kidney, small intestine, etc.), but the expression level in PCa tissues is 100–1,000 times higher than that in normal prostate tissues, and is positively correlated with the severity of PCa (such as stage and grade).
- (II) When patients enter the stage of castration resistance, PCa cells will lose a lot of PSAs, while PSMA is still highly expressed. Due to the high expression of PSMA in LNM area, PSMA-PET has

a great advantage in the diagnosis of PLNM in PCa.

- (III) When PSMA ligand binds to its enzyme active region, it can migrate and stay in PCa cells after internalization, which makes its enzyme active region an ideal site for imaging studies (22,23). <sup>68</sup>Ga-PSMA PET/CT technique has good biological characteristics and half-life. By using radionuclide <sup>68</sup>Ga to label PSMA, relevant lesions (primary lesions, metastases) can be shown (13).

Our research found that compared with mpMRI, <sup>68</sup>Ga-PSMA PET/CT was more sensitive to the diagnosis of PLNM in patients with LAPC. Similar results have been found in other studies. Hövels *et al.* reported that the sensitivity of MRI and CT in the diagnosis of LNMs of PCa was about 40%, but 30% of patients had LNMs smaller than 5 mm, which was likely to cause patients' disease recurrence (20,24). Abufaraj *et al.* retrospectively reviewed 149 high-risk PCa patients who underwent <sup>68</sup>Ga-PSMA-PET before RP, and found that <sup>68</sup>Ga-PSMA-PET had high diagnostic accuracy in monitoring regional LNM. Regional lymph node analysis in 65 patients showed that the sensitivity of the left and right lymph node monitoring reached more than 90% (25). All the above studies indicate that <sup>68</sup>Ga-PSMA-PET is expected to become an effective method for the early detection of metastatic lymph nodes in PCa, and provide assistance for the formulation of treatment strategies (20), so as to benefit PCa patients.

Overall, <sup>68</sup>Ga-PSMA PET/CT showed higher sensitivity and accuracy compared to mpMRI. Therefore, <sup>68</sup>Ga-PSMA PET/CT may be a more suitable approach for detecting PLNM in LAPC patients, highlighting the importance of utilizing advanced imaging techniques to accurately detect LNM in PCa patients which may have significant implications for treatment outcomes of LAPC patients.

However, the number of patients with <sup>68</sup>Ga-PSMA PET/CT and mpMRI examination included in this study was relatively small, which may have some influence on the results. Therefore, we will conduct prospective randomized controlled studies with a larger sample size to further confirm the research conclusions in the future.

## Conclusions

To sum up, this study shows that for the detection of pelvic lymph nodes in patients with LAPC, the sensitivity of <sup>68</sup>Ga-PSMA PET/CT is higher than that of mpMRI, which is of

great significance for preoperative assessment of PLNM and accurate staging, guiding surgeons to optimize treatment plans, and achieve personalized precision medicine.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (No. 2019CR101) and individual consent for this retrospective analysis was waived.

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## References

1. Siegel RL, Miller KD, Wagle NS, et al. Cancer statistics, 2023. *CA Cancer J Clin* 2023;73:17-48.
2. Hofbauer LC, Bozec A, Rauner M, et al. Novel approaches to target the microenvironment of bone metastasis. *Nat Rev Clin Oncol* 2021;18:488-505.
3. Moris L, Cumberbatch MG, Van den Broeck T, et al. Benefits and Risks of Primary Treatments for High-risk Localized and Locally Advanced Prostate Cancer: An International Multidisciplinary Systematic Review. *Eur Urol* 2020;77:614-27.
4. Rebello RJ, Oing C, Knudsen KE, et al. Prostate cancer. *Nat Rev Dis Primers* 2021;7:9.
5. Mottet N, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol* 2021;79:243-62.
6. Briganti A, Larcher A, Abdollah F, et al. Updated nomogram predicting lymph node invasion in patients with prostate cancer undergoing extended pelvic lymph node dissection: the essential importance of percentage of positive cores. *Eur Urol* 2012;61:480-7.
7. Cacciamani GE, Maas M, Nassiri N, et al. Impact of Pelvic Lymph Node Dissection and Its Extent on Perioperative Morbidity in Patients Undergoing Radical Prostatectomy for Prostate Cancer: A Comprehensive Systematic Review and Meta-analysis. *Eur Urol Oncol* 2021;4:134-49.
8. Stabile A, Giganti F, Rosenkrantz AB, et al. Multiparametric MRI for prostate cancer diagnosis: current status and future directions. *Nat Rev Urol* 2020;17:41-61.
9. Wang Y, Galante JR, Haroon A, et al. The future of PSMA PET and WB MRI as next-generation imaging tools in prostate cancer. *Nat Rev Urol* 2022;19:475-93.
10. Roberts MJ, Maurer T, Perera M, et al. Using PSMA imaging for prognostication in localized and advanced prostate cancer. *Nat Rev Urol* 2023;20:23-47.
11. Wüstemann T, Haberkorn U, Babich J, et al. Targeting prostate cancer: Prostate-specific membrane antigen based diagnosis and therapy. *Med Res Rev* 2019;39:40-69.
12. Chavoshi M, Mirshahvalad SA, Metser U, et al. (68)Ga-PSMA PET in prostate cancer: a systematic review and meta-analysis of the observer agreement. *Eur J Nucl Med Mol Imaging* 2022;49:1021-9.
13. Farolfi A, Calderoni L, Mattana F, et al. Current and Emerging Clinical Applications of PSMA PET Diagnostic Imaging for Prostate Cancer. *J Nucl Med* 2021;62:596-604.
14. Bukavina L, Luckenbaugh AN, Hofman MS, et al. Incorporating Prostate-specific Membrane Antigen Positron Emission Tomography in Management Decisions for Men with Newly Diagnosed or Biochemically Recurrent Prostate Cancer. *Eur Urol* 2023;83:521-33.
15. Bergengren O, Pekala KR, Matsoukas K, et al. 2022 Update on Prostate Cancer Epidemiology and Risk Factors-A Systematic Review. *Eur Urol* 2023;84:191-206.
16. Vale CL, Fisher D, Kneebone A, et al. Adjuvant or early salvage radiotherapy for the treatment of localised and locally advanced prostate cancer: a prospectively planned systematic review and meta-analysis of aggregate data. *Lancet* 2020;396:1422-31.
17. Pignot G, Maillat D, Gross E, et al. Systemic treatments for high-risk localized prostate cancer. *Nat Rev Urol* 2018;15:498-510.
18. Thoeny HC, Barbieri S, Froehlich JM, et al. Functional and Targeted Lymph Node Imaging in Prostate Cancer: Current Status and Future Challenges. *Radiology* 2017;285:728-43.
19. Schlemmer HP, Krause BJ, Schütz V, et al. Imaging of Prostate Cancer. *Dtsch Arztebl Int* 2021;118:713-9.
20. Hope TA, Eiber M, Armstrong WR, et al. Diagnostic Accuracy of 68Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection: A Multicenter Prospective Phase 3 Imaging Trial. *JAMA Oncol* 2021;7:1635-42.
21. He Y, Xu W, Xiao YT, et al. Targeting signaling pathways in prostate cancer: mechanisms and clinical trials. *Signal Transduct Target Ther* 2022;7:198.
22. Perera M, Papa N, Roberts M, 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.
23. Han S, Woo S, Kim YJ, et al. Impact of 68Ga-PSMA PET on the Management of Patients with Prostate Cancer: A Systematic Review and Meta-analysis. *Eur Urol* 2018;74:179-90.
24. Hövels AM, Heesackers RA, Adang EM, et al. The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis. *Clin Radiol* 2008;63:387-95.



25. Abufaraj M, Grubmüller B, Zeitlinger M, et al. Prospective evaluation of the performance of [68Ga]Ga-PSMA-11 PET/CT(MRI) for lymph node staging in patients

undergoing superextended salvage lymph node dissection after radical prostatectomy. *Eur J Nucl Med Mol Imaging* 2019;46:2169-77.

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