

REVIEW

Diagnostic accuracy of MRI and PSMA PET/CT for detection of histologically confirmed lymph node metastasis in prostate cancer: A systematic review

Emeka Ihechi Udeh¹, Solomon Anyimba², Loius Okolie³, Rotimi David¹, Maureen O. Udeh⁵

¹ Department of Urology, Dorset County Hospital NHS, Dorchester, England, United Kingdom;

² University of Nigeria Teaching Hospital Enugu Nigeria;

³ University of Nigeria Teaching Hospital Enugu Nigeria;

⁴ Kingston University, England, United Kingdom.

Summary

Objective: To compare the diagnostic accuracy of prostate-specific membrane antigen

positron emission tomography/computed tomography (PSMA PET/CT) and multiparametric magnetic resonance imaging (mpMRI) for the detection of histologically confirmed pelvic lymph node metastases in patients with intermediate- and high-risk prostate cancer.

Methods: A systematic review and meta-analysis were conducted according to PRISMA guidelines. PubMed, Embase, and Cochrane Library databases were searched from January 2011 to March 2026. Studies evaluating PSMA PET/CT and/or mpMRI for preoperative pelvic lymph node staging using histopathology as the reference standard were included. Study quality was assessed using the Quality Assessment of Diagnostic Performance Studies-2 tool (QUADAS-2). Pooled sensitivity and specificity were estimated using a hierarchical bivariate random-effects (Reitsma) model, and hierarchical summary receiver operating characteristic (HSROC) curves were generated.

Results: Sixteen studies comprising 1,999 patients met the inclusion criteria. Fourteen studies contributed to the PSMA PET/CT analysis and six studies to the mpMRI analysis. For PSMA PET/CT, pooled sensitivity was 54.6% (95% CI 43.7-65.1%) and pooled specificity was 92.7% (95% CI 90.5-94.4%). The HSROC area under the curve (AUC) was 0.909. For mpMRI, pooled sensitivity was 33.0% (95% CI 18.7-51.3%) and pooled specificity was 94.9% (95% CI 92.2-96.8%), with an HSROC AUC of 0.941. Indirect comparison of pooled estimates suggested that PSMA PET/CT had higher sensitivity and a higher diagnostic odds ratio than mpMRI. However, because these estimates were derived from separate bodies of evidence rather than direct head-to-head comparative studies, this comparison should be interpreted with caution.

Conclusions: PSMA PET/CT demonstrated higher pooled sensitivity than mpMRI while maintaining similarly high specificity for detecting pelvic lymph node metastases. However, the moderate sensitivity of both imaging modalities indicates that a negative PSMA PET/CT scan cannot reliably exclude microscopic nodal disease. Furthermore, this comparison between pooled estimates should be interpreted with caution because it is based on an indirect comparison rather than a formal head-to-head meta-analysis. Consequently, extended pelvic lymph node dissection remains the reference standard for pathological nodal staging in appropriately selected patients, and prospective head-to-

head comparative studies are required to define the relative diagnostic performance of PSMA PET/CT and mpMRI.

KEY WORDS: Prostate cancer; PSMA PET/CT; Multiparametric MRI; Lymph node metastasis; Diagnostic accuracy; Systematic review; Meta-analysis.

Submitted 4 June 2026; Accepted 5 July 2026

INTRODUCTION

Prostate cancer remains one of the most diagnosed malignancies in men worldwide and is a leading cause of cancer-related mortality (1). Accurate staging is crucial for guiding treatment decisions, particularly in determining the need for pelvic lymph node dissection (PLND) and multimodal therapy (2). Lymph node metastasis (LNM) is a key prognostic factor associated with increased risk of biochemical recurrence and reduced survival (3).

Conventional imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) have historically demonstrated limited sensitivity for nodal staging due to reliance on morphological criteria, including lymph node size and shape (4). Consequently, small metastatic deposits within normal-sized lymph nodes are frequently missed (4). Despite the limitations of morphologic imaging, certain characteristics - such as the absence of a fatty hilum, irregular or poorly defined nodal margins exceeding size criteria, a rounded shape in all dimensions, reduced signal intensity on T2-weighted images, and heterogeneous parenchymal signal - can aid in identifying metastatic involvement in prostate cancer nodal staging (5). Nonetheless, this method is contingent upon experience and may be challenging to replicate.

The development of PSMA PET/CT has significantly improved the imaging landscape by enabling functional detection of tumour-specific tracer uptake (6). Early studies have demonstrated improved diagnostic performance compared to conventional imaging (7); however, the ability of PSMA PET/CT to detect micrometastatic disease remains limited (8).

Despite these advances, histopathological evaluation following PLND or extended PLND (ePLND) remains the

gold standard for nodal staging. Given the morbidity associated with surgical staging, there is a growing need to assess the reliability of non-invasive imaging modalities (9). Previous meta-analyses have evaluated PSMA PET and MRI for lymph node staging; however, many included studies used heterogeneous or non-histological reference standards. Our study uniquely restricts inclusion to studies with histopathological confirmation (ePLND), thereby providing a more robust and clinically reliable estimate of diagnostic accuracy. This study aims to systematically evaluate the diagnostic accuracy of MRI and PSMA PET/CT for detecting LNM in prostate cancer using histopathology as the reference standard.

METHODS

Study design and reporting standards

This systematic review and meta-analysis was conducted to evaluate and compare the diagnostic accuracy of PSMA PET/CT and mpMRI for the detection of pelvic lymph node metastases in patients with intermediate- and high-risk prostate cancer. The review was performed in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA 2020) statement and the PRISMA extension for Diagnostic Test Accuracy Studies (PRISMA-DTA). The methodology was developed a priori and registered with the International Prospective Register of Systematic Reviews - PROSPERO 2026 CRD420261380019.

Eligibility criteria

Eligibility criteria were defined according to the *Population, Index Test, Comparator, Outcome, and Study Design* (PICOS) framework.

Population: Studies involving adult men (≥ 18 years) with biopsy-proven prostate adenocarcinoma undergoing pre-operative lymph node staging prior to radical prostatectomy and pelvic lymph node dissection were considered eligible. Studies enrolling patients with intermediate-risk, high-risk, or locally advanced disease were included.

Index Tests: The index tests of interest were the following: 1) PSMA PET/CT using any clinically approved PSMA tracer, including ^{68}Ga -PSMA-11, ^{18}F -PSMA-1007, ^{18}F -DCFPyL, and other PSMA-targeted radiotracers. 2) Multiparametric MRI performed according to institutional or contemporary guideline-based protocols.

Reference Standard: The reference standard was histopathological examination of lymph nodes obtained during PLND or ePLND. Histopathological confirmation was required for study inclusion to minimise verification bias and ensure that diagnostic accuracy estimates were based on the highest available standard.

Outcomes: Studies were required to report sufficient information to determine: 1) *True positives* (TP) 2) *False positives* (FP) 3) *False negatives* (FN) 4) *True negatives* (TN) or provide data from which these values could be derived.

The primary outcome was diagnostic accuracy for the detection of pelvic lymph node metastases.

Study Design: Prospective and retrospective cohort studies, diagnostic accuracy studies, and clinical trials were eligible. Conference abstracts, narrative reviews, system-

atic reviews, editorials, letters, case reports, and animal studies were excluded.

Literature search strategy

A comprehensive literature search was conducted in the following electronic databases: 1) PubMed/MEDLINE 2) Embase 3) Cochrane Central Register of Controlled Trials (CENTRAL) The search covered the period from January 2011 to March 2026.

The search strategy combined *Medical Subject Headings* (MeSH) and free-text terms relating to prostate cancer, PSMA imaging, MRI, lymph node metastases, and diagnostic accuracy.

Search terms included: ("prostate cancer" OR "prostatic neoplasm") AND ("PSMA PET" OR " ^{68}Ga -PSMA" OR " ^{18}F -PSMA" OR " ^{18}F -DCFPyL" OR " ^{18}F -PSMA-1007") AND ("multiparametric MRI" OR "mpMRI") AND ("lymph node metastasis" OR "pelvic lymph node" OR "nodal staging")

Reference lists of eligible studies and relevant review articles were manually screened to identify additional studies not captured during electronic database searches.

The complete database-specific search strategies for MEDLINE, Embase and the Cochrane Library have been provided as supplementary material (**Supplementary Table S2**).

Study selection

All search results were imported into Rayyan software for screening and duplicate removal. Study selection was performed independently by two reviewers in two stages: *Stage 1: Title and Abstract Screening:* Titles and abstracts were screened against the predefined eligibility criteria. Irrelevant records were excluded at this stage. *Stage 2: Full-Text Review:* Potentially eligible studies underwent full-text assessment. Studies meeting all inclusion criteria were included in the final review. Disagreements between reviewers were resolved through discussion and consensus. Where necessary, a third reviewer was consulted. The study selection process was documented using a PRISMA flow diagram.

Data extraction

Data extraction was performed independently by two reviewers using a standardised extraction template.

The following information was collected: Study Characteristics: First author, Year of publication, Country, Study design, Sample size, Mean or median age, PSA level, Risk group classification, Clinical stage, Imaging modality, PSMA tracer type.

Diagnostic accuracy data

The following values were extracted directly or reconstructed from published data: TP, FP, FN, TN. Where studies reported sensitivity, specificity, prevalence, or contingency tables without explicit TP/FP/FN/TN values, these were derived mathematically.

Imaging characteristics

For PSMA PET studies: Tracer type, Imaging protocol, Interpretation criteria.

For MRI studies: MRI field strength, PI-RADS version, Nodal assessment criteria.

Risk of bias assessment

Methodological quality was assessed independently by two reviewers using the QUADAS-2 tool. The following domains were evaluated: Patient selection, Index test, Reference standard, Flow and timing. Each domain was classified as: Low risk of bias, Some concerns, High risk of bias. Applicability concerns were also assessed across patient selection, index test, and reference standard domains. Discrepancies were resolved through consensus. Retrospective study design alone was considered insufficient to classify a study as having a high risk of bias. Assessments were based on the signalling questions within each QUADAS-2 domain. Studies were judged as having "some concerns" for patient selection when consecutive or random recruitment was unclear or when retrospective inclusion introduced potential selection bias. Similarly, studies were judged as having "some concerns" in the flow and timing domain when exclusions, withdrawals, or verification of all enrolled participants were incompletely reported.

Statistical analysis

A diagnostic accuracy meta-analysis was performed using R statistical software (version 4.5.0) with the mada package.

Bivariate Random-Effects Meta-analysis

Pooled sensitivity and specificity were estimated using the hierarchical bivariate random-effects model described by Reitsma et al. This model jointly analyses sensitivity and specificity while accounting for their inherent correlation and between-study heterogeneity. The model was fitted using *restricted maximum likelihood* (REML) estimation.

Hierarchical summary receiver operating characteristic analysis

Hierarchical summary receiver operating characteristic (HSROC) curves were generated for both PSMA PET/CT and mpMRI. For each modality, the following were calculated: Pooled sensitivity, Pooled specificity, False-positive rate, Area under the HSROC curve (AUC), Partial AUC, Summary operating points, confidence regions, and prediction regions were plotted.

Diagnostic odds ratio analysis

Univariate random-effects diagnostic meta-analysis was performed using the mada function. Pooled *diagnostic odds ratios* (DORs) with 95% confidence intervals were calculated for each imaging modality.

Assessment of heterogeneity

Between-study heterogeneity was assessed using: Cochran's Q statistic, Higgins' I^2 statistic, Zhou and Dendukuri I^2 estimates, Holling sample-size adjusted I^2 estimates. Heterogeneity was interpreted according to conventional thresholds: < 25%: low, 25-50%: moderate, 50%: substantial.

Subgroup analysis

Prespecified subgroup analyses were performed according to study design (prospective versus retrospective studies). Tracer-specific subgroup analyses were planned; however, insufficient numbers of studies within individual tracer categories prevented reliable hierarchical modelling.

Assessment of publication bias

A formal assessment of publication bias was not performed. Conventional approaches, such as funnel plots or Deeks' asymmetry test, have limited validity in diagnostic test accuracy meta-analyses, particularly when few studies are available. Because the mpMRI analysis included a small number of studies and publication bias methods are not well adapted to hierarchical diagnostic models, a formal evaluation was not considered appropriate.

Statistical Significance

All statistical tests were two-sided. A p-value < 0.05 was considered statistically significant.

RESULTS

Study selection

A comprehensive literature search identified 736 records from MEDLINE, Embase, and Cochrane databases. After removal of 73 duplicate records, 663 studies underwent title and abstract screening. Following screening, 631 records were excluded for not meeting the inclusion criteria, leaving 32 articles for full-text assessment. Sixteen studies were subsequently excluded because of inappropriate comparators, interventions, study design, patient population, or outcomes. Ultimately, 16 studies met the eligibility criteria and were included in the qualitative and quantitative synthesis (Figure 1).

Study characteristics

The systematic review and meta-analysis included 16 studies with a total of 1,999 patients. The studies were published between 2019 and 2026 and were conducted across Australia, Austria, Sweden, Turkey, China, Italy, Spain, and the United States. Six studies were prospective in design, including three multicentre trials, while ten studies were retrospective cohort studies.

Histopathological examination of PLND specimens served as the reference standard in all included studies. Most studies enrolled patients with intermediate- and high-risk prostate cancer undergoing preoperative nodal staging prior to radical prostatectomy and pelvic lymph node dissection. PSMA PET tracers included ^{68}Ga -PSMA-11, ^{18}F -PSMA-1007, and ^{18}F -DCFPyL, while MRI studies used multiparametric MRI according to institutional protocols. Detailed study characteristics are presented in Table 1.

Diagnostic accuracy of PSMA PET/CT

Fourteen studies contributed to the pooled analysis of PSMA PET/CT for the detection of histologically confirmed pelvic lymph node metastases. Using the bivariate random-effects Reitsma model, the pooled sensitivity was 54.6% (95% CI 43.7-65.1%), while the pooled false-positive rate was 7.3% (95% CI 5.6-9.5%), corresponding to a pooled specificity of 92.7% (95% CI 90.5-94.4%). The *hierarchical summary receiver operating characteristic* (HSROC) model demonstrated excellent overall diagnostic discrimination with an *area under the curve* (AUC) of 0.909. Between-study heterogeneity was low to moderate. The Zhou and Dendukuri I^2 estimate was 9.7%, while unadjusted Holling estimates ranged from 32.3% to 59.9%. The pooled *diag-*

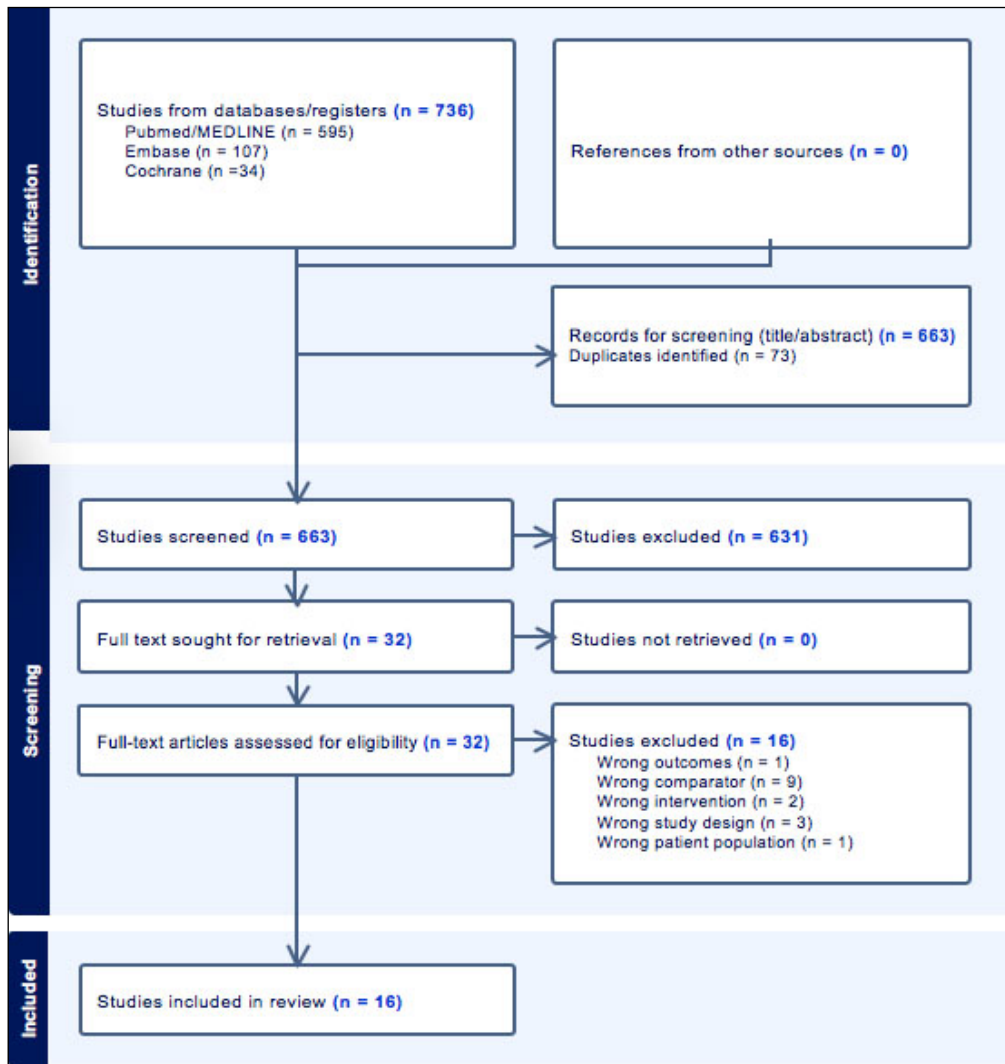


Figure 1.
The PRISMA flow chart.

Table 1.
Characteristics of included studies.

Study	Year	Country	Design	n	Population Detail	Reference Standard
Yaxley et al. (10)	2019	Australia	Prospective	208	RP + PLND after ⁶⁸ Ga-PSMA PET/CT	Histopathology (PLND)
Szigeti et al. (11)	2022	Austria	Prospective	52	mpMRI and ⁶⁸ Ga-PSMA-11 PET/CT before RP + ePLND	Histopathology (ePLND)
Franklin et al. (12)	2021	Australia	Retrospective cohort	233	mpMRI and ⁶⁸ Ga-PSMA PET/CT before RALP + PLND	Histopathology (PLND)
Hope et al. (6)	2021	USA	Prospective multicentre Phase III	277	⁶⁸ Ga-PSMA-11 PET before RP + PLND	Histopathology (PLND)
Pienta et al. (OSPREY)(13)	2021	USA/Canada	Prospective multicentre Phase 2/3	252	¹⁸ F-DCFPyL PET/CT before RP + ePLND	Histopathology (ePLND)
Ingvar et al. (8)	2022	Sweden	Retrospective cohort	104	¹⁸ F-PSMA-1007 PET/CT before RALP + ePLND	Histopathology (ePLND)
Arslan et al. (14)	2022	Turkey	Retrospective	39	mpMRI and ⁶⁸ Ga-PSMA PET/CT before RP + ePLND	Histopathology (ePLND)
Tang et al. (15)	2023	China	Retrospective single-centre	130	mpMRI and ¹⁸ F-PSMA-1007 PET/CT before RP	Histopathology ± LND
Maestroni et al. (16)	2023	Italy	Retrospective	42	⁶⁸ Ga-PSMA PET/CT before RP + ePLND	Histopathology (ePLND)
Xiong et al. (17)	2024	China	Retrospective single-centre	50	mpMRI and ⁶⁸ Ga-PSMA PET/CT before RP + ePLND	Histopathology (ePLND)
Pepe et al. (18)	2024	Italy	Prospective	78	PSMA PET/CT before RP + ePLND	Histopathology (ePLND)
Dinckal et al. (19)	2025	Turkey	Retrospective	78	mpMRI and ⁶⁸ Ga-PSMA PET/CT before RP	Histopathology
Arena et al. (20)	2025	Italy	Retrospective	156	PSMA PET/CT before RARP + LND	Histopathology (LND)
Eraky et al. (21)	2025	USA	Retrospective	189	¹⁸ F-DCFPyL PET/CT before RP + PLND	Histopathology
Talavera Cobo et al. (22)	2026	Spain	Retrospective	53*	mpMRI and ⁶⁸ Ga-PSMA-11 PET/CT before RP + ePLND	Histopathology (ePLND)
Daouacher et al. (23)	2026	Sweden	Prospective multicentre	99	MRI before ePLND	Histopathology (ePLND)

*53 patients included in nodal accuracy analysis.

nostic odds ratio (DOR) from the univariate model was 16.88 (95% CI 10.32-27.60), indicating a strong overall association between PSMA PET findings and histologically

confirmed nodal metastases. Cochran's Q test showed no statistically significant heterogeneity ($Q = 17.05$, $p = 0.197$), with Higgins' I^2 of 23.7% (Table 2).

Table 2.

Diagnostic accuracy of PSMA PET for detection of pelvic lymph node metastasis in 14 selected studies.

Study	Tracer	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)
Yaxley 2019	^{68}Ga -PSMA PET/CT	21	10	34	143	38.2	93.5
Szigeti 2022	^{68}Ga -PSMA-11	6	3	4	35	60.0	91.0
Franklin 2021	^{68}Ga -PSMA PET	28	14	30	161	48.3	92.0
Hope 2021	^{68}Ga -PSMA-11	30	10	45	192	40.0	95.0
Pienta (OSPREV) 2021	^{18}F -DCFPyL	25	4	37	186	40.3	97.9
Ingvar 2022	^{18}F -PSMA-1007	7	3	19	75	26.9	96.2
Tang 2023	^{18}F -PSMA-1007	10	11	6	103	62.5	90.4
Maestroni 2023	^{68}Ga -PSMA PET	6	0	1	35	85.7	100.0
Xiong 2024	^{68}Ga -PSMA PET/CT	15	0	1	34	93.8	100.0
Pepe 2024	PSMA PET/CT	14	2	4	58	77.8	96.7
Dinckal 2025	^{68}Ga -PSMA PET/CT	5	3	5	55	50.0	94.8
Arena 2025	PSMA PET/CT	9	12	16	119	36.0	90.8
Eraky 2025	^{18}F -DCFPyL	4	24	1	160	80.0	86.9
Talavera Cobo 2026	^{68}Ga -PSMA-11	11	1	1	40	91.7	97.6

Table 3.

Diagnostic accuracy of PSMA PET for detection of pelvic lymph node metastasis in 14 selected studies.

Study	Modality	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)
Szigeti 2022	mpMRI	5	1	5	37	50.0	97.4
Franklin 2021	3T mpMRI	13	9	45	166	22.4	94.9
Xiong 2024	mpMRI	11	1	5	33	68.8	97.1
Dinckal 2025	mpMRI	3	5	7	53	30.0	91.4
Daouacher 2026	Conventional MRI	10	3	29	57	24.5	95.0
Talavera Cobo 2026	mpMRI	1	1	11	40	8.3	97.6

Table 4.

Pooled diagnostic performance of PSMA PET/CT and mpMRI for detection of histologically confirmed pelvic lymph node metastases.

Parameter	PSMA PET/CT	mpMRI
Studies included (n)	14	6
Pooled sensitivity (95% CI)	54.6% (43.7-65.1)	33.0% (18.7-51.3)
Pooled specificity (95% CI)	92.7% (90.5-94.4)	94.9% (92.2-96.8)
False positive rate (95% CI)	7.3% (5.6-9.5)	5.1% (3.2-7.8)
HSROC AUC	0.909	0.941
Diagnostic Odds Ratio (95% CI)	16.88 (10.32-27.60)	8.35 (3.78-18.42)
Cochran's Q (p value)	17.05 ($p = 0.197$)	5.45 ($p = 0.364$)
Higgins' I^2 (%)	23.7%	8.2%
Between-study SD (Sensitivity)	0.660	0.755
Between-study SD (False Positive Rate)	0.334	0.127

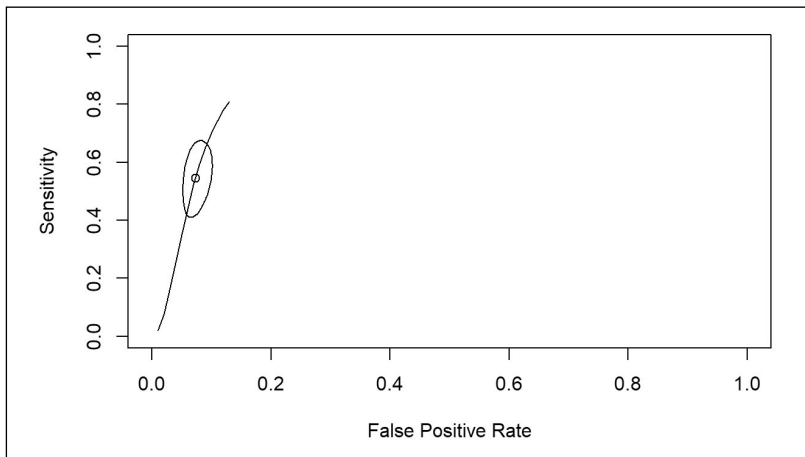
HSROC = Hierarchical Summary Receiver Operating Characteristic; AUC = Area Under the Curve; CI = Confidence Interval; DOR = Diagnostic Odds Ratio.

Diagnostic accuracy of multiparametric MRI

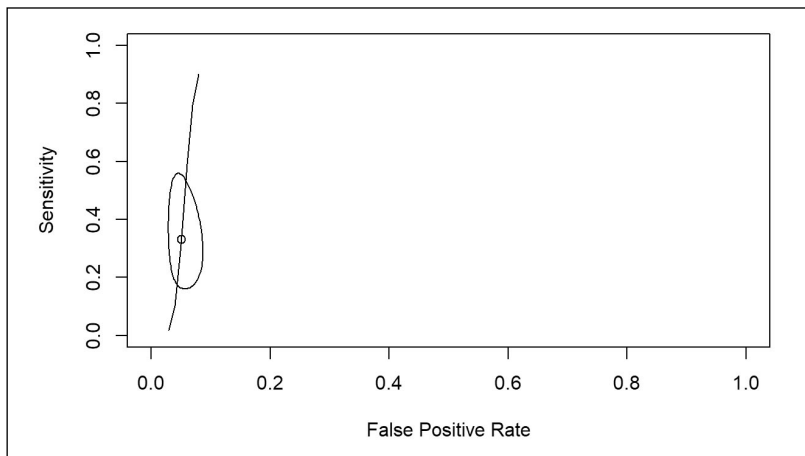
Six studies were included in the pooled analysis of multiparametric MRI. The bivariate Reitsma model demonstrated a pooled sensitivity of 33.0% (95% CI 18.7-51.3%) and a pooled false-positive rate of 5.1% (95% CI 3.2-7.8%), corresponding to a pooled specificity of 94.9% (95% CI 92.2-96.8%). The HSROC analysis demonstrated good overall discrimination with an AUC of 0.941. The pooled diagnostic odds ratio was 8.35 (95% CI 3.78-18.42). Between-study heterogeneity was low, with Higgins' I^2 of 8.2% and a non-significant Cochran's Q statistic ($Q = 5.45$, $p = 0.364$) (Tables 3, 4). Pooled sensitivity and specificity were estimated using the Reitsma bivariate random-effects model. Diagnostic odds ratios were obtained using univariate random-effects meta-analysis.

Comparative diagnostic performance of PSMA PET/CT and mpMRI

PSMA PET/CT demonstrated higher pooled sensitivity

**Figure 2.**

HSROC curve of PSMA PET/CT for detection of pelvic lymph node metastases in prostate cancer.

**Figure 3.**

HSROC curve of multiparametric MRI for pelvic lymph node staging in prostate cancer.

than mpMRI (54.6% vs. 33.0%) while maintaining similarly high specificity (92.7% vs. 94.9%). The pooled diagnostic odds ratio was also higher for PSMA PET/CT (16.88 vs. 8.35) (Figure 2).

The open circle represents the pooled estimate of sensitivity and specificity. The inner ellipse represents the 95% confidence region around the pooled estimate, while the outer ellipse represents the 95% prediction region. The solid curve denotes the *hierarchical summary receiver operating characteristic* (HSROC) model fitted using a bivariate random-effects approach (Figure 3).

The open circle represents the pooled estimate of sensitivity and specificity. The inner ellipse represents the 95% confidence region around the pooled estimate, while the outer ellipse represents the 95% prediction region. The solid curve denotes the HSROC model fitted using a bivariate random-effects approach.

The HSROC analyses demonstrated good overall diagnostic performance for both modalities, with AUC values of 0.909 for PSMA PET/CT and 0.941 for MRI.

Subgroup analysis

Subgroup analyses were performed according to study design. Among prospective PSMA PET studies, pooled sensitivity was higher than that observed in retrospective studies, while specificity remained consistently high across both subgroups. Retrospective studies demonstrat-

ed a pooled sensitivity of 60.7% (95% CI 43.3-75.8%) and specificity of 90.6% (95% CI 87.9-92.8%), with an AUC of 0.908. Heterogeneity remained low following stratification by study design. Tracer-specific subgroup analyses were explored; however, the limited number of studies with complete TP, FP, FN and TN data within individual tracer categories precluded reliable HSROC modelling and formal pooled estimates.

Diagnostic odds ratio analysis

Univariate diagnostic meta-analysis demonstrated a pooled DOR of 16.88 (95% CI 10.32-27.60) for PSMA PET/CT.

For MRI, the pooled DOR was 8.35 (95% CI 3.78-18.42), approximately half that observed for PSMA PET/CT.

Heterogeneity was low for both modalities. PSMA PET/CT demonstrated a Cochran's Q statistic of 17.05 ($p = 0.197$) with $I^2 = 23.7\%$, while MRI demonstrated a Cochran's Q statistic of 5.45 ($p = 0.364$) with $I^2 = 8.2\%$.

Risk of bias assessment

The methodological quality of the included studies was assessed using the QUADAS-2 tool (Figures 4, 5). Overall, study quality was high. Six studies (37.5%) were evaluated to have a low risk of bias in patient selection, while ten studies (62.5%) were assessed as having some concerns, primarily due to retrospective patient recruitment or unclear sam-

Figure 4.

QUADAS-2 Risk-of-Bias Traffic-Light Plot.

Traffic-light representation of risk-of-bias assessment for each included study across the four QUADAS-2 domains: patient selection, index test, reference standard, and flow and timing.

Study	QUADAS-2 Domain			
	Patient Selection	Index Test	Reference Standard	Flow and Timing
Yaxley et al., 2019	●	●	●	●
Szigeti et al., 2022	●	●	●	●
Franklin et al., 2021	●	●	●	●
Hope et al., 2021	●	●	●	●
Pienta et al. (OSPREDY), 2021	●	●	●	●
Ingvar et al., 2022	●	●	●	●
Arslan et al., 2022	●	●	●	●
Tang et al., 2023	●	●	●	●
Maestroni et al., 2023	●	●	●	●
Xiong et al., 2024	●	●	●	●
Pepe et al., 2024	●	●	●	●
Dinckal et al., 2025	●	●	●	●
Arena et al., 2025	●	●	●	●
Eraky et al., 2025	●	●	●	●
Talavera Cobo et al., 2026	●	●	●	●
Daouacher et al., 2026	●	●	●	●

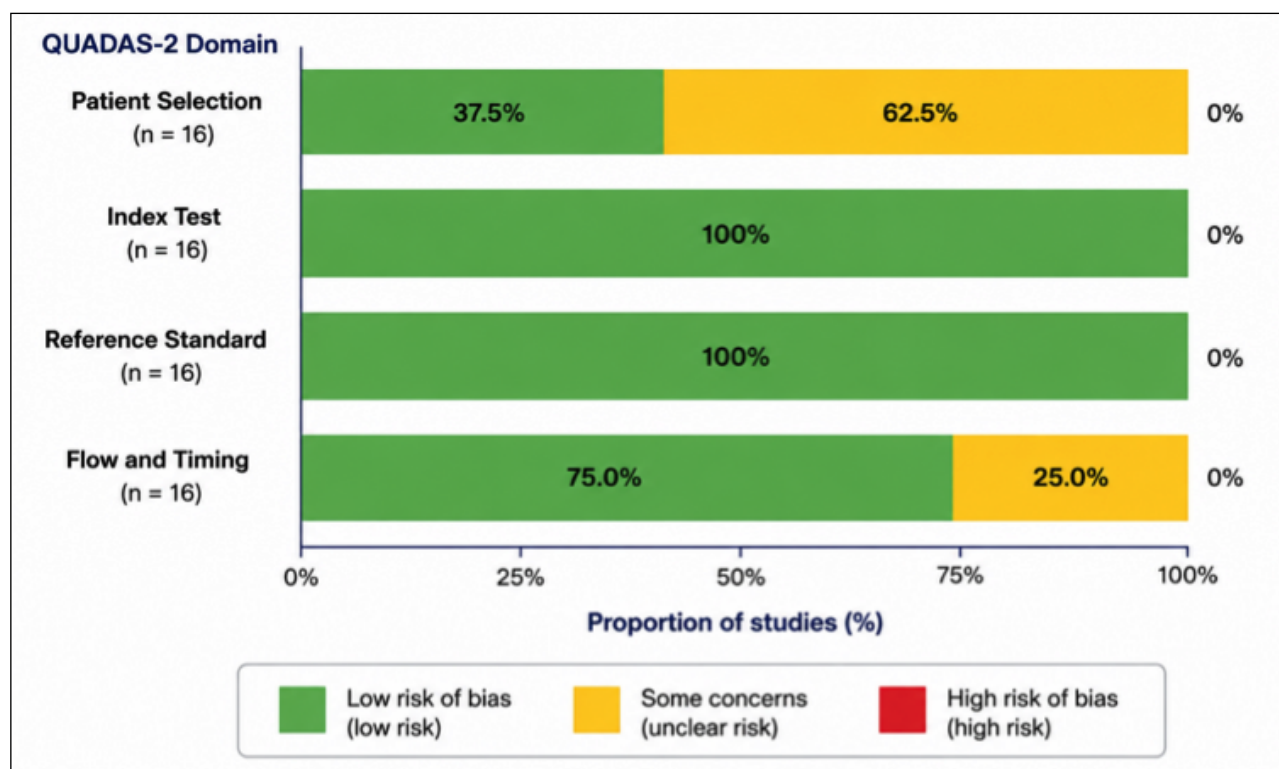
● Low risk of bias ● Some concerns (Unclear risk) ● High risk of bias

Figure 5.

QUADAS-2 Risk-of-Bias Summary Plot.

Proportion of studies judged as low risk of bias, some concerns, or high risk of bias across each QUADAS-2 domain.

Most studies demonstrated low risk of bias in the index test and reference standard domains, while concerns were primarily related to patient selection and flow and timing.



pling strategies. All studies demonstrated low risk of bias for both the index test and reference standard domains. In the flow and timing domain, twelve studies (75.0%) were judged to have low risk of bias, while four studies (25.0%) had some concerns related to patient exclusions or incomplete verification. No study was considered to have a high risk of bias in any QUADAS-2 domain.

DISCUSSION

Principal findings

This systematic review and meta-analysis evaluated the diagnostic performance of PSMA PET/CT and mpMRI for the detection of histologically confirmed pelvic lymph node metastases in patients with intermediate- and high-risk prostate cancer. Across 16 studies comprising 1,999 patients, PSMA PET/CT demonstrated substantially higher pooled sensitivity than mpMRI while maintaining similarly high specificity. The pooled sensitivity and specificity of PSMA PET/CT were 54.6% and 92.7%, respectively, compared with 33.0% and 94.9% for mpMRI. PSMA PET/CT also demonstrated a higher pooled diagnostic odds ratio (16.9 vs. 8.3). However, these findings should be interpreted with caution because the pooled estimates were derived from different sets of included studies, and not all studies evaluated both imaging modalities within the same patient population.

Consequently, the comparison reflects pooled estimates from separate study groups rather than evidence from a formal head-to-head meta-analysis. The HSROC analyses further supported these findings. PSMA PET/CT demonstrated excellent diagnostic accuracy with an AUC of 0.909, while mpMRI achieved a numerically higher AUC of 0.941. This apparent discrepancy should be interpreted cautiously. The MRI estimate was derived from only six studies compared with fourteen studies for PSMA PET/CT, making the HSROC curve and corresponding AUC more susceptible to instability. Furthermore, the HSROC AUC reflects overall test performance across all possible decision thresholds, whereas the diagnostic odds ratio summarises the discriminatory ability of a test at the observed study thresholds. Consequently, despite a slightly lower AUC, PSMA PET/CT demonstrated substantially higher pooled sensitivity and a higher DOR, indicating better discrimination between patients with histologically confirmed lymph node metastases within the available evidence.

Comparison with existing literature

The findings of the present study are consistent with an expanding body of evidence supporting the use of PSMA PET/CT for preoperative lymph node staging in prostate cancer. However, the comparison with mpMRI should be interpreted with caution because the pooled estimates were derived from different groups of studies, and not all studies evaluated both imaging modalities within the same patient population. Large prospective multicentre investigations, including the OSPREY trial by Pienta *et al.* (13) and the phase III study by Hope *et al.* (6), reported sensitivities ranging from approximately 40% to 50% with specificity exceeding 90%, findings that closely mir-

ror the pooled sensitivity of 54.6% and specificity of 92.7% observed in the present analysis.

Similarly, Franklin *et al.* (12) demonstrated superior nodal detection using PSMA PET/CT compared with mpMRI in patients undergoing radical prostatectomy and pelvic lymph node dissection, while Arena *et al.* (20) reported sensitivity of 36% and specificity approaching 91%, further reinforcing the recurring pattern of excellent specificity but only moderate sensitivity. Comparable findings were reported by Ingvar *et al.* (8), who observed sensitivity of 26.9% and specificity of 96.2% using ¹⁸F-PSMA-1007 PET/CT, highlighting the persistent challenge of detecting microscopic nodal deposits despite advances in molecular imaging.

Studies by Szigeti *et al.* (11), Maestroni *et al.* (16), and Tang *et al.* (15) similarly demonstrated high specificity with variable sensitivity, reflecting differences in patient selection, prevalence of nodal disease, pathological burden of metastases, and tracer characteristics. The variation observed among studies likely reflects differences in metastatic tumour volume, with smaller nodal deposits remaining below the spatial resolution of current PET technology. Previous pathological correlation studies have shown that sensitivity decreases substantially for metastatic lymph nodes measuring less than 3–5 mm, which may explain the moderate pooled sensitivity observed in the present analysis.

The findings of the present review are also supported by more recent investigations. Eraky *et al.* (21) reported excellent specificity for ¹⁸F-DCFPyL PET/CT but similarly identified limitations in detecting microscopic nodal disease. Talavera Cobo *et al.* (22) also showed that ⁶⁸Ga-PSMA-11 PET/CT, had high specificity, but its sensitivity was still not good enough to reliably rule out nodal involvement. Collectively, these studies reinforce the conclusion that PSMA PET/CT performs best as a rule-in test rather than a rule-out test for lymph node metastases.

In contrast, mpMRI demonstrated substantially lower pooled sensitivity (33.0%) despite maintaining high specificity (94.9%). The numerically higher HSROC AUC observed for mpMRI should not be interpreted as evidence of superior diagnostic performance. HSROC AUC estimates are influenced by the shape of the summary ROC curve and may be unstable when derived from a limited number of studies. In contrast, the higher pooled sensitivity and diagnostic odds ratio observed for PSMA PET/CT indicate greater discriminatory ability at the thresholds reported in the included studies. These complementary metrics should therefore be interpreted together rather than in isolation. This finding is biologically plausible because MRI relies primarily on size-based and morphological criteria for nodal assessment. Small metastatic deposits may therefore remain undetected within morphologically normal lymph nodes. Daouacher *et al.* (23) similarly reported limited sensitivity for MRI-based nodal staging, supporting current guideline recommendations that MRI alone should not be relied upon for lymph node assessment.

Several studies not eligible for quantitative synthesis provide additional context. Rosales *et al.* (24) reported sensitivity of approximately 75% and specificity of 82% for PSMA PET/CT; however, the absence of complete

histopathological verification limited direct comparability with the studies included in the pooled analysis. Similarly, Gültekin *et al.* (25) demonstrated specificity approaching 100% with sensitivity of approximately 50%, further supporting the recurring observation that PSMA PET/CT is highly reliable for confirming nodal disease but less effective for excluding microscopic metastases.

Overall, the consistency of findings across prospective and retrospective cohorts, different PSMA tracers, and multiple healthcare systems supports the robustness of the present findings despite the indirect comparison between imaging modalities. The pooled estimates observed in this study closely mirror those reported by Stabile *et al.* (9), who found a sensitivity of 58% and specificity of 95% for PSMA PET/CT, further validating the moderate sensitivity and high specificity demonstrated in our analysis.

Contextualisation of excluded studies

Several studies identified during the systematic search were not eligible for quantitative synthesis but provide important contextual information regarding contemporary approaches to lymph node staging in prostate cancer (**Supplementary Table S1**).

Evangelista *et al.* (26) previously conducted a systematic review and meta-analysis evaluating PSMA PET imaging for nodal staging and similarly concluded that PSMA PET demonstrates high specificity but only moderate sensitivity for the detection of lymph node metastases. Although not included in the present analysis because it was a secondary evidence synthesis, its findings are broadly consistent with the pooled estimates observed in our study. Several recent investigations have focused on predictive modelling rather than direct diagnostic accuracy. Li *et al.* (27) evaluated MRI-based radiomic models for predicting lymph node metastases, while Madendere *et al.* (28) assessed modifications of the Briganti nomogram incorporating contemporary imaging parameters. These studies suggest that integrating imaging findings with clinical and pathological variables may improve risk stratification; however, they do not directly evaluate the diagnostic accuracy of MRI or PSMA PET/CT and therefore could not be included in the present meta-analysis. Other studies were excluded because histopathological confirmation was unavailable or incomplete. Chikatamarla *et al.* (29) evaluated the performance of ¹⁸F-PSMA-1007 PET/CT using imaging findings rather than histopathology as the reference standard, while Barbosa *et al.* (30) reported outcomes using mixed verification methods with incomplete pathological confirmation. Although these studies reported favourable diagnostic performance, the absence of a uniform histopathological reference standard introduces verification bias and limits direct comparison with studies included in the present review. Narrative reviews by Lin *et al.* (31) highlighted the rapidly evolving role of PSMA PET imaging in prostate cancer staging. However, these publications did not provide original patient-level diagnostic accuracy data and therefore were not suitable for quantitative synthesis. Importantly, the exclusion of these studies reflects a deliberate methodological decision to maximise internal validity. By restricting inclusion to studies reporting histologically confirmed lymph node status with extractable TP, FP, FN, and TN data, the present meta-

analysis minimised verification bias and ensured that pooled estimates were derived from the highest level of available diagnostic evidence. Nevertheless, the consistency of findings across included and excluded studies supports the robustness of the present findings, although the comparison between imaging modalities remains indirect and should be interpreted with appropriate caution.

Clinical implications

The high specificity of PSMA PET/CT indicates that positive findings are highly reliable and may assist treatment planning, including surgical planning, radiotherapy field design, and systemic treatment decisions. However, the moderate sensitivity observed in this meta-analysis represents an important clinical limitation. A Negative PSMA PET/CT scans should not be used alone to exclude extended pelvic lymph node dissection in carefully chosen patients since they cannot securely rule out microscopic lymph node metastases. Imaging findings should always be interpreted alongside established clinical risk factors, including PSA level, tumour grade, clinical stage, and validated nomograms. Despite advances in molecular imaging, extended pelvic lymph node dissection remains the reference standard for pathological nodal staging when accurate assessment will influence treatment decisions. Beyond imaging, alternative approaches have been developed to improve prediction of lymph node involvement. Traditional nomograms such as the Briganti and Memorial Sloan Kettering models demonstrate high sensitivity but often at the expense of lower specificity, resulting in a substantial number of unnecessary lymph node dissections. More recently, machine learning and artificial intelligence-based models incorporating imaging, clinical variables, and pathological parameters have demonstrated promising discriminatory performance. Nevertheless, their positive predictive value remains limited, particularly in cohorts with a low prevalence of nodal metastases, and external validation remains insufficient for routine clinical implementation.

Quality assessment and risk of Bias

Overall, methodological quality was favourable. Although most included studies were retrospective, no study was judged to be at high risk of bias in any QUADAS-2 domain. Retrospective design alone was not considered sufficient to warrant a high-risk judgement; rather, assessments were based on the predefined QUADAS-2 signalling questions. Most concerns related to patient selection, where retrospective recruitment and unclear consecutive inclusion introduced the possibility of selection bias. Additional concerns arose in the flow and timing domain when participant exclusions or verification of all enrolled patients were incompletely reported. In contrast, the index test and reference standard domains were consistently judged to be at low risk of bias because imaging interpretation and histopathological confirmation were generally well described and applied consistently across studies.

Strengths and limitations

The present study has several important strengths. First, only studies using histopathological confirmation as the

reference standard were included, minimising verification bias and ensuring a robust assessment of diagnostic performance. Second, pooled estimates were derived using hierarchical bivariate random-effects modelling, the recommended statistical approach for diagnostic accuracy meta-analyses. Third, the review incorporated contemporary PSMA PET tracers and MRI techniques that reflect current clinical practice.

Several limitations should be acknowledged. The number of MRI studies available for quantitative synthesis was relatively small compared with the PSMA PET literature, reducing the precision of pooled MRI estimates. In addition, comparisons between PSMA PET/CT and mpMRI were based on indirect pooled estimates derived from different sets of included studies rather than direct head-to-head comparisons. Although statistical heterogeneity was low, important clinical heterogeneity remained with respect to PSMA tracers, MRI acquisition protocols, patient risk profiles, the prevalence of nodal metastases, and the extent of pelvic lymph node dissection, which may limit the generalisability of the findings. The predominance of retrospective studies may also have introduced selection bias, while the limited number of studies prevented detailed subgroup and tracer-specific analyses. Finally, only English-language studies were included, and publication bias could not be formally assessed because of the limited number of eligible diagnostic accuracy studies. These methodological limitations should be considered when interpreting the findings.

Future directions

Future research should prioritise prospective head-to-head studies directly comparing contemporary PSMA

PET/CT and mpMRI within the same patient population using standardised imaging protocols and uniform histopathological reference standards. Further investigation is also required to evaluate combined imaging strategies integrating PSMA PET/CT and mpMRI, as well as emerging radiomics, artificial intelligence, and genomic approaches. Such integrated diagnostic models may improve risk stratification and help overcome the persistent challenge of detecting microscopic nodal metastases.

CONCLUSIONS

PSMA PET/CT demonstrated higher pooled sensitivity than mpMRI while maintaining similarly high specificity for detecting pelvic lymph node metastases. However, these findings should be interpreted with caution because the comparison was based on pooled estimates derived from different sets of included studies rather than from direct head-to-head comparative studies. A negative PSMA PET/CT scan cannot reliably exclude microscopic nodal metastases and should not be used as the sole basis for omitting extended pelvic lymph node dissection in appropriately selected patients. Extended pelvic lymph node dissection therefore remains the reference standard for pathological nodal staging.

REFERENCES

1. Raychaudhuri R, Lin DW, Montgomery RB. Prostate Cancer. JAMA 2025; 333:1433.
2. European Association of Urology. EAU Guidelines on Prostate Cancer. <https://UrowebOrg/Guidelines/Prostate-Cancer/Chapter/Diagnostic-Evaluation> 2025.
3. 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.
4. 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.
5. Thoeny HC, Froehlich JM, Triantafyllou M, et al. Metastases in Normal-sized Pelvic Lymph Nodes: Detection with Diffusion-weighted MR Imaging. Radiology 2014; 273:125-35.
6. Hope TA, Eiber M, Armstrong WR, et al. Diagnostic Accuracy of 68 Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection. JAMA Oncol 2021; 7:1635.
7. Yang B, Dong H, Zhang S, et al. PSMA PET vs. mpMRI for Lymph Node Metastasis of Prostate Cancer: A Systematic Review and Head-to-Head Comparative Meta-analysis. Acad Radiol 2025; 32:2797-814.
8. Ingvar J, Hvittfeldt E, Trägårdh E, et al. Assessing the accuracy of (18F)PSMA-1007 PET/CT for primary staging of lymph node metastases in intermediate- and high-risk prostate cancer patients. EJNM-MI Res 2022; 12.
9. Stabile A, Pellegrino A, Mazzone E, et al. Can Negative Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography Avoid the Need for Pelvic Lymph Node Dissection in Newly Diagnosed Prostate Cancer Patients? A Systematic Review and Meta-analysis with Backup Histology as Reference Standard. Eur Urol Oncol 2022; 5:1-17.

DECLARATIONS

Ethical approval and consent for participate: No ethics requirement.

Availability of data and material: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: Authors declare no financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

Data Availability declaration: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Funding: The authors did not receive support from any organization for the submitted work.

Authors' contributions: EU: Conceptualisation, methodology, literature search, study selection, data extraction, statistical analysis, interpretation of results, manuscript drafting, and manuscript revision; SA: Independent study screening, data extraction, interpretation of results, and manuscript revision; LO: Data verification, interpretation of results, and manuscript revision; RD: Methodological supervision, interpretation of results, critical review of the manuscript, and manuscript revision; MU: Literature review, manuscript editing, manuscript revision and critical review of the manuscript. All authors read and approved the final manuscript.

10. Yaxley JW, Raveenthiran S, Nouhaud FX, et al. Outcomes of Primary Lymph Node Staging of Intermediate and High Risk Prostate Cancer with 68Ga-PSMA Positron Emission Tomography/Computerized Tomography Compared to Histological Correlation of Pelvic Lymph Node Pathology. *J Urol* 2019; 201:815-20.
11. Szigeti F, Schweighofer-Zwink G, Meissnitzer M, et al. Incremental Impact of (68 Ga)Ga-PSMA-11 PET/CT in Primary N and M Staging of Prostate Cancer Prior to Curative-Intent Surgery: a Prospective Clinical Trial in Comparison with mpMRI. *Mol Imaging Biol* 2022; 24:50-9.
12. Franklin A, Yaxley WJ, Raveenthiran S, et al. Histological comparison between predictive value of preoperative 3-T multiparametric MRI and 68Ga-PSMA PET/CT scan for pathological outcomes at radical prostatectomy and pelvic lymph node dissection for prostate cancer. *BJU Int* 2021; 127:71-9.
13. Pienta KJ, Gorin MA, Rowe SP, et al. A Phase 2/3 Prospective Multicenter Study of the Diagnostic Accuracy of Prostate Specific Membrane Antigen PET/CT with 18F-DCFPyL in Prostate Cancer Patients (OSPReY). *J Urol* 2021; 206:52-61.
14. Arslan A, Karaarslan E, Güner AL, et al. Comparing the Diagnostic Performance of Multiparametric Prostate MRI Versus 68Ga-PSMA PET-CT in the Evaluation Lymph Node Involvement and Extraprostatic Extension. *Acad Radiol* 2022; 29:698-704.
15. Tang Y, Ji X, Lin Q, et al. Status of 18F-PSMA-1007-PET/CT compared with multiparametric MRI in preoperative evaluation of prostate cancer. *World J Urol* 2023; 41:1017-24.
16. Maestroni UV, Campobasso D, Guarino G, et al. Lymph node staging with 68Ga-PSMA PET in patients with intermediate and high-risk prostate cancer suitable for radical prostatectomy managed in a prostate cancer unit. *Chin Clin Oncol* 2023; 12:22-22.
17. Xiong Z, Ge Y, Ma S, et al. Comparing the diagnostic value of 68Ga-prostate-specific membrane antigen PET/CT and multiparametric MRI in pelvic lymph node metastasis of locally advanced prostate cancer. *Transl Androl Urol* 2024; 13:1219-27.
18. Pepe L, Fiorentino V, Curduman M, et al. PSMA PET/CT Accuracy in Diagnosing Prostate Cancer Nodes Metastases. *In Vivo (Brooklyn)* 2024; 38:2880-5.
19. Dinckal M, Ergun KE, Kalemci MS, et al. Head-to-head comparison of GA-68 PSMA PET/CT and multiparametric MRI findings with postoperative results in preoperative locoregional staging and localization of prostate cancer. *Prostate* 2025; 85:48-57.
20. Arena P, Fasulo V, Gelardi F, et al. An Evaluation of the Diagnostic Accuracy of (68Ga)Ga-PSMA-11 vs. (18F)F-PSMA-1007 PET/CT for Lymph Node Staging in Patient Candidates for Radical Prostatectomy and Lymph Node Dissection: A Single Institutional Analysis. *Diagnostics* 2025; 15.
21. Eraky A, Tillu N, Ben-David R, et al. Diagnostic Accuracy of (18 F)-DCFPyL Prostate-Specific Membrane Antigen Positron Emission Tomography/Computerized Tomography in Intermediate-Risk Prostate Cancer Undergoing Radical Prostatectomy: Is Pelvic Lymph Node Dissection Still Necessary? *J Urol* 2025; 214:365-73.
22. Talavera Cobo V, Yáñez Ruiz CA, Tapia Tapia MD, et al. Diagnostic Accuracy of PSMA-PET/CT vs. mpMRI in Primary Staging of Intermediate- and High-Risk Prostate Cancer. *Med Sci (Basel)* 2026; 14.
23. Daouacher G, Carlsson J, Voulgarakis N, et al. Diagnostic performance of conventional MRI using T1W and T2W for primary lymph node staging in intermediate- and high-risk prostate cancer patients prior to pelvic lymph node dissection. *Abdominal Radiology* 2025.
24. Rosales JJ, Beteach Antar V, Mínguez F, et al. Comparison of staging using (68Ga)Ga-PSMA-11 PET/CT and histopathological results in intermediate- and high-risk prostate cancer patients treated with radical prostatectomy and pelvic lymph node dissection. *Revista Española de Medicina Nuclear e Imagen Molecular (English Edition)* 2025; 44:500076.
25. Gultekin MH, Demirci E, Turegun FA, et al. The Role of 68Ga-PSMA PET/CT Scan In Patients with Prostate Adenocarcinoma who Underwent Radical Prostatectomy. *Urol J* 2020; 18:58-65.
26. Evangelista L, Zattoni F, Cassarino G, et al. PET/MRI in prostate cancer: a systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2021; 48:859-73.
27. Li C, Hu J, Zhang Z, et al. Biparametric MRI of the prostate radiomics model for prediction of pelvic lymph node metastasis in prostate cancers: a two-centre study. *BMC Med Imaging* 2024; 24.
28. Madendere S, Kılıç M, Gürses B, et al. Can the Briganti 2019 nomogram be modified to predict lymph node metastasis risk in patients with prostate cancer detected with in-bore biopsy? *Int J Urol* 2024; 31:1269-77.
29. Chikatamarla VA, Okano S, Jenvey P, et al. Risk of metastatic disease using (18F)PSMA-1007 PET/CT for primary prostate cancer staging. *EJNMMI Res* 2021; 11.
30. Barbosa ÁRG, Amaral BS, Lourenço DB, et al. Accuracy of 68Ga-PSMA PET-CT and PET-MRI in lymph node staging for localized prostate cancer. *Einstein (Sao Paulo)* 2022; 20:eAO6599.
31. Lin Y, Johnson LA, Fennessy FM, Turkbey B. Prostate Cancer Local Staging with Magnetic Resonance Imaging. *Radiol Clin North Am* 2024; 62:93-108.

Correspondence

Emeka I Udeh (Corresponding Author)
ihechiudeh@yahoo.com; emeka.udeh1@nhs.net

Department of Urology, Dorset County Hospital NHS Foundation
Dorchester, England, United Kingdom

Rotimi David
rotimi.david1@nhs.net

Department of Urology, Dorset County Hospital NHS, Dorchester,
England, United Kingdom

Solomon Anyimba
sanyimba@yahoo.com
University of Nigeria Teaching Hospital Enugu Nigeria

Loius Okolie
louisokolie@gmail.com
University of Nigeria Teaching Hospital Enugu Nigeria

Maureen O. Udeh
udehmaureen91@gmail.com
Kingston University, England, United Kingdom