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Diagnostic performance of ^{18}F-DCFPyL PET vs. ^{68}Ga-PSMA PET/CT in patients with suspected prostate cancer: A systemic review and meta-analysis

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Abstract. In this systematic review and meta-analysis, the diagnostic performance of ^{68}Ga-prostate-specific membrane antigen (PSMA) positron emission tomography (PET)/CT was compared with that of ^{18}F-DCFPyL PET for patients with suspected prostate cancer (PCa). Up to September 2023, the PubMed, Embase and Web of Science databases were thoroughly searched for relevant papers. Studies examining the diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in patients with suspected PCa were included in the present review. The Quality Assessment of Diagnostic Performance Studies-2 tool was used to rate the diagnostic performance of each study. The diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT for primary PCa was examined by 13 studies included, comprising 1,178 patients. The pooled sensitivity and specificity of ^{18}F-DCFPyL PET were 0.92 (95% CI, 0.85-0.96) and 0.59 (95% CI, 0.08-0.96), respectively. For ^{68}Ga-PSMA PET/CT, the pooled sensitivity and specificity were 0.96 (95% CI, 0.88-0.99) and 0.71 (95% CI, 0.57-0.82), respectively. ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT both had an area under the receiver operating characteristic curve of 0.92 (95% CI, 0.89-0.94). In addition, the Fagan nomogram revealed that the post-test probabilities for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT could rise to 69 and 77% when the pre-test probability was set at 50%. In conclusion, a comparable diagnostic performance for patients with suspected PCa was determined for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT. However, it is crucial to keep in mind that the findings of the present meta-analysis come from investigations with modest sample sizes. Therefore, more extensive research is required to obtain more solid data.

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Introduction

The second most frequent disease globally and the fifth most common cause of cancer-related mortality in men is prostate cancer (PCa) (1). Digital rectal examination and serum prostate-specific antigen (PSA) testing, followed by transrectal ultrasonography (TRUS)-guided biopsy, have historically been used to identify PCa (2). Despite being the preferred approach for PCa diagnosis, TRUS-guided biopsy has several inherent drawbacks. A TRUS-guided biopsy may ignore abnormalities in the anterior and apical prostate, producing false-negative findings in addition to being an invasive treatment with a chance of potentially life-threatening infections (3). As a result, it is critical to investigate alternative strategies that may decrease the number of needless prostate biopsies or perhaps completely replace puncture biopsy to diagnose PCa (4,5).

A non-invasive diagnostic called multiparametric MRI (mpMRI) has great potential for identifying and staging PCa (6). The Prostate Imaging Reporting and Data System version 2.1 (PI-RADS v2.1), the most recent version of the structured reporting system for mpMRI, aims to improve inter-reader agreement and streamline the evaluation of prostate mpMRI using PI-RADS criteria (7). Despite these developments, mpMRI also has numerous defects, such as false-positive results (8) and new histopathological patterns (9), and alternative non-invasive diagnostic modalities still need to be researched and used.

A type II transmembrane glycoprotein called prostate-specific membrane antigen (PSMA) is overexpressed in almost all cases of PCa (10-12). However, the clinical use of the nuclide ^{68}Ga has been constrained by the cost, its short half-life and high electron energy during synthesis. Specifically, producing ^{68}Ga is costly due to the need for specialized equipment. Its short half-life requires rapid use, challenging for centers far from production sites. The high electron energy needed for creating ^{68}Ga compounds adds to the complexity and cost, limiting its wider clinical use (13). The most frequently utilized positron nuclide in clinical practice has been ^{18}F-DCFPyL, based on a glutamate-urea-lysine

structure. In contrast to ^{68}Ga-PSMA-11, ^{18}F-DCFPyL has excellent affinity, advantageous *in vivo* pharmacokinetics, good solubility and the possibility for a better rate of minor lesion detection. As a result, it performs better and is more appropriate for broader usage in clinical practice (14-16).

Only a few studies have evaluated the use of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in the diagnosis of patients with suspected PCa; most of this research involved patients with biopsy-proven PCa. In the present study, a meta-analysis was performed using previously published data to acquire complete comprehension of the diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in evaluating patients with suspected PCa.

Methods

Search strategy. The guidelines for preferred reporting items for systematic reviews and meta-analyses (PRISMA) (17) were followed when conducting this study. The protocol for this study was registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols database on February 13, 2024 (INPLASY202420059) and is available in full on inplasy (https://doi.org/10.37766/inplasy2024.2.0059).

Using the PubMed (http://pubmed.ncbi.nlm.nih.gov/), Embase (www.embase.com) and Web of Science (https://www.webofscience.com/) databases, a comprehensive search for literature up until September 2023 was conducted. 'Positron-Emission Tomography' OR 'PET' OR 'Positron Emission Tomography Imaging' OR 'PET Scan' OR 'PET Imaging' AND 'Prostate Specific Membrane Antigen' OR 'PSMA' AND 'Prostate Neoplasms' OR 'Prostatic Cancers' OR 'Prostatic Cancer' OR 'Prostatic Neoplasm' OR 'Prostate Neoplasm' OR 'Prostate tumor' were the key words used (Table SI). Two researchers (JG and LH) independently integrated computer-generated search results with manual searches to ensure diversity and prevent omitting pertinent literature. In addition, the list of references included in the study was screened to find any other articles that were left out in the initial search.

Inclusion and exclusion criteria. Studies were considered eligible for inclusion if they met all of the following criteria: i) They involved untreated patients with suspected PCa, which included individuals whose prostates had abnormalities found during an abnormal PSA test, an abnormal MRI scan or a digital rectal examination; ii) diagnostic imaging was performed using an ^{18}F-DCFPyL PET scan or a ^{68}Ga-PSMA PET/CT scan; iii) the reference standard used for comparison was histological biopsy and histopathology; and iv) the number of subjects was ≥10.

The following exclusion criteria were applied: i) Duplicate articles; ii) abstracts, editorial comments, letters, case reports, reviews or meta-analyses; iii) titles and abstracts that were clearly irrelevant; iv) insufficient data to perform calculations; and v) articles not written in English.

Two researchers (JG and LH) meticulously assessed the titles and abstracts of the retrieved papers whilst applying the above-mentioned inclusion and exclusion criteria. Following this initial screening procedure, the full-text versions of the remaining articles were carefully examined to determine whether they were appropriate for inclusion in the ensuing stage. The researchers reached a consensus in a discussion with a third author (ZJ) to resolve any disagreements during the evaluation.

Quality assessment and data extraction. Using the Quality Assessment of Diagnostic Performance Studies (QUADAS-2) method, two researchers (SY and BM) independently assessed the quality of the included articles (18). The following areas of each study were evaluated: Patient selection, the index test, the reference standard and the flow and timing of the study. These domains were assessed for risk of bias and given a high, low or unclear applicability rating. Discussions with a third reviewer (ZJ) helped to settle any differences that came up.

For each study, two researchers independently extracted the data. General information, characteristics of the literature, demographic information regarding the patients, technical information and outcomes related to the total number of patients, as well as true positive (TP), false positive (FP), true negative (TN) and false negative (FN) counts, were all included in the data. These values were computed using test findings for sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) in cases where they weren't expressly provided. The sensitivity was calculated as the ratio of TP to the sum of TP and FN [sensitivity=TP/(TP + FN)], while specificity was calculated as the ratio of TN to the sum of TN and FP [specificity=TN/(TN + FP)]. The PPV was derived as the ratio of TP to the sum of TP and FP [PPV=TP/(TP + FP)], and the NPV as the ratio of TN to the sum of TN and FN [NPV=TN/(TN + FN)]. These formulas allowed for a consistent and objective assessment of the diagnostic performance across the included studies.

Statistical analysis. The best outcome was chosen for analysis when the included publications provided a range of diagnostic performances based on cut-off thresholds for classifying positive and negative scans. Stata 16.0 (StataCorp LP) and Meta-Disc 1.4 (http://www.hrc.es/investigacion/metadisc_en.htm) were used to examine the data of a four-grid table. As the bivariate random-effects model can simultaneously adapt to the inherent correlation between the sensitivity and specificity of different studies, it also explains the heterogeneity between studies (19). Using a bivariate random random-effects model, the pooled sensitivity and specificity for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT were reported as estimates with 95% confidence intervals (CIs). In addition, because the summary receiver operating characteristic (SROC) model facilitates the interpretation of diagnostic test accuracy in the presence of heterogeneity and varying threshold effects, this model was used to generate the SROC curve and determine the area under the curve (AUC) (19,20). The difference of the pooled AUC between ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT was analyzed using Z test statistics (21,22).

Using the I^2 statistic, the heterogeneity between the pooled studies was evaluated. Meta-regression analysis was used to explore potential causes of heterogeneity when there was significant heterogeneity (I^2>50%) (23). The funnel plot test developed by Deek was used to evaluate publication bias. Stata 16.0 and Meta-Disc 1.4 were used for all statistical calculations. Statistical significance was defined as $P<0.05$.

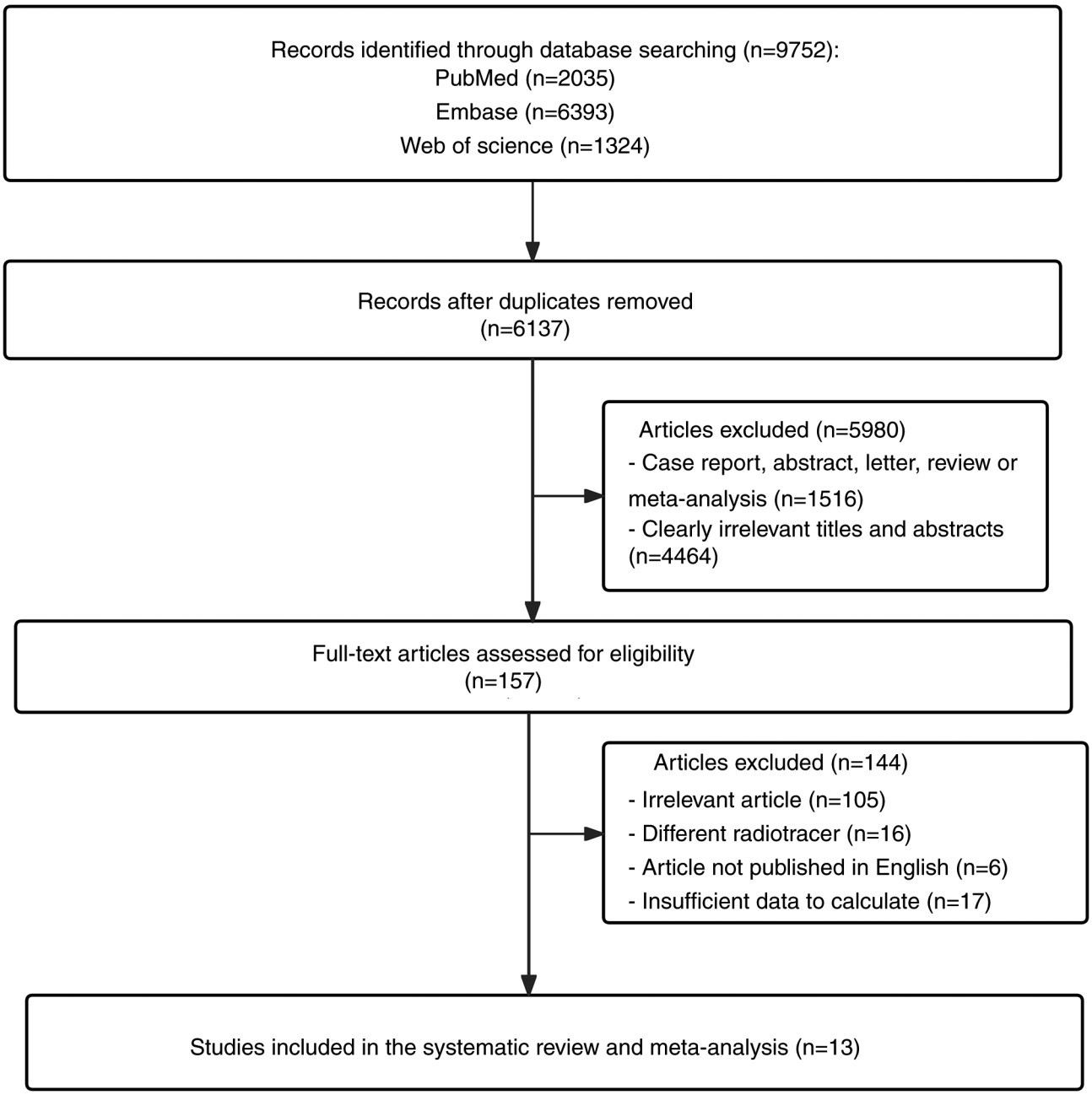

Figure 1. PRISMA flow diagram of the study selection process.

Results

Literature search and study selection. A total of 9,752 entries were found in the original search and 3,615 duplicates were removed, leaving 6,137 articles for further analysis. After examining the titles and abstracts, 5,980 items were deemed unrelated and discarded. The 105 unrelated studies, 6 articles not published in English, 16 articles using various radiotracers and 17 articles not providing sufficient data for the computation were all eliminated after further study of the remaining articles. Finally, 13 studies (24-36) assessing the diagnostic performance of ^{18}F-DCFPyL PET or ^{68}Ga-PSMA PET/CT were considered eligible for meta-analysis. The study selection procedure is depicted by a PRISMA flow diagram in Fig. 1.

Study description and quality assessment. There were 1,178 patients with suspected PCa in the 13 qualifying studies. The mean of the median and mean ages of the patients in the evaluable articles was 67.4 years (range, 43-90 years). The study and patient characteristics are listed in Table I and the technical details of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT are provided in Table II.

Fig. 2 shows the results of the risk of bias assessment for these 13 studies, which was performed using the QUADAS-2 technique. The included studies' quality was deemed to be adequate.

Quantitative synthesis. The analysis comprised a total of 13 trials with 1,178 patients. The pooled sensitivity and specificity of ^{18}F-DCFPyL PET for suspected PCa were 0.92 (95% CI,

Table I. Study and patient characteristics of the included articles.

		Study characteristics			Patient characteristics				
Author(s), year	Modality	Country	Study design	Analysis	Number of patients	PSA level, ng/ml	Age, years	Gleason score	(Refs.)
Metser *et al*, 2021	^{18}F-DCFPyL PET	Canada	Pro	PB	55	8.8±5.3	65.1±7.2	NA	(25)
Zhang *et al*, 2022	^{18}F-DCFPyL PET	China	Retro	PB	56	20.4 (1.9-1000)	Mean: 68 (43-83)	≤7: 33.9%; ≥8: 55.3%; Unknown: 10.7%	(26)
Bodar *et al*, 2020	^{18}F-DCFPyL PET	Netherlands	Pro	LB	420	Median: 11.1	Mean: 68.5	≤7, 53.3%; ≥8, 46.7%	(24)
Liu *et al*, 2021	^{18}F-DCFPyL PET	China	Retro	PB	52	18.3±16.0	Mean: 65 (48-79)	≤7, 38.4%; ≥8, 61.6%	(27)
Parathithasan *et al*, 2022	^{18}F-DCFPyL PET	Australia	Retro	PB	65	14.3±11.6	Mean: 67 (44-80)	≤7, 64.7%; ≥8, 35.3%	(28)
Hoffmann *et al*, 2017	^{68}Ga-PSMA PET/CT	Germany	Retro	PB	25	20.4±33.5	67.0±8.1	≤7: 60%; ≥8: 40%	(29)
Lopci *et al*, 2018	^{68}Ga-PSMA PET/CT	Italy	Pro	PB	45	Median: 7.24	Median: 64	NA	(30)
Sasikumar *et al*, 2018	^{68}Ga-PSMA PET/CT	India	Pro	PB	66	11.56 (0.85-4156)	67 (48-90)	≤7: 72%; ≥8: 28%	(31)
Kumar *et al*, 2019	^{68}Ga-PSMA PET/CT	India	Pro	PB	15	Mean: 9.9 (5.1-19.5)	Mean: 66.2 (57-73)	≤7: 53%; ≥8: 7%; Unknown: 40%	(32)
Zhang *et al*, 2018	^{68}Ga-PSMA PET/CT	China	Retro	PB	58	15.46 (1.31-49.07)	70 (55-85)	≤7: 69%; ≥8: 31%	(33)
Liu *et al*, 2020	^{68}Ga-PSMA PET/CT	China	Pro	PB	31	18 (5.48-49.77)	65 (53-81)	NA	(34)
Lopci *et al*, 2020	^{68}Ga-PSMA PET/CT	Italy	Pro	PB	97	7.6 (1.86-32.6)	74.7 (43-81)	≤7: 92%; ≥8: 8%	(35)
Jiao *et al*, 2021	^{68}Ga-PSMA PET/CT	China	Pro	PB	193	NA	68.21±9.37	≤7: 29%; ≥8: 71%	(36)

Values are expressed as the median (range) or mean ± standard deviation unless otherwise indicated. NA, not available; Pro, prospective; Retro, retrospective; PB, patient-based; LB, lesion-based; PSMA, prostate-specific membrane antigen; PSA, prostate-specific antigen; PET, positron emission tomography.

Table II. Technical aspects of included studies.

Author(s), year	Scanner modality	Ligand dose	Image analysis	TP	FP	FN	TN	Total	(Refs.)
Metser *et al*, 2021	Siemens Healthcare: Biograph mMR; PET/MRI, Siemens Healthineers	329.5 MBq/kg	Quantitative	39	12	3	1	55	(25)
Zhang *et al*, 2022	Siemens Medical Solutions: PET/CT, Siemens Healthineers	4.44 MBq/kg	Quantitative	45	0	5	6	56	(26)
Bodar *et al*, 2020	Philips Healthcare®: PET/CT system	313 MBq/kg	Quantitative	103	9	19	289	420	(24)
Liu *et al*, 2022	Siemens Healthcare: Biograph 64 PET/CT Biograph mMR; PET/MRI, Siemens Healthineers	NA	Quantitative	40	2	3	7	52	(27)
Parathithasan *et al*, 2022	General Electric Medical Systems: PET/CT	250 MBq/kg	Quantitative	59	4	2	0	65	(28)
Hoffmann *et al*, 2017	Siemens Healthcare: Biograph 64, PET/CT scanner, Siemens Healthineers	176 MBq/kg	Quantitative	21	0	2	2	25	(29)
Lopci *et al*, 2018	Siemens Healthcare: Biograph LSO 6 scanner; PET/CT, Siemens Healthineers	Range: 250-400 MBq/kg	Quantitative	11	14	0	20	45	(30)
Sasikumar *et al*, 2018	NA	100 MBq/kg	Quantitative	50	6	0	10	66	(31)
Kumar *et al*, 2019	Siemens Healthcare: PET/CT, Siemens Healthineers	Range: 1.8-2.2 MBq/kg	Quantitative	8	2	1	4	15	(32)
Zhang *et al*, 2018	Siemens Medical Solutions: Biograph 40 system, PET/CT, Siemens Healthineers	206.09 MBq/kg	Quantitative	33	4	3	18	58	(33)
Liu *et al*, 2020	Philips Medical Systems: PET/CT	206.09 MBq/kg	Quantitative	14	4	1	12	31	(34)
Lopci *et al*, 2020	Siemens Medical Solutions: Biograph LSO 6 scanner, PET/CT, Siemens Healthineers	Range: 250-400 MBq/kg	Quantitative	23	41	0	33	97	(35)
Jiao *et al*, 2021	Siemens Medical Solutions: Biograph 40 system, PET/CT, Siemens Healthineers	NA	Quantitative	126	7	22	48	193	(36)

NA, not available; PET, positron emission tomography; TP, true positive; FP, false positive; TN, true negative; FN, false negative; mMR, magnetic resonance imaging with molecular imaging.

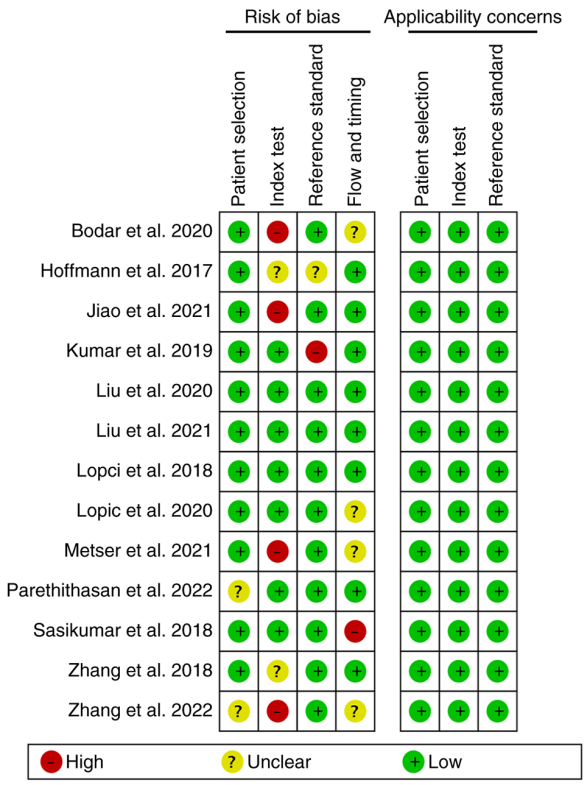

Figure 2. Graph of risk of bias and applicability of all eligible studies based on the Quality Assessment of Diagnostic Performance Studies-2 tool.

0.85-0.96) and 0.59 (95% CI, 0.08-0.96), respectively. The pooled sensitivity and specificity for ^{68}Ga-PSMA PET/CT were, respectively, 0.96 (95% CI, 0.88-0.99) and 0.71 (95% CI, 0.57-0.82) (Fig. 3).

In the SROC analysis, the AUC for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT were calculated to be 0.92 (95% CI, 0.89-0.94) and 0.92 (95% CI, 0.89-0.94) and there was no statistically significant difference according to Z-test statistics (Z<0.001, P<0.999) (Fig. 4).

Furthermore, the Fagan nomogram in Fig. 5 showed that the post-test probabilities for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT could rise to 69 and 77%, respectively, when the pre-test probability was 50%.

Heterogeneity analysis. The I^2 values for ^{18}F-DCFPyL PET's pooled sensitivity and specificity for primary cancer were 49.29 and 97.07%, respectively. The corresponding I^2 values for ^{68}Ga-PSMA PET/CT's heterogeneity were 50.49 and 79.57% (Fig. 3). It was attempted to identify the cause of heterogeneity by using meta-regression analysis. It demonstrated that diversities in geographical region and study design were two potential causes of heterogeneity for these two imaging agents (Tables III and IV).

In addition, Deek's funnel plot showed no evidence of publishing bias for both imaging modalities, with P-values of 0.17 and 0.90 (Fig. 6).

Discussion

Currently, there is a scarcity of studies investigating the application of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in the diagnosis of suspected PCa. The present study was the first meta-analysis on the comparative efficacy of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in the detection of PCa in patients with a suspicion of the disease. The purpose of the present study was to quantitatively assess and evaluate the diagnostic accuracy of two different diagnostic methods for patients with suspected PCa. Based on the results, ^{18}F-DCFPyL PET demonstrated a pooled sensitivity, specificity and AUC of 0.92, 0.59 and 0.92, respectively. ^{68}Ga-PSMA PET/CT exhibited a pooled sensitivity, specificity and AUC of 0.96, 0.71 and 0.92, respectively. This suggests that both ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT have the potential to serve as 'rule-out' tests for patients suspected of having PCa based on clinical or biochemical evidence. Consequently, these tests can help avoid unnecessary biopsies.

Numerous PCa cases progress slowly and typically do not produce severe symptoms, thereby not necessitating immediate active treatment or intervention (37,38). Therefore, there is a strong emphasis on detecting clinically relevant PCa at an early stage. Clinically relevant PCa often refers to tumors with a Gleason score of 3+4 or higher (39). The present findings indicate that both ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT had a high level of accuracy in detecting clinically significant tumors. The pooled sensitivity for ^{18}F-DCFPyL PET was 0.92, while that for ^{68}Ga-PSMA PET/CT was 0.96. These findings have the potential to impact the categorization of risk and improve the decision-making process for treating such patients (40).

In the present meta-analysis, a comprehensive evaluation of the efficacy of two imaging methods in identifying suspected PCa was performed. The AUC for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT in identifying suspected PCa was 0.92 (95% CI: 0.89-0.94) for both. Although there was no statistical difference by Z-test statistics (Z<0.001, P<0.999), ^{68}Ga-PSMA PET/CT was indicated to have higher sensitivity, specificity and post-test probability compared to ^{18}F-DCFPyL PET. The present results indicated that ^{18}F-DCFPyL and ^{68}Ga-PSMA PET/CT have similar diagnostic accuracy in detecting suspected PCa. Van Kalmthout *et al* (41) discovered in their earlier research that the diagnostic performance of both ^{18}F-DCFPyL and ^{68}Ga-PSMA PET/CT in the setting of biochemical recurrence of PCa post-prostatectomy is comparable. Perhaps the similarity in biodistribution patterns of ^{18}F-DCFPyL and ^{68}Ga-PSMA in normal tissues is due to their comparable characteristics (42). In addition, it has been indicated that ^{68}Ga-PSMA PET/CT remains highly valuable due to its accessibility and cost-effectiveness (43), although ^{18}F-DCFPyL PET may offer slight advantages in terms of imaging clarity and patient safety in certain contexts (44). However, the finding was derived from a limited sample size and thus, the reliability of the results may be limited.

In the present study, papers that assessed the diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT for suspected PCa were analyzed using various thresholds for detecting positive and negative scans. Of note, a consensus on the precise diagnostic threshold choice for different imaging techniques has yet to be obtained. Studies have used measurements such as the standardized uptake value threshold and the choline/creatinine ratio. The reported sensitivity and specificity of the imaging technique may change depending

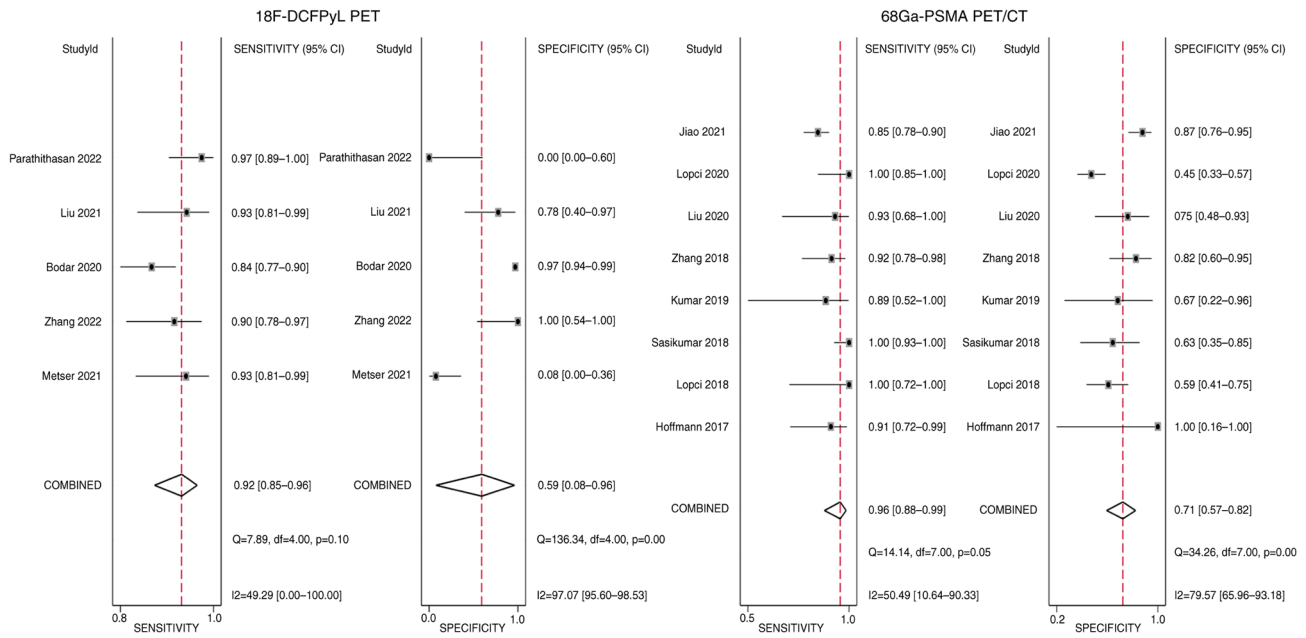

Figure 3. Forest plot showing the sensitivity and specificity of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT for primary prostate cancer. PSMA, prostate-specific membrane antigen; PET, positron emission tomography; df, degrees of freedom.

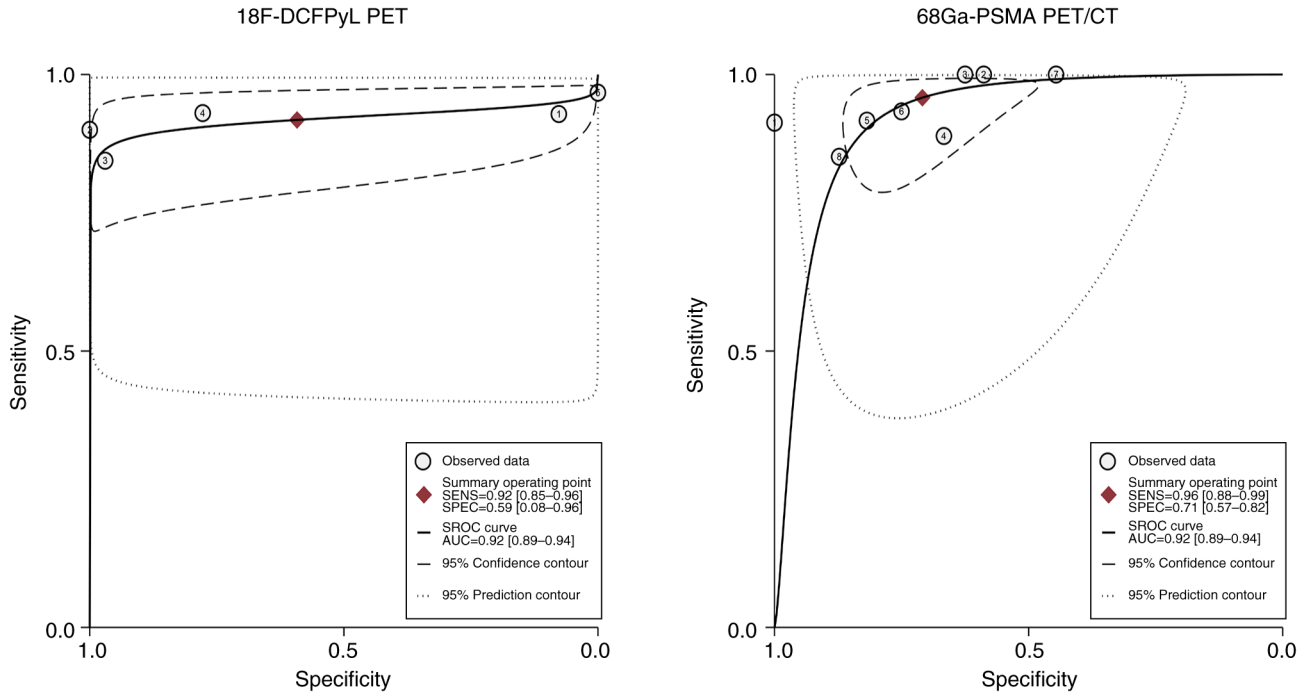

Figure 4. SROC curve of the diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT for detecting prostate cancer. SROC, summary receiver operating characteristic; PSMA, prostate-specific membrane antigen; PET, positron emission tomography; SENS, sensitivity; SPEC, specificity; AUC, area under the curve. In the ^{18}F-DCFPyL PET section: 1, Metser *et al* (25), 2021; 2, Zhang *et al* (26), 2022; 3, Bodar *et al* (24), 2020; 4, Liu *et al* (27), 2022; 5, Parathithasan *et al* (28), 2022. In the ^{68}Ga-PSMA PET/CT section: 1, Hoffmann *et al* (29), 2017; 2, Lopci *et al* (30), 2018; 3, Sasikumar *et al* (31), 2018; 4, Kumar *et al* (32), 2019; 5, Zhang *et al* (33), 2018; 6, Liu *et al* (34), 2020; 7, Lopci *et al* (35), 2020; 8, Jiao *et al* (36), 2021.

on the choice of diagnostic thresholds (45). In some of the included articles, ROC curves were generated to assess diagnostic performance, and the diagnostic threshold that produced the highest sensitivity and specificity products was chosen. Although this method of determining the ideal diagnostic threshold is frequently utilized, it may only be suitable under certain circumstances, mainly when there is a trade-off between sensitivity and specificity. Therefore, additional research examining the ideal diagnostic cutoff for ^{68}Ga-PSMA PET/CT and ^{18}F-DCFPyL PET in patients with suspected PCa is necessary.

The identification of significant heterogeneity in the present examination of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT, as evidenced by an I^2-value exceeding 50%, highlights the

Table III. Meta-regression and subgroup analysis of ^{18}F-DCFPyL positron emission tomography.

Covariate	Studies, n	Sensitivity (95%Cl)	P-value	Specificity (95% CI)	P-value
Analysis			0.48		0.13
Patient-based	4	0.94 (0.90-0.97)		0.42 (-0.28-1.00)	
Lesion-based	1	0.84 (0.75-0.94)		0.97 (0.83-1.00)	
Region			0.24		0.03
Western	3	0.92 (0.87-0.98)		0.24 (-0.47-0.95)	
Asian	2	0.92 (0.84-0.99)		0.95 (0.75-1.00)	
Sample size			0.48		0.13
≤60	4	0.94 (0.90-0.97)		0.42 (-0.28-1.00)	
>60	1	0.84 (0.75-0.94)		0.97 (0.83-1.00)	
Study design			0.02		0.80
Prospective	2	0.89 (0.81-0.97)		0.61 (-0.50-1.00)	
Retrospective	3	0.94 (0.89-0.99)		0.67 (-0.29-1.00)	

Table IV. Meta-regression and subgroup analyses of ^{68}Ga-prostate-specific membrane antigen positron emission tomography/CT.

Covariate	Studies, n	Sensitivity (95%Cl)	P-value	Specificity (95% CI)	P-value
Year of publication			0.71		0.65
2017-2018	4	0.96 (0.92-1.00)		0.72 (0.55-0.89)	
2019-2021	4	0.95 (0.87-1.00)		0.71 (0.52-0.89)	
Region			0.42		<0.001
Western	5	0.97 (0.95-1.00)		0.54 (0.41-0.67)	
Asian	3	0.88 (0.80-0.95)		0.83 (0.75-0.92)	
Sample size			0.85		0.93
≤60	5	0.95 (0.88-1.00)		0.74 (0.59-0.89)	
>60	3	0.97 (0.92-1.00)		0.66 (0.47-0.85)	
Study design			0.50		0.44
Prospective	6	0.97 (0.92-1.00)		0.67 (0.54-0.80)	
Retrospective	2	0.92 (0.81-1.00)		0.84 (0.65-1.00)	

complex and diverse characteristics of diagnostic accuracy research in this field. In the following meta-regression analysis, it was attempted to find the underlying factors that contribute to the observed heterogeneity. It was indicated that the diversity in geographical region among the research populations, as well as the combination of prospective and retrospective study designs, were significant factors. However, it is crucial to recognize that the observed heterogeneity can also be attributed to methodological differences, such as variations in imaging techniques, thresholds for determining positives and discrepancies in the criteria used to choose patients among the studies included. These factors indicate that, although specific variables have a significant impact on heterogeneity, a wider range of methodological and clinical factors should be considered when interpreting the results of diagnostic accuracy meta-analyses in PCa imaging.

The present study acknowledges several methodological limitations that warrant careful consideration. First, the relatively small sample size, with only 13 studies included, restricts the statistical power and robustness of the present findings. This limitation underscores the need for caution when extrapolating the present results to broader populations. Furthermore, the heterogeneity introduced by differing diagnostic cutoffs and design of the included studies was a challenge. Such heterogeneity may lead to biases in the synthesis of data, particularly in deciding which results are emphasized, potentially skewing the overall interpretation of diagnostic efficacy. In addition, the study's selection criteria may have inadvertently resulted in a narrow representation of geographical region. This limitation is significant because the diagnostic performance of the tests under review may vary across different regional groups, thereby affecting the applicability of the conclusions across diverse populations. Finally, the reliance on histology and follow-up as the gold standard for confirming tumor recurrence is a critical point for consideration. The fact that not all patients in the included studies had accessible confirmatory pathology results introduces an element of uncertainty regarding the diagnostic precision of the imaging modalities evaluated. This limitation is particularly pertinent, as it may compromise the reliability

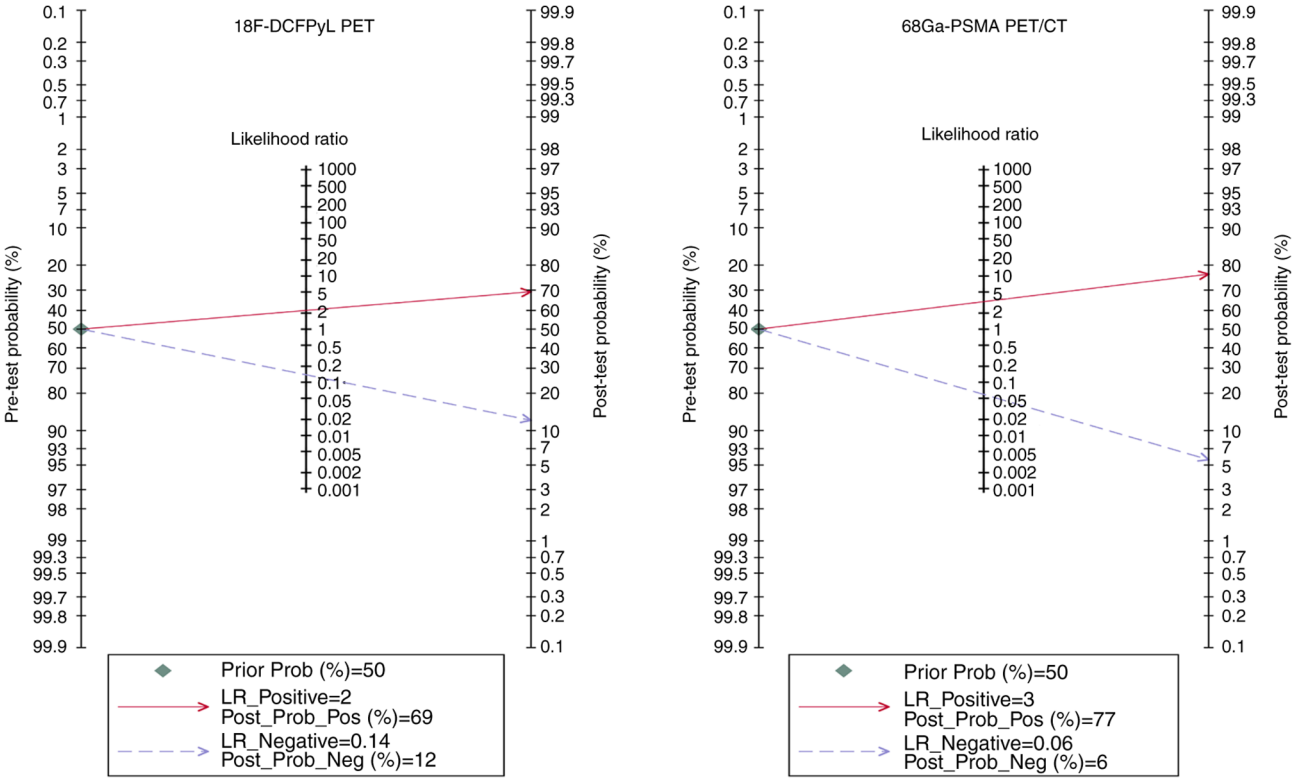

Figure 5. Fagan nomogram for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT. The pre-test probability was set at 50%. PSMA, prostate-specific membrane antigen; PET, positron emission tomography; LR, likelihood ratio; Prob, probability/probably; Neg, negative; Pos, positive.

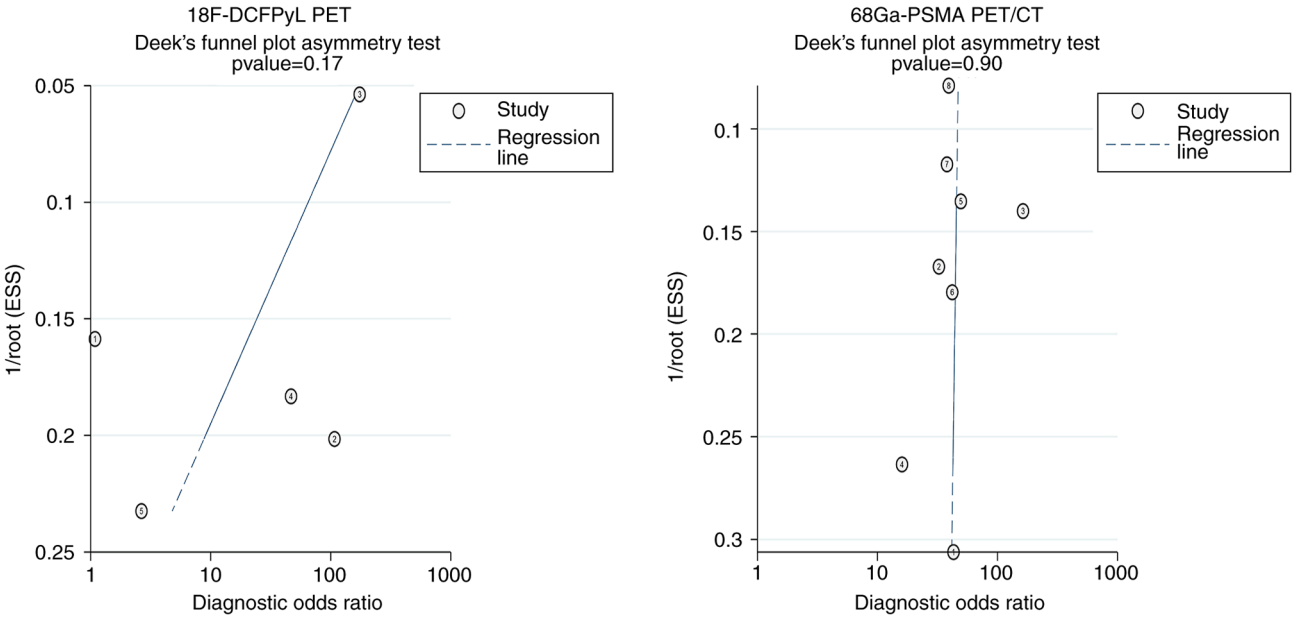

Figure 6. Deeks' funnel plot tests for ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT. PSMA, prostate-specific membrane antigen; PET, positron emission tomography. ESS, effective sample size. In the ^{18}F-DCFPyL PET section: 1, Metser *et al* (25), 2021; 2, Zhang *et al* (26), 2022; 3, Bodar *et al* (24), 2020; 4, Liu *et al* (27), 2022; 5, Parathithasan *et al* (28), 2022. In the ^{68}Ga-PSMA PET/CT section: 1, Hoffmann *et al* (29), 2017; 2, Lopci *et al* (30), 2018; 3, Sasikumar *et al* (31), 2018; 4, Kumar *et al* (32), 2019; 5, Zhang *et al* (33), 2018; 6, Liu *et al* (34), 2020; 7, Lopci *et al* (35), 2020; 8, Jiao *et al* (36), 2021.

of the current findings. Considering these limitations, the conclusions of the present study should be interpreted with caution. The identified weaknesses and sources of heterogeneity highlight the need for additional, more comprehensive research to validate and extend the current findings, ensuring their relevance and applicability to a wide range of clinical contexts.

From the pooled data it was inferred that the diagnostic performance of ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT is comparable in patients with suspected PCa. Although only

a small number of studies have been carried out thus far, it is significant to emphasize that the comparative evidence in this field currently needs to be more extensive. Therefore, subsequent studies concentrating on direct head-to-head comparisons of these two radiotracers may produce fresh and intriguing findings, offering new insight into the diagnostic capacities of these imaging modalities.

In conclusion, comparable diagnostic performance is seen for patients with suspected PCa using ^{18}F-DCFPyL PET and ^{68}Ga-PSMA PET/CT. It is suggested that both modalities can be valuable tools in the diagnostic arsenal against this prevalent disease, underscoring the potential for flexibility in clinical choices, based on availability and patient-specific factors. However, given the modest sample sizes of the studies included in the present meta-analysis, it is crucial to interpret these results with caution. Further studies with larger, more diverse populations are essential to solidify our understanding and refine suspected PCa diagnostic protocols. Such research will also help in addressing the limitations identified, ultimately contributing to more effective and personalized patient care.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

QT and ZJ conceived of and designed the study. JG, SY and BM performed data acquisition, data analysis and manuscript preparation. ZJ, JG, LH and SY assisted with data acquisition, data analysis and statistical analysis. ZJ and BM confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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