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Head-to-head comparison of PSMA PET/CT and mpMRI for detecting biochemical recurrence of prostate cancer: A systematic review and meta-analysis

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Abstract

Objectives: This study aimed to evaluate the performance of prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) in comparison to multiparametric magnetic resonance imaging (mpMRI) for detecting biochemical recurrence of prostate cancer (PCa).

Materials and methods: We conducted a comprehensive search for articles published in PubMed, Web of Science, Embase, and the Cochrane Library, spanning the inception of the database until October 26, 2022, which included head-to-head comparisons of PSMA PET/CT and mpMRI for assessing the biochemical recurrence of PCa.

Results: A total of 5 studies including 228 patients were analyzed. The overall positivity rates of PSMA PET/CT and mpMRI for detecting biochemical recurrence of PCa after final treatment were 0.68 (95% confidence interval [CI], 0.52–0.89) and 0.56 (95% CI, 0.36–0.88), respectively. The positivity rates of PSMA PET/CT and mpMRI for detecting local recurrence, lymph node metastasis, and bone metastases were 0.37 (95% CI, 0.30–0.47) and 0.38 (95% CI, 0.22–0.67), 0.44 (95% CI, 0.35–0.56) and 0.25 (95% CI, 0.17–0.35), and 0.19 (95% CI, 0.11–0.31) and 0.12 (95% CI, 0.05–0.25), respectively. Compared with mpMRI, PSMA PET/CT exhibited a higher positivity rate for detecting biochemical recurrence and lymph node metastases, and no significant difference in the positivity rate of local recurrence was observed between these 2 imaging modalities.

Conclusions: Compared with mpMRI, PSMA PET/CT appears to have a higher positivity rate for detecting biochemical recurrence of PCa. Although both imaging methods showed similar positivity rates of detecting local recurrence, PSMA PET/CT outperformed PSMA PET/CT in detecting lymph node involvement and overall recurrence.

Keywords: Prostate-specific membrane antigen; Positron emission tomography/computed tomography; Multiparametric magnetic resonance imaging; Prostate cancer; Biochemical recurrence; Positive rate

1. Introduction

According to the latest National Cancer Report 2022[1] released by the National Cancer Center, the incidence and mortality rates of prostate cancer (PCa) in men are increasing every year. Early treatment is crucial for favorable prognosis of PCa, and radical prostatectomy is the most effective treatment.[2] Approximately 40% of patients with radically treated PCa experience biochemical recurrence (BCR) during their lifetime; however, only 10%–20% of them experience clinically detectable recurrence. Biochemical recurrence, a commonly used endpoint in PCa studies, is defined as a sustained increase in prostate-specific antigen (PSA) levels beyond a certain threshold after the initial treatment. It is often evaluated using imaging-based criteria, such as radiographic evidence of disease progression or the initiation of new therapy in response to rising PSA levels.[3,4] The Society for Nuclear Medicine and Molecular Imaging[5] defines BCR as an elevation of PSA to ≥0.2 ng/mL measured 6–13 weeks after prostatectomy and confirmed by a subsequent PSA level of >0.2 ng/mL. Managing BCR remains a major challenge for patients undergoing radical prostatectomy.

Targeting early BCR to plan the initial and subsequent treatment strategies is a major clinical need. Various conventional imaging modalities, such as thoracoabdominal computed tomography (CT), pelvic multiparametric magnetic resonance imaging (mpMRI), and bone scintigraphy, are available for biochemically recurrent PCa; however, these modalities are usually unable to detect disease sites, especially in low-level recurrent diseases. The use of positron emission tomography (PET) imaging in medicine is evolving, and it is commonly used for PCa staging, assessing BCR after radiotherapy, and detecting metastatic involvement; however, its role in diagnosing BCR of PCa is limited. Positron emission tomography/computed tomography is a novel diagnostic tool that has demonstrated its unique diagnostic properties in cancer, particularly for PCa. The ability to develop radiolabeled tracers for functional imaging based on PCa cell characteristics could potentially provide additional information by exploiting key features of these cells, such as metabolic activity, increased proliferation, and receptor expression.[6] A study showed that prostate-specific membrane antigen (PSMA)–based tracers exhibit higher tumor detection rates in patients with

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BCR of PCa after radical prostatectomy.[7] Prostate-specific membrane antigen is a transmembrane protein expressed in secretory cells of the prostate epithelium, as well as in nonprostatic normal and malignant tissues. Almost all prostate adenocarcinomas exhibit PSMA expression in most primary and metastatic lesions. Currently, PSMA-PET/CT is being increasingly used to localize recurrent diseases.[8] A noteworthy advancement in the past decade has been the introduction of prostate mpMRI, characterized by a set of images, including at least 1 sequence in addition to anatomical T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI), such as diffusion-weighted imaging (DWI), apparent diffusion coefficient maps, and dynamic contrast-enhanced sequences (DCEs).[9] Diffusion-weighted imaging and DCE are particularly important among these. Diffusion-weighted imaging measures the Brownian motion of water molecules in the tissue and can be used to identify the peripheral regions of the prostate, which can be sampled using different *b* values, with lower *b* values providing more DWI and T2WI information and higher *b* values highlighting only DWI effects. In contrast, DCE emphasizes the vascular perfusion of the tissue and helps diagnose and capture abnormal vascular distribution. Therefore, mpMRI is widely used for detecting BCR of PCa because of its superior anatomical and tissue resolutions. Researchers have extensively used mpMRI to detect biochemically recurrent PCa.

Although both PSMA PET/CT and mpMRI can improve disease detection, their detection rates for BCR of PCa are still controversial; therefore, the aim of this study was to compare the diagnostic performance of PSMA PET/CT with mpMRI for detecting BCR of PCa. To reduce the heterogeneity between studies, we included only those investigations incorporating both modalities in the same population.

2. Materials and methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[10]

2.1. Search strategy

We conducted a comprehensive search for articles published in PubMed, Web of Science, Embase, and the Cochrane Library from the inception of the database until October 26, 2022. The search MESH terms were as follows: [(PET OR positron emission tomography) AND (mpMRI OR multiparametric magnetic resonance imaging OR multiparametric MRI) AND (regeneration OR biochemical OR recurrent OR relapse OR recrudescence) AND (Prostatic Cancers OR Prostatic Cancer OR Prostate Cancers OR Prostate Cancer OR Prostatic Neoplasm OR Prostate Neoplasm OR Prostate Neoplasms OR Prostate tumor OR prostatic tumor)]. In addition, we manually searched the reference lists of the identified publications for potentially relevant studies.

2.2. Inclusion and exclusion criteria

Studies that met all the following criteria were included: (1) BCR of PCa; (2) head-to-head comparison of PSMA PET/CT and mpMRI; (3) studies with positivity detection rates; and (4) studies in the English language.

The exclusion criteria were as follows: (1) case reports, abstracts, letters, editorial comments, meta-analyses, and reviews; (2) clearly irrelevant titles and abstracts; (3) no head-to-head comparison between the 2 modalities; and (4) data not retrievable for analysis.

Using the inclusion and exclusion criteria described previously, 2 researchers independently screened the titles and abstracts of the retrieved articles and evaluated the full-text versions to determine eligibility for inclusion in the subsequent step. Disagreements between the researchers were resolved through consensus.

2.3. Quality assessment

Two investigators independently assessed the quality of the included studies using the Quality Assessment of Diagnostic Performance Studies (QUADAS-2) tool.[11] Each study was assessed on the following domains: patient selection, index test, reference standard, flow, and time. These domains were assessed based on the risk of bias, and their applicability was categorized as high, low, or unclear.

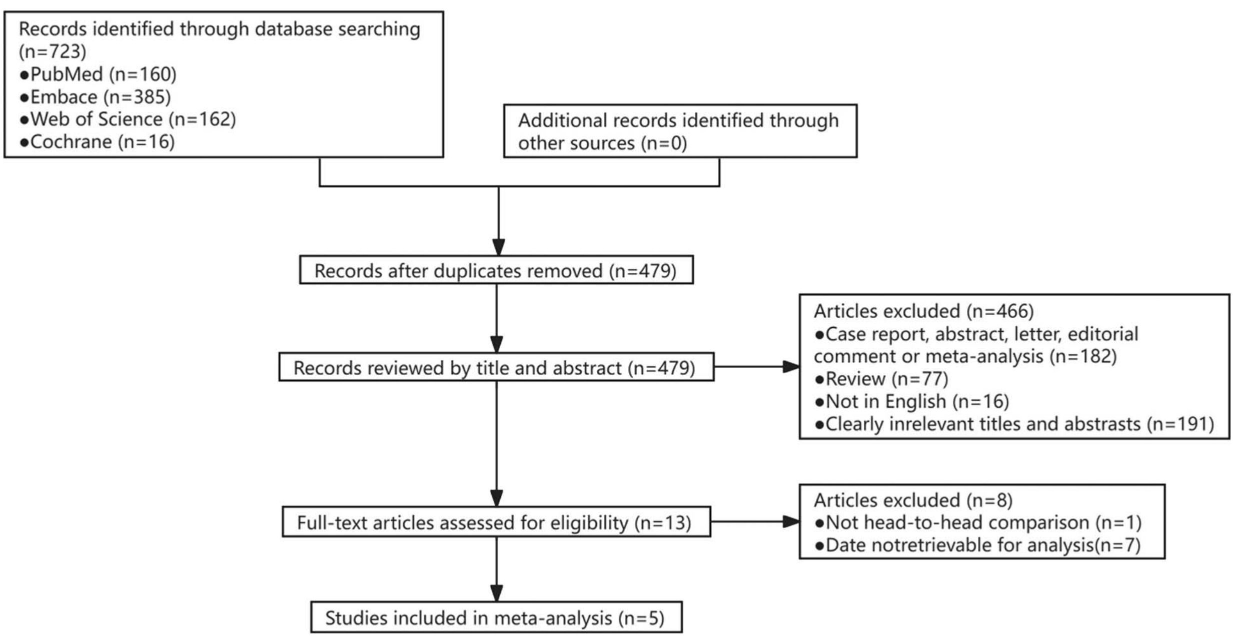

Figure 1. The PRISMA flow diagram of study selection process.

Table 1

Study and patient characteristics of the included studies.

Author	Year	Study characteristics: Country	Study design	Patient characteristics: No. patients	Mean age (range), yr	PSA level (ng/mL)	Gleason score
Laura Saule et al.[13]	2021	Latvia	Prospective	28	67 (52–84)	1.05 (0.21–5.0)	7 (5–9)
Jing-Ren Tseng et al.[16]	2020	Taiwan, China	Prospective	34	67 (56–79)	0.51 (0.2–13.10)	≤7 (76.5%) ≥8 (23.5%)
Maija Radzina et al.[14]	2020	Latvia	Prospective	32	63 (49–81)	2.27 (0.22–10.10)	≤7 (75%) ≥8 (25%)
Ali Afshar-Oromieh et al.[15]	2019	Switzerland	Retrospective	43	69.8 (59–86)	4.1 (0.2–20)	NA
Louise Emmett et al.[12]	2018	Australia	Prospective	91	64 (59–69)	0.42 (0.29–0.93)	6–7 (67%) 8–10 (32%)

NA = not accessed; PSA = prostate-specific antigen.

2.4. Data extraction

Two researchers independently performed data extraction for all the included articles. The extracted data included authors, year, study characteristics (country and study design), patient characteristics (number of patients, age, median PSA level, and Gleason score), and technical aspects (scanner model, field strength, MRI sequence, ligand, injection dose, time from injection to acquisition, and image analysis). Total, local recurrence, lymph node metastasis, and bone metastasis positivity rates were tabulated using the corresponding raw data from each included study. Disagreements between the investigators were resolved through consensus.

2.5. Statistical analysis

Statistical analyses were performed using R software version 4.2.2 (R Core Team, Vienna, Austria). Heterogeneity was assessed using the I^2 statistic; if significant heterogeneity was observed ($I^2 > 50\%$), forest plots were constructed with a random-effects model; otherwise, a fixed model was applied. The inverse variance and DerSimonian-Laird methods, using logarithmic transformation were applied, and the Clopper-Pearson method was used to calculate confidence intervals (CIs). Owing to the limited number of included studies, we did not perform subgroup analysis or meta-regression to identify sources of heterogeneity and performed a sensitivity analysis to explore the sources of heterogeneity. Egger test using R software version 4.2.2 was used to assess possible publication bias.

3. Results

3.1. Literature search and study selection

A total of 723 studies were identified by searching databases and publications. After excluding 244 duplicate studies; 182 case

Table 2

Technical aspects of mpMRI and PSMA PET/CT scans.

Author	Year	mpMRI: Scanner modality	Field strength	MRI sequence	PSMA PET/CT: Scanner modality	Radiotracers	Ligand dose	Time from injection to acquisition (min)	Image analysis
Laura Saule et al.[13]	2021	Magnetom/Avanto, Siemens, Germany; Ingenia, Philips Healthcare, Best, the Netherlands	1.5 T 3 T	T1WI T2WI DWI DCE	Ge-mini TF64, Philips, Koninklijke Philips NV, Best, the Netherlands	^{18}F-PSMA-1007	1.8–2.2 MBq/kg BW	54 (52–78)	Quantitative
Jing-Ren Tseng et al.[16]	2020	Siemens Healthineers	3 T	T1WI T2WI DWI DCE	Siemens Healthineers	^{68}Ga-PSMA-11	135.8 MBq (88.4–182.8)	60	Quantitative
Maija Radzina et al.[14]	2020	Magnetom/Avanto, Siemens, Germany; Ingenia, Philips Healthcare, Best, the Netherlands	1.5 T 3 T	T1WI T2WI DWI DCE ADC	Gemini TF64, Philips, Koninklijke Philips NV, Best, the Netherlands	^{68}Ga-PSMA-11	1.8–2.2 MBq/kg BW	55 (51–81)	Quantitative
Ali Afshar-Oromieh et al.[15]	2019	Siemens Skyra, Siemens Healthineers, Erlangen, Germany	3 T	T1WI T2WI DWI ADC	Siemens, Erlangen, Germany	^{68}Ga-PSMA-11	194.6 MBq	60	Quantitative
Louise Emmett et al.[12]	2018	NA	NA	Small field-of-view, pelvic T2 axial and coronal sequences	NA	Gallium-68 HBED-CC-PSMA-11	2.0 MBq/kg	60	Quantitative

ADC = apparent diffusion coefficient; DCE = dynamic contrast-enhanced sequence; DWI = diffusion-weighted imaging; mpMRI = multiparametric magnetic resonance imaging; NA = not accessed; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography; T1WI = T1-weighted imaging; T2WI = T2-weighted imaging.

Table 3

Positivity rates at different locations.

	mpMRI				PSMA PET/CT			
Author, year	Overall PR	PR in local recurrence	PR in lymph node metastasis	PR in bone metastasis	Overall PR	PR in local recurrence	PR in lymph node metastasis	PR in bone metastasis
Laura Saule et al., 2021[13]	NA	0.32 (9/28)	0.25 (7/28)	NA	NA	0.36 (10/28)	0.46 (13/28)	0.21 (6/28)
Jing-Ren Tseng et al., 2020[16]	0.82 (28/34)	0.76 (26/34)	0.26 (9/34)	0.12 (4/34)	0.68 (23/34)	0.44 (15/34)	0.32 (11/34)	0.15 (5/34)
Maija Radzina et al., 2020[14]	0.56 (18/32)	0.37 (11/30)	0.22 (7/32)	0.11 (2/18)	0.72 (23/32)	0.38 (12/32)	0.50 (16/32)	0.22 (7/32)
Ali Afshar-Oromieh et al., 2019[15]	0.70 (30/43)	NA	NA	NA	0.88 (38/43)	NA	NA	NA
Louise Emmett et al., 2018[12]	0.28 (25/88)	0.22 (19/88)	0.08 (7/88)		0.42 (13/31)	0.19 (6/31)	0.31 (10/31)	

mpMRI = multiparametric magnetic resonance imaging; NA = not accessed; PR = positive rate; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

studies, abstracts, letters, reviews, and meta-analyses; 77 reviews; 16 non-English articles; and 191 irrelevant studies, 13 articles were identified for full evaluation. Subsequently, 8 additional articles were excluded for the following reasons: not meeting head-to-head comparisons (n = 1) and unavailable or incomplete data (n = 7). Finally, 5 articles[12–16] focusing on the detection of BCR of PCa with head-to-head comparisons of PSMA PET/CT and mpMRI were deemed eligible for analysis. A PRISMA flowchart of the study selection process is shown in Figure 1.

3.2. Study description and quality assessment

The 5 included studies, published between 2018 and 2021, with sample sizes ranging from 28 to 91, comprised 228 patients with BCR of PCa. Table 1 summarizes the studies and patient characteristics from the included studies. Table 2 lists the technical aspects of PSMA PET/CT and mpMRI. Table 3 presents the detection rates at different locations. Variations in the definitions of BCR across included studies were noted, reflecting differences in imaging techniques, biomarker thresholds, and other factors. A summary of the definitions used in each study is presented in Table 4. Figure 2 presents our assessment of the risk of bias in these studies using the QUADAS-2 tool. The quality of the included studies was satisfactory according to the QUADAS-2 recommendations.

3.3. Quantitative synthesis

Among the 228 patients in 5 studies, the overall positivity rates of PSMA PET/CT and mpMRI for BCR of PCa after final treatment were 0.68 (95% CI, 0.52–0.89) and 0.56 (95% CI, 0.36–0.88), respectively; for local recurrence, the positivity rates were 0.37 (95% CI, 0.30–0.47) and 0.38 (95% CI, 0.22–0.67), respectively; for lymph node metastasis, the positivity rates were 0.44 (95% CI, 0.35–0.56) and 0.25 (95% CI, 0.17–0.35), respectively; and for bone metastases, the positivity rates were 0.19 (95% CI, 0.11–0.31) and 0.12 (95% CI, 0.05–0.25), respectively (Figs. 3–6). Because of the limited number of literature reporting the number of bone metastases, the positivity rate of bone metastases has not been reported. A statistically significant difference in the overall positivity rate was observed between the 2 imaging modalities (χ^2, 10.96, $p \leq 0.001$); in addition, no significant difference in the positivity rate for local recurrence ($p = 0.76$) and a significant difference in the positivity rate for lymph node metastasis ($p = 0.009$) was observed.

Table 4

Definitions of biochemical recurrence in the included studies.

Study/author, year	Definition of BCR
Laura Saule et al., 2021[13]	PSA level 0.2–5.0 ng/mL after radical prostatectomy or PSA level 0.2–5.0 ng/mL after prostatectomy with following radiation therapy in BCR
Jing-Ren Tseng et al., 2020[16]	PSA increase by >0.2 ng/mL on 2 or more consecutive measurements
Maija Radzina et al., 2020[14]	PSA level 0.2–10.0 ng/mL after radical prostatectomy, radical pelvic radiation therapy, or radical prostatectomy and adjuvant radiotherapy
Ali Afshar-Oromieh et al., 2019[15]	PSA level 0.2–20.0 ng/mL after radical prostatectomy
Louise Emmett et al., 2018[12]	PSA level ≥0.2 ng/mL after radical prostatectomy

BCR = biochemical recurrence; PSA = prostate-specific antigen.

3.4. Heterogeneity analysis

Regarding the overall positivity rate of BCR for PCa on PSMA PET/CT and mpMRI, I^2 values were 81% and 91%, respectively, indicating high heterogeneity in both the imaging modalities. Sensitivity analysis revealed moderate to high heterogeneity after excluding data for the analysis (Table 5); therefore, the source of heterogeneity could not be identified for either PSMA PET/CT or mpMRI. For mpMRI, we observed a high heterogeneity in local recurrence (I^2, 92%) and no heterogeneity in lymph node metastasis (I^2, 0%), whereas PSMA PET/CT showed low heterogeneity in both local recurrence and lymph node metastasis, with I^2 of 27% and 6%, respectively.

Regarding publication bias, Egger test for mpMRI did not reach significance ($p = 0.09$), confirming that the results had a publication bias for PSMA PET/CT ($p = 0.01$). After analyzing publication bias using the cut-and-patch method and supplementing the 2 studies by Tseng et al. and Emmett et al., the results remained unchanged, indicating that publication bias had little effect and that the results were relatively robust.

4. Discussion

To our knowledge, this study represents the first head-to-head comparison of PSMA PET/CT and mpMRI for detecting BCR of PCa, with the aim to compare the detection rates of both diagnostic modalities.

This meta-analysis pooled patient-based data from 5 studies that compared PSMA-PET/CT and mpMRI in the same population. By systematically reviewing the ability of both imaging methods for detecting BCR, the final results revealed that the overall positivity rates of PSMA PET/CT and mpMRI for detecting BCR after PCa treatment were 0.68 and 0.56, respectively. Evidence from this study suggests that PSMA PET/CT has a higher positivity detection rate for BCR and lymph node metastases than that of mpMRI. Notably, no significant difference in the positivity rate for local recurrence was observed between the 2 imaging modalities. A previous study by Radzina et al.[14] confirmed the excellent diagnostic ability of PSMA-PET/CT and mpMRI for the staging of early recurrent PCa at low PSA levels. Although mpMRI demonstrated better

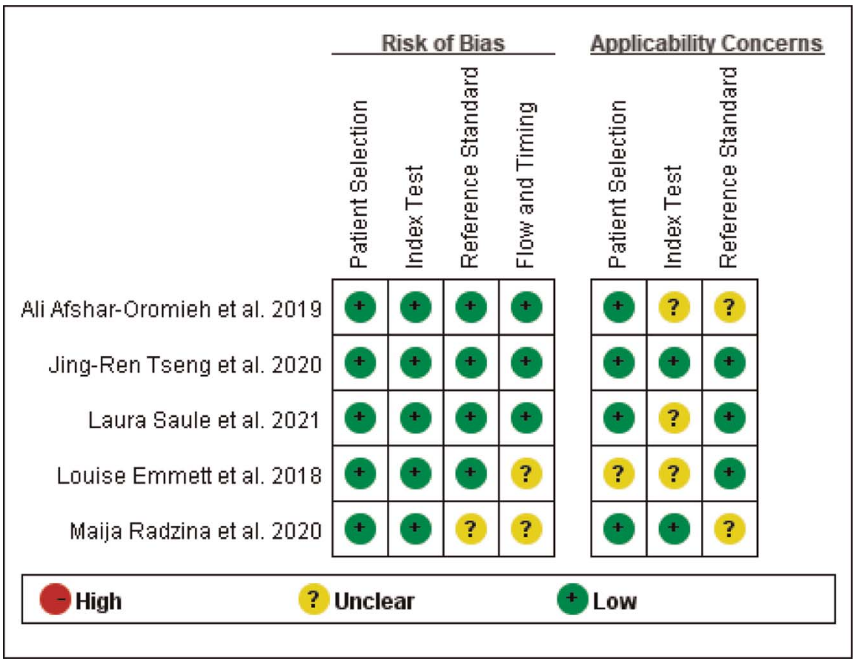

Figure 2. Summary of the risk of bias and applicability concerns of the included studies.

diagnostic accuracy for detecting local recurrence, PSMA PET/CT was superior in detecting distant and lymph node metastases. Because their study was based on a small sample size, caution is warranted in interpreting these results.

Analysis of the total positivity rate of PSMA PET/CT and mpMRI for detecting BCR of PCa indicated that both were highly heterogeneous and did not reach acceptable levels of heterogeneity even after sensitivity analysis. Although mpMRI displayed no heterogeneity in lymph node metastasis, PSMA PET/CT exhibited low heterogeneity in both local recurrence and lymph node metastasis. The high heterogeneity in the overall positivity rate may be due to the small sample size or variations in patients, methods, and study design.

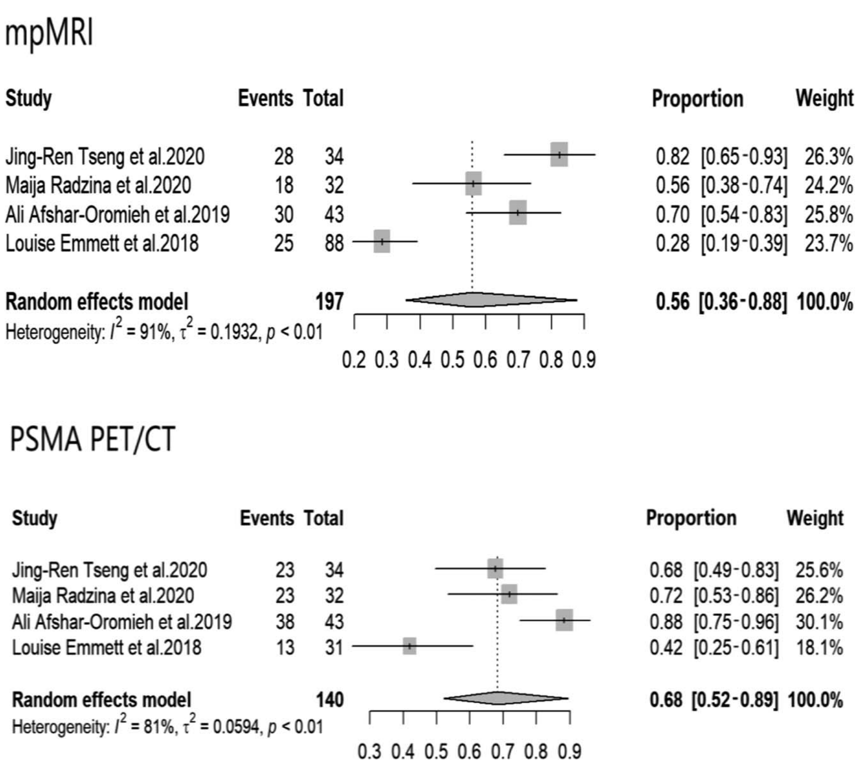

Figure 3. Forest plot showing the pooled overall positive rate of mpMRI and PSMA PET/CT in BCR. BCR = biochemical recurrence; mpMRI = multiparametric magnetic resonance imaging; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

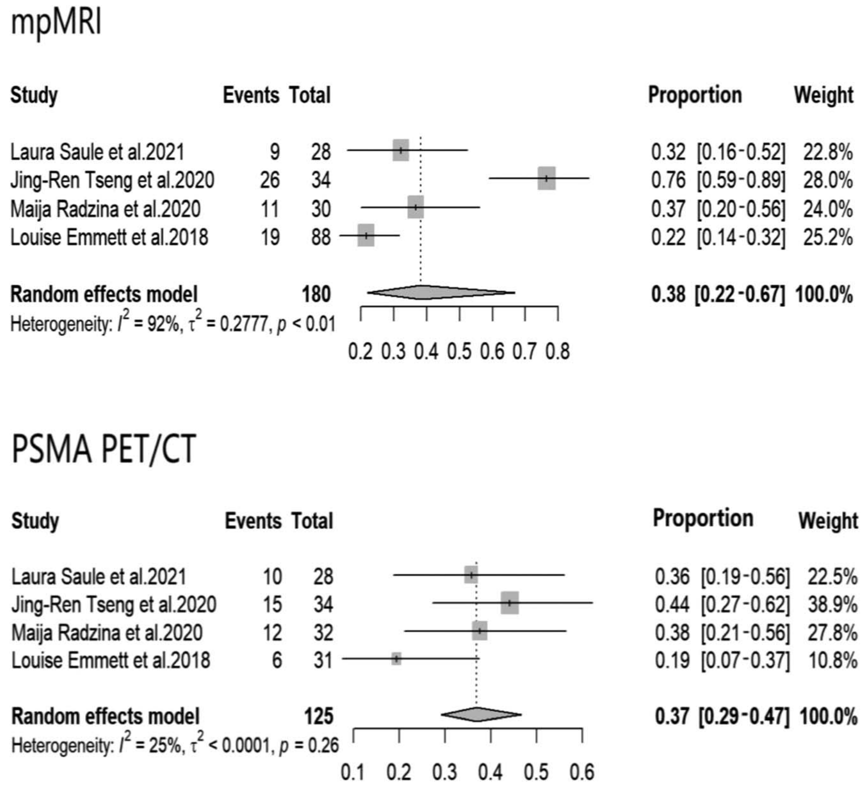

Figure 4. Forest plot showing the pooled positive rate of mpMRI and PSMA PET/CT for detecting in local recurrence in BCR. BCR = biochemical recurrence; mpMRI = multiparametric magnetic resonance imaging; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

Therefore, the reliability of the results should be viewed with caution. Egger test confirmed the existence of publication bias in PSMA PET/CT, and additional studies did not reverse this bias, indicating that publication bias had little effect and the results were relatively robust.

In reviewing the definitions of BCR, we observed variations and discrepancies across studies, such as differences in biomarker thresholds, imaging modalities, and duration of follow-up. These discrepancies could have significant implications for the interpretation of results, introducing heterogeneity and limiting comparability between studies. For instance, the use of lower biomarker thresholds or more sensitive imaging techniques may lead to the earlier identification of cases of BCR compared with that of higher thresholds or

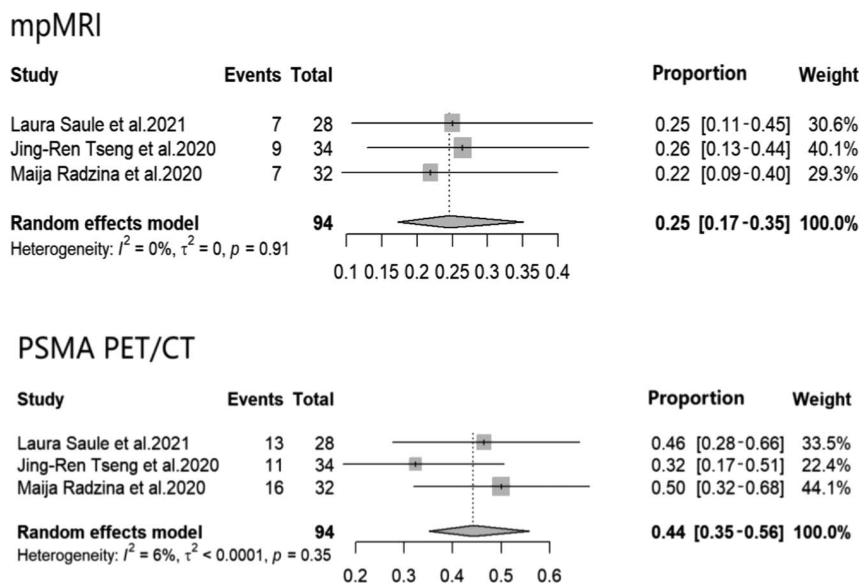

Figure 5. Forest plot showing the pooled positive rate of mpMRI and PSMA PET/CT for detecting lymph node metastasis in BCR. BCR = biochemical recurrence; mpMRI = multiparametric magnetic resonance imaging; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

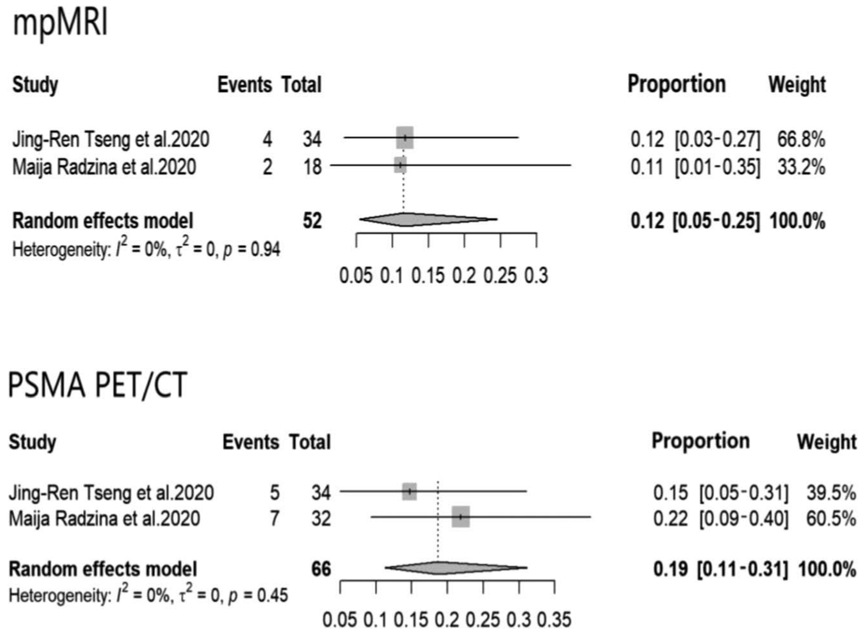

Figure 6. Forest plot showing the pooled positive rate of mpMRI and PSMA PET/CT for detecting in bone metastasis in BCR. BCR = biochemical recurrence; mpMRI = multiparametric magnetic resonance imaging; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

less sensitive methods, resulting in differences in the reported rates of recurrence and effect sizes. To address these challenges, future research should aim to establish standardized criteria for defining BCR to promote consistency and comparability across studies, facilitating accurate assessments of treatment outcomes and meaningful comparisons among different interventions or patient populations.

International guidelines,[17] including the European Association of Urology guidelines,[18,19] have recommended the use of PSMA PET/CT in patients with elevated PSA levels after radical prostate treatment, making it an essential imaging tool for detecting BCR.[20] However, the performance of PSMA-PET/CT may be limited by the availability of the PET/CT scanner or PSMA radiotracer. First, PET/CT is a combination of 2 different imaging principles, PET scanner and spiral CT, where the obtained images are superimposed by a computer to generate a new image. Although PET/CT examination uses radiation, which is harmful to human body, the degree of harm is minimal and completely within the acceptable safety limits. Second, radiolabeled PSMA ligands are increasingly used in clinical practice,[21] especially in patients with BCR or metastasis. Notably, antibodies binding to the extracellular structural domain of monoclonal antibodies demonstrate excellent affinity and specificity for PSMA.[22] The 2 main ligands currently used are ^{68}Ga-PSMA and ^{18}F-PSMA. Among the ^{68}Ga-PSMA ligands, ^{68}Ga labeled with Glu-NH-CO-NH-Lys-(Ahx) (^{68}GaHBED-CC or ^{68}Ga-PSMA-11) is one of the earliest PET tracers widely used in clinical practice. Ga-PSMA-11 exhibits a high receptor affinity for PSMA and excellent tissue penetration, allowing its effective diffusion into prostate tumor cells.[23] ^{68}Ga-PSMA-11 uptake in the lacrimal gland, salivary gland, liver, spleen, kidney, and some parts of the intestine is considered physiological, with PSMA expression levels significantly lower than those in prostate tumor cells.[24] In addition, the free form of ^{68}Ga-PSMA-11 is excreted through the kidneys and urethra.[25] Recent clinical studies have demonstrated the superiority of ^{18}F-based PET to ^{68}Ga-based PET in terms of availability, yield, and image resolution.[26] Conversely, because ^{18}F is produced by a cyclotron and can be produced in larger quantities than ^{68}Ga, which is serially produced by generators,[27] a potential advantage of ^{18}F compared with ^{68}Ga is the lower positron energy, and thus improved spatial resolution. In contrast, ^{18}F-PSMA-1007, a novel PSMA ligand, has been developed with a good preclinical profile; it exhibits rapid blood clearance, and only a very minimal amount of the radiotracer is excreted through the urethra,[28] contributing to the assessment of the prostate bed by reducing the urinary clearance rate. Therefore, ^{18}F-PSMA PET/CT may greatly improve diagnostic performance in the future detection of BCR of PCa. Simultaneously, PSMA ligand PET data[5] suggest that increased PSMA expression can also be found in the neovascularization of nonprostatic solid tumors or benign tumors, and we should carefully evaluate the possibility of other tumors resulting from increased PSMA expression.

Table 5

Sensitivity analysis of the overall positivity rate for mpMRI and PSMA PET/CT.

	mpMRI		PSMA PET/CT	
Omitting studies	Positive rate (95% CI)	I^2 (%)	Positive rate (95% CI)	I^2 (%)
Jing-Ren Tseng et al., 2020[16]	0.49 (0.29–0.82)	90.4	0.67 (0.45–1.00)	85.0
Maija Radzina et al., 2020[14]	0.55 (0.29–1.00)	93.8	0.66 (0.44–0.98)	86.2
Ali Afshar-Oromieh et al., 2019[15]	0.52 (0.28–0.95)	94.1	0.62 (0.47–0.82)	61.8
Louise Emmett et al., 2018[12]	0.71 (0.58–0.87)	61.9	0.77 (0.65–0.92)	66.0

CI = confidence interval; mpMRI = multiparametric magnetic resonance imaging; PSMA PET/CT = prostate-specific membrane antigen positron emission tomography/computed tomography.

Limitations

This study has some limitations. First, our meta-analysis included only 5 studies, comprising a small sample size, mainly because we only included studies that used PET/CT and mpMRI for detecting

BCR within the same patient cohort. Second, the main purpose of this study was to compare positivity rates. We only evaluated positive lesions without assessing benign lesions and were unable to calculate other parameters of diagnostic performance, such as specificity or accuracy. Therefore, cautious interpretation of the final results is recommended, and a larger sample size is needed to draw more accurate conclusions. This meta-analysis of head-to-head comparative studies affirms that PSMA PET/CT appears to have a higher positive rate for detecting BCR of PCa than that of mpMRI.

Acknowledgments

None.

Statement of ethics

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Conflict of interest statement

The authors have no relevant financial or nonfinancial interests to disclose.

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Author contributions

XZ, ZM: Material preparation, data collection, and analysis;
XZ: Writing of the first draft of the manuscript;
XZ, ZM: Study conception and design;
XZ, ZM: Commenting on previous versions of the manuscript;
XZ, ZM: Reading and approval of the final manuscript.

Data availability

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

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