Prostate Cancer

The performance of $^{18}$F-PSMA PET/CT in the detection of prostate cancer: a systematic review and meta-analysis

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This paper presents a meta-analysis regarding the detection rate (DR) of fluorine-18 ($^{18}$F)-labeled prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) in the management of patients with prostate cancer (PCa). Relevant studies regarding $^{18}$F-PSMA PET/CT in the management of PCa published until June 1, 2021, were electronically searched in online databases including EMBASE, PubMed, and Web of Science. The primary outcome was the DR of $^{18}$F-PSMA PET/CT in managing PCa patients, while the secondary outcome was the DR of $^{18}$F-PSMA PET/CT according to Gleason scores and serum prostate-specific antigen (PSA) level. The pooled DR was calculated on a per-patient basis, with pooled odd ratios and 95% confidence intervals (CIs). In total, 17 observational studies evaluating 1019 patients with PCa met the inclusion criteria. The DR of $^{18}$F-PSMA PET/CT was 0.83 (95% CI: 0.78–0.88), in the random-effects model. Subsequently, the analysis of DR of $^{18}$F-PSMA PET/CT in PCa patients using Gleason score ($\leq$7 vs $\geq$8), showed a significant difference in PCa patients. Based on the above results, the higher Gleason score of PCa patients, the higher DR of $^{18}$F-PSMA PET/CT. The DR of $^{18}$F-PSMA PET/CT in PCa was 0.57 for PSA $<$0.5 ng ml$^{-1}$; 0.75 for PSA $\geq$0.5 ng ml$^{-1}$ and $<$1.0 ng ml$^{-1}$; 0.93 for PSA $\geq$1.0 ng ml$^{-1}$ and $<$2.0 ng ml$^{-1}$; and 0.95 for PSA $\geq$2.0 ng ml$^{-1}$. Therefore, the significant diagnostic value was found in terms of the DR of $^{18}$F-PSMA PET/CT in managing PCa patients and was associated with Gleason score and serum PSA level.

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INTRODUCTION

Prostate cancer (PCa) is one of the most frequently diagnosed cancers in men and the fifth leading cause of death worldwide. The incidence of PCa varies greatly depending on the continent. In the recent past, incidences of PCa have been increasingly reported in regions like Asia, which were traditionally considered low-incidence areas. Regardless of this, the diagnostic rate of PCa is still low due to the existing suboptimal imaging modalities used for diagnosis and treatment. There have been efforts to develop novel imaging tools that will promote diagnostic and therapeutic strategies for PCa. Therapeutic and management options for PCa are highly informed by the accurate staging of primary or recurrent PCa. Various imaging tools and techniques have been employed to assess the progression of PCa. They include transrectal ultrasound (TRUS), computed tomography (CT), magnetic resonance imaging (MRI), and bone scintigraphy (BS), which have been recommended for the diagnosis of primary and recurrence PCa by the European Association of Urology (EAU). These imaging techniques are, however, not always effective for the early and reliable management of primary/recurrence PCa due to their low sensitivity and specificity. Recently developed metabolic imaging techniques are aimed at improving the diagnosis of PCa when an increase in prostate-specific antigen (PSA) serum values is detected following curative primary treatments. In patients with low but rising values of PSA serum, after definitive local therapy, it is important to identify the sites of recurrence to maximize the effects of treatment. Therefore, imaging with radiotracers targeting the prostate-specific membrane antigen (PSMA) has received increasing attention as a promising novel technique for PCa detection. The PSMA is a protein expressed in dysplastic prostate cells with expression levels of 100–1000 times that of normal cells. The overexpression of PSMA may further be caused by the advanced stage and grade of PCa. It is important to note that PSMA is not prostate-specific, and it may be expressed in other tissues and tumors. The physiological expression of PSMA has also been revealed in the kidneys, the lacrimal and salivary glands, parts of the small and large intestines, the liver, the spleen, the neuronal ganglia, and various solid malignant and benign tumors.

The clinical breakthrough in PSMA-based imaging was achieved with the introduction of gallium-68 ($^{68}$Ga)-PSMA-11 in May 2011 as a PET tracer. In addition to $^{68}$Ga, several PSMA ligands, such as fluorine-18 ($^{18}$F) and copper-64 ($^{64}$Cu), can be radiolabeled with various positron-emitter isotopes to produce positron emission...
tomography (PET) radiopharmaceuticals for PCa therapy. The $^{68}$Ga PSMA PET/CT method of imaging has rapidly spread worldwide and is regarded as a significant step forward in the detection of PCa.\textsuperscript{16} It is characterized by excellent tumor uptake, low background signal, high specificity, and very fast pharmacokinetics. These features enhance superior tumor visibility compared with other imaging.\textsuperscript{17,18} Currently available $^{18}$F-labeled PSMA agents ($^{18}$F-PSMA-1007, $^{18}$F-DCFPyL, and $^{18}$F-DCFBC) provide a more accurate and earlier detection of prostate disease than conventional imaging.\textsuperscript{2,19} The labeling of PSMA agents as $^{18}$F has several advantages over $^{68}$Ga. They include a larger amount of activity from $^{18}$F production by cyclotron, compared with the limited activity of $^{68}$Ga derived from the elution of Germanium-68 ($^{68}$Ge)/$^{68}$Ga generators.\textsuperscript{19} This is in addition to improved image resolution and a longer half-life.\textsuperscript{19} Due to the lower positron energy, the theoretical achievable resolution of $^{18}$F is relatively better compared to that of $^{68}$Ga.

To date, numerous studies have explored the detection rate (DR) of $^{68}$Ga-labeled PSMA PET/CT in PCa patients. Conversely, this study aimed to perform a meta-analysis concerning the DR of $^{18}$F-PSMA PET/CT in the management of patients with PCa.

MATERIALS AND METHODS

**Research question**

A meta-analysis was performed to explore the DR of $^{18}$F-PSMA PET/CT for PCa patients in the management of localized or metastatic PCa.

**Search strategy**

This study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.\textsuperscript{20} The existing studies from EMBASE, PubMed, and Web of Science electronic databases were searched from the inception of the databases to June 1, 2021. The search query was formulated based on the following keywords: “$^{18}$F-PSMA” or “$^{18}$F-prostate-specific membrane antigen” and “diagnosis accuracy” or “detection” and “management” and “PCa” or “prostate cancer”. Besides, we also hand-searched the relevant studies from the reference lists of the selected articles, to identify more relevant publications and avoid relevant information being missed. The search was only limited to human studies and no language restrictions were posted in the setting.

**Inclusion and exclusion criteria**

Studies were included based on “Patient/Intervention/Outcome/Study design” criteria: (1) “patients” with PCa, regardless of the clinical setting of primary staging or biochemical failure (BCF; biochemical persistence or recurrence); (2) studies using $^{18}$F-PSMA PET/CT as an “intervention”; (3) patient-specific overall detection rate or proportion of PCa patients who experience change as an “outcome”; and (4) “study design” of clinical trials and prospective or retrospective studies published as original articles or brief communications.

The following were the exclusion criteria: (1) small number of patients (<10); (2) other publication types, including conference abstracts, review articles, editorials, and letters; (3) papers irrelevant

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**Table 1: Characteristics and methodology assessment of individual studies included in the meta-analysis**

| Publication year | Study | Country/region | Patient enrolment period | Institution | Prospective or retrospective | Responding entity | Prior imaging |
|------------------|-------|----------------|--------------------------|-------------|----------------------------|-------------------|--------------|
| 2020             | Dietlein et al.\textsuperscript{12} | Germany | 04/2017–03/2018 | University Hospital of Cologne | R | The institutional review board | NR |
| 2020             | Kuten et al.\textsuperscript{26} | Israel | NR | Tel Aviv Sourasky Medical Center | P | The institutional ethical committee | NR |
| 2020             | Witkowska-Patena et al.\textsuperscript{37} | Poland | NR | Military Institute of Medicine | P | Military Medical Chamber ethics committee | NR |
| 2020             | Sachpekidis et al.\textsuperscript{38} | Germany | NR | German Cancer Research Center | R | Ethical Committee of the University of Heidelberg | NR |
| 2020             | Rowe et al.\textsuperscript{46} | USA | 05/2016–11/2016 | Johns Hopkins University School of Medicine | P | Institutional Review Board of Johns Hopkins Medicine | NR |
| 2020             | Rowe et al.\textsuperscript{34} | USA | 08/2017–02/2018 | University Hospital of Cologne | R | The ethics committee | NR |
| 2020             | Dietlein et al.\textsuperscript{35} | Germany | 03/2017–12/2017 | University of British Columbia, Vancouver | P | UBC/BC Cancer Research Ethics Board | NR |
| 2019             | Rousseau et al.\textsuperscript{31} | Canada | 02/2017–01/2018 | Technical University of Munich | R | The ethics committee | NR |
| 2018             | Rahbar et al.\textsuperscript{23} | Switzerland | 10/2017–05/2018 | University Hospital of Heidelberg | R | CT/MRI/BS | NR |
| 2018             | Rahbar et al.\textsuperscript{26} | Switzerland | 10/2017–01/2018 | University Hospital of Heidelberg | R | CT/MRI/BS | NR |
| 2018             | Giesel et al.\textsuperscript{24} | Germany | 05/2016–07/2017 | University Hospital of Heidelberg | R | The Institutional review board | NR |
| 2018             | Giesel et al.\textsuperscript{27} | South Africa | 02/2017–01/2018 | University of Heidelberg | P | The Institutional Ethics Committee | NR |
| 2017             | Kesch et al.\textsuperscript{28} | Germany | 2016 | University Hospital of Heidelberg | R | The institutional review board | MRI |
| 2017             | Wondergem et al.\textsuperscript{29} | The Netherlands | 11/2016–03/2017 | University Hospital of Heidelberg | R | The institutional review board | NR |
| 2018             | Mena et al.\textsuperscript{30} | USA | 07/2014–11/2016 | National Cancer Institute, NIH | P | The institutional review board | MRI |

NR: not reported; P: prospective; R: retrospective; CT: computed tomography; MRI: magnetic resonance imaging; BS: bone scintigraphy
to the research question; (4) insufficient information provided in the study to calculate the DR of $^{18}$F-PSMA PET/CT in the management of PCa; and (5) overlapping study population. In the case of overlapping study populations, the article that provided more comprehensive information required for this meta-analysis was included.

**Data extraction and quality assessment**

Data extraction and study quality assessment were conducted blindly by two researchers (ZQQ and GJP). In the case of any inconsistency occurring in the results, a third reviewer (ZX) was consulted to reach a consensus. For each eligible article, clinicopathological and $^{18}$F-PSMA PET/CT characteristics were extracted using a standardized form, as follows:

1. Basic studies: origin (first author, publication year, patient enrolment period, institution, and country), design (prospective vs retrospective, and consecutive enrolment vs nonconsecutive), and methods for data acquisition (review of medical records vs questionnaires)

2. Clinicopathological: number of patients, age, and level of serum PSA at initial diagnosis and before $^{18}$F-PSMA PET/CT, Gleason score, and clinical setting (primary staging vs BCF)

3. PET: vendor, scanner model, ligands, injected dose, uptake time, acquisition time, and PET positivity (proportion of patients with positive $^{68}$Ga-PSMA PET scans).

**Statistical analyses**

The primary outcome of this meta-analysis was "the impact of $^{18}$F-PSMA PET/CT on the detection of PCa" according to the proportion of patients who had their PCa care changed following imaging findings detected on $^{18}$F-PSMA PET/CT. The secondary outcomes compared the DR of $^{18}$F-PSMA PET/CT in PCa patients, based on Gleason scores and the level of serum PSA. Pooled odds ratios (ORs) analyses were carried out using data retrieved from individual studies about the DR of $^{18}$F-PSMA PET/CT in the management of PCa. Pooled data were plotted with its specific 95% confidence interval (95% CI) values. A fixed-effects model (the Mantel–Haenszel method) or a random-effects model (the DerSimonian and Laird method) was used for statistical pooling of the data. During pooling, consideration was given to heterogeneity between the selected studies. The heterogeneity was assessed among studies using the $I^2$ test and the $F$ statistic. The $F$ value typically ranges from 0 (no observed heterogeneity) to 100% (maximal heterogeneity). If the heterogeneity across studies was not identified, then the fixed-effects model was used; otherwise, the random-effects model was used in the meta-analysis. All statistical analyses were performed using STATA software (version 12.0; StataCorp LP, College Station, TX, USA). $P < 0.05$ was regarded as statistically significant.

**RESULTS**

**Literature search**

In total, 486 articles were initially identified through a primary search of the relevant online databases and reference lists. After reviewing titles and abstracts, 424 articles were excluded. The remaining 62 articles were selected and reviewed in full-text version. Consequently, 45 full-text articles were excluded due to the following reasons: no original data available (n = 13), meta-analysis (n = 9), review articles (n = 20), and overlapping articles (n = 3). Ultimately, 17 full-text studies met the inclusion criteria and were involved in the present meta-analysis. The studies were accrued from May 2017 to June 2021.\textsuperscript{24-38} The literature search and selection procedure is presented in Figure 1.

**Table 2: Characteristics about fluorine-18-labeled prostate-specific membrane antigen positron emission tomography/computed tomography of individual studies included in the meta-analysis**

| Publication year | First author | Vendor | Model | Ligand | Dose (MBq) | Uptake time (min) | Acquisition time (min per bed) |
|------------------|--------------|--------|-------|--------|------------|-------------------|-------------------------------|
| 2020             | Dietlein et al.\textsuperscript{22} | Siemens | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 3.28 ± 358.97\textsuperscript{a} | NR |
| 2020             | Kuten et al.\textsuperscript{26} | NR | Biograph mCT | $^{18}$F-PSMA-1007 | NR | 60 | NR |
| 2020             | Witkowska-Patena et al.\textsuperscript{37} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 295.5 ± 14.1\textsuperscript{a} | 95 ± 12\textsuperscript{a} | NR |
| 2020             | Wueschke et al.\textsuperscript{38} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 237 (131–266)\textsuperscript{a} | 70 | 2 |
| 2020             | Rowe et al.\textsuperscript{48} | Siemens | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 333 \textsuperscript{c} | 60 | NR |
| 2020             | Wueschke et al.\textsuperscript{39} | Siemens | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 333 \textsuperscript{c} | 60 | NR |
| 2020             | Rauscher et al.\textsuperscript{33} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 325 ± 40\textsuperscript{a} | 94 ± 22\textsuperscript{a} | NR |
| 2020             | Dietlein et al.\textsuperscript{35} | Siemens | Biograph mCT | $^{18}$F-JK-PSMA | 141 ± 30\textsuperscript{a} | 230 | NR |
| 2019             | Rousseau et al.\textsuperscript{31} | NR | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 237–474\textsuperscript{a} | 120 | 2–4\textsuperscript{a} |
| 2019             | Giesel et al.\textsuperscript{34} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 301 ± 46\textsuperscript{a} | 92 ± 26\textsuperscript{a} | 3–4\textsuperscript{a} |
| 2018             | Rahbar et al.\textsuperscript{23} | Siemens | Siemens mCT | $^{18}$F-PSMA-1007 | 338 ± 44.3\textsuperscript{a} | 120 | 3 |
| 2018             | Rahbar et al.\textsuperscript{25} | Siemens | Siemens mCT | $^{18}$F-PSMA-1007 | 336.7 ± 46\textsuperscript{a} | 120/60 | 3 |
| 2018             | Giesel et al.\textsuperscript{26} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 251.5 (154–326)\textsuperscript{a} | 180 ± 5\textsuperscript{a} | NR |
| 2018             | Giesel et al.\textsuperscript{27} | Siemens | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 240–260\textsuperscript{a} | 120 | 3 |
| 2017             | Kesch et al.\textsuperscript{28} | Siemens | Biograph mCT | $^{18}$F-PSMA-1007 | 15.9 (10.6–54.9)/27.5 (14.8–76.2)\textsuperscript{a} | 60/180 | NR |
| 2017             | Wondergem et al.\textsuperscript{29} | Siemens | Biograph mCT | $^{18}$F-DCFPyL | $^{18}$F-PSMA-1007 | 314 (243–369)\textsuperscript{a} | 120/60 | NR |
| 2018             | Mena et al.\textsuperscript{30} | NR | Biograph mCT | $^{18}$F-DCFBC | $^{18}$F-PSMA-1007 | 292.3 (255.3–299.7)\textsuperscript{a} | 120/60 | 2 |

\textsuperscript{a}Data are shown as mean(s.d.); \textsuperscript{b}data are shown as mean (range); \textsuperscript{c}data are shown as range. NR: not reported; CT: computed tomography; PSMA: prostate-specific membrane antigen; $^{18}$F: fluorine-18; s.d.: standard deviation.
Characteristics of included studies

The characteristics and methodology assessment of individual studies included in the meta-analysis are described in Table 1. Briefly, seven prospective and ten retrospective studies were included. To ensure homogenous calibration between sites, all articles were approved by the Ethics Committee of each university or hospital. The patients from the included studies were consecutive enrolment. Besides, the data acquisition was based on the review of medical records in all these studies. Table 2 and 3 show the clinicopathologic features and PET characteristics of individual studies included in this meta-analysis. The number of PCa patients ranged from 10 to 251, with ages of 45–86 years. Median levels of PSA reported before 18F-PSMA PET/CT in all the included studies ranged between 0.03 ng ml\(^{-1}\) and 1481 ng ml\(^{-1}\). Of the total studies, only six studies reported the outcomes separately for primary staging and BCF; ten studies reported outcomes for BCF; and one study reported outcomes for primary staging. Besides, PET positivity was reported in all studies,\(^{15-28}\) with values ranging from 60% to 100% (overall, 82.8%).

Quality assessment

A total of 17 articles, enrolling 1019 patients, were identified and included in the analysis. According to the random-effects model, the DR of 18F-PSMA PET/CT was 0.83 (95% CI: 0.78–0.88) increase in the odds of the management of PCa (Figure 2a). Subsequently, the performance of 18F-PSMA PET/CT on the detection of PCa patients was compared with the DR of 18F-PSMA PET/CT based on Gleason scores and serum PSA level. The results of Gleason score showed that there was a statistically significant diagnostic value in two groups of PCa patients. According to the random-effects model, the DR of 18F-PSMA PET/CT on the detection of PCa patients was 0.57 for PSA <0.5 ng ml\(^{-1}\) and 0.83 for PSA ≥0.5 ng ml\(^{-1}\) (95% CI: 0.72–0.93; Figure 2b). Moreover, in the PCa patients with Gleason scores ≥7, the DR of 18F-PSMA PET/CT was 0.83 (95% CI: 0.78–0.88) increase in the management of PCa patients. In the subgroup analysis using serum PSA level, the DR of 18F-PSMA PET/CT prominently increased (OR: 0.89, 95% CI: 0.83–0.96) in the management of PCa patients with serum PSA level of PCa patients correlated with DR of 18F-PSMA PET/CT in the management of PCa.

DISCUSSION

In recent years, increased studies in cancer research have focused on the diagnosis of tumors, which includes but is not limited to serum biomarkers, tissue pathology examination, and imaging tools.\(^{9,10}\) It has emerged that the most ideal methods in the field of cancer screening should be specific, noninvasive, and convenient, especially at an early stage.\(^{9,10}\) Screening tools such as PSA, DRE, TRUS, CT, and MRI are significant in the clinical diagnosis and management of PCa.\(^{9,10,19}\) Previous studies have, however, found that morphologic imaging, such as TRUS and CT, is limited in terms of diagnostic value (management rate <5%), especially when the PSA levels are <20 ng ml\(^{-1}\) or the PSA velocity is <2 ng ml\(^{-1}\) per year. Their sensitivity to detecting local PCa relapse remains relatively low (25%–54%) and is only moderately improved with functional MRI techniques.\(^{40,41}\) Moreover, the sensitivity of CT and MRI for the management of lymph node metastases of PCa is reported to be 30%–80%.\(^{42}\) In view of the low sensitivity of morphologic imaging, there has been an urgent need to find more effective and reliable diagnostic methods to better manage primary/recurrence PCa.\(^{9,10,19}\) As a new method of staging and restaging PCa patients, recent studies have recommended 18F-PSMA PET/CT. This method has the potential to improve the management of approximately half of PCa patients.\(^{23-38}\) Elsewhere, studies have reported overexpression of PSMA in PCa tissue compared with normal tissue, which increased even further at advanced stage and grade of PCa.\(^{15,20}\) These findings suggest that PSMA is a novel and promising biomarker.\(^{5,20}\) Thus, this meta-analysis aimed to evaluate the DR of 18F-PSMA PET/CT in the management of patients with PCa.
Table 3: Patient characteristics of individual studies included in the meta-analysis

| Publication year | First author            | Patients (n) | Age (year) | PSA (ng ml\(^{-1}\)) | Clinical setting                  | PSMA-positive patients (n) | Gleason score ≥7 (%) | Gleason score, n/total | PSA (ng ml\(^{-1}\)), n/total |
|------------------|-------------------------|--------------|------------|-----------------------|----------------------------------|--------------------------|----------------------|------------------------|-----------------------------|
| 2020             | Dietlein et al.\(^{32}\) | 27           | NR         | NR                    | BCF                              | 23                       | NR                   | NA                     | NA                          |
| 2020             | Kuten et al.\(^{36}\)   | 16           | 56.0–72.0\(^{a}\) | 3.5–14.4\(^{a}\) | Primary staging/BCF              | 16                       | 87.5                 | 14/14                  | 2/2                         |
| 2020             | Witkowska-Patena et al.\(^{37}\) | 40           | 66.6±6.5\(^{b}\) | 0.7±0.6\(^{b}\)     | BCF                              | 24                       | 62.5                 | 16/30                  | 8/10                        |
| 2020             | Sachpekidis et al.\(^{38}\) | 25           | 66.0 (48.0–84.0)\(^{a}\) | 1.2 (0.2–237.3)\(^{a}\) | BCF                              | 15                       | 68.0                 | NA                     | NA                          |
| 2020             | Rowe et al.\(^{46}\)    | 31           | 63.0 (45.0–74.0)\(^{a}\) | 0.4 (0.2–28.3)\(^{a}\) | BCF                              | 21                       | NR                   | NA                     | NA                          |
| 2020             | Rowe et al.\(^{31}\)    | 15           | 65.8 (52.0–77.0)\(^{a}\) | 4.4 (0.2–224.5)\(^{a}\) | Primary staging/BCF              | 11                       | NR                   | NA                     | NA                          |
| 2020             | Rauscher et al.\(^{33}\) | 102          | 71.0±8.0\(^{b}\) | 0.87 (0.2–13.6)\(^{b}\) | BCF                              | 88                       | NR                   | NA                     | NA                          |
| 2020             | Dietlein et al.\(^{35}\) | 75           | 69.2±8.1\(^{b}\) | 0.5–14.9\(^{b}\)    | BCF                              | 56                       | NR                   | NA                     | NA                          |
| 2019             | Rousseau et al.\(^{34}\) | 130          | 69.1±6.5\(^{b}\) | 5.2±6.5\(^{b}\)     | BCF                              | 110                      | 86.2                 | NA                     | 3/5                         |
| 2019             | Giesel et al.\(^{24}\)  | 251          | 70.0 (48.0–86.0)\(^{a}\) | 10.9 (0.6–250.0)\(^{a}\) | Primary staging/BCF              | 204                      | 83.7                 | 106/139                | 72/83                        |
| 2018             | Rahbar et al.\(^{25}\)  | 100          | 68.7±7.6\(^{b}\) | 3.4±6.1\(^{b}\)    | BCF                              | 95                       | 71.0                 | 44/49                  | 26/28                       |
| 2018             | Rahbar et al.\(^{25}\)  | 40           | 68.7±8.1\(^{b}\) | 35.4 (0.03–939.0)\(^{b}\) | Primary staging/BCF              | 38                       | 60.0                 | NA                     | 6/8                         |
| 2018             | Giesel et al.\(^{24}\)  | 12           | 70.0 (54.0–79.0)\(^{a}\) | 0.60 (0.08–6.90)\(^{a}\) | BCF                              | 9                        | 91.6                 | 6/7                    | 3/5                         |
| 2018             | Giesel et al.\(^{27}\)  | 12           | 66.0 (54.0–82.0)\(^{a}\) | 85.0 (10.0–279.8)\(^{a}\) | Primary staging/BCF              | 12                       | 91.6                 | 6/6                    | 6/6                         |
| 2017             | Kesch et al.\(^{28}\)   | 10           | 67.0 (62.0–77.0)\(^{a}\) | 13.1 (5.8–58.0)\(^{a}\) | Primary staging/BCF              | 10                       | 100.0                | 3/3                    | 7/7                         |
| 2017             | Wondergem et al.\(^{29}\) | 65           | 62.0 (52.0–84.0)\(^{a}\) | 56.0 (0.1–1481.0)\(^{a}\) | Primary staging/BCF              | 59                       | 67.7                 | NA                     | NA                          |
| 2018             | Mena et al.\(^{30}\)    | 68           | 64.0 (51.0–74.0)\(^{a}\) | 4.4±7.3\(^{a}\)     | BCF                              | 41                       | NR                   | NA                     | 2/13                        |

\(^{a}\) Data are shown as range; \(^{b}\) data are shown as mean±s.d.; \(^{c}\) data are shown as median (range). NR: not reported; BCF: biochemical failure; PSA: prostate-specific antigen; PSMA: prostate-specific membrane antigen; NA: not available; s.d.: standard deviation
Recently, some studies have evaluated the clinicopathologic characteristics of 18F-PSMA PET/CT in the management of PCa. Nevertheless, the study’s outcomes remain inconsistent due to the relatively small sample size, the different ethnicities, and the possible limited effect of individual patient data in the 18F-PSMA PET/CT. The meta-analysis had explored the results of the DR of 18F-PSMA PET/CT in the management of biochemical recurrent PCa, but such studies remain unreliable due to the disparity between the individual studies involved. Limited research on 18F-PSMA PET/CT limits the comprehensive understanding of the disparity in the management of PCa based on Gleason scores and serum PSA level. The present study pooled data reported in various studies to explore the DR of 18F-PSMA PET/CT in the management of PCa.

According to the current meta-analysis findings, the DR of 18F-PSMA PET/CT significantly increased in patients with PCa. The meta-analysis could also provide the most comprehensive information about different subgroups. Results of the stratified analysis using Gleason scores (≤7 or ≥8), suggested that higher DR of 18F-PSMA PET/CT was found in PCa patients with Gleason scores ≥8. In addition, the DR of 18F-PSMA PET/CT in PCa increased with the increase in the serum PSA level.

The present meta-analysis was not without limitations. First, there were a limited number of studies and an insufficient number of PCa patients for the meta-analysis. Thus, the results were based on unadjusted estimates due to slight variations in the inclusion criteria for each individual patient. Second, many factors could affect the DR of 18F-PSMA PET/CT, such as reagent resources, tumor size, assay type, cutoff value, and the proficiency of a particular physician. These factors were, however, not considered in the subgroup analysis. Prospect studies should focus on exploring better diagnostic strategies for PCa. Third, there were no studies reporting on adverse events in 18F-PSMA PET/CT in all the included trials. As a result, additional exploration to determine adverse events should be prospected for and studied. In addition, the PET/CT scan may underestimate the burden of the recurrence of PCa patients with a PSA below 1.5 ng ml⁻¹ and a limited nodal tumor load. This may be so regardless of the tracer used.  

Figure 3: Forest plots showing the detection rate of 18F-labeled prostate-specific membrane antigen positron emission tomography/computed tomography for prostate cancer based on serum PSA level. (a) PSA <0.5 ng ml⁻¹; (b) 0.5 ng ml⁻¹ ≤ PSA <1.0 ng ml⁻¹; (c) 1.0 ng ml⁻¹ ≤ PSA <2.0 ng ml⁻¹; (d) PSA ≥2.0 ng ml⁻¹. PSA: prostate-specific antigen; 18F: fluorine-18; CI: confidence interval; ES: Elastic Search.
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