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Review

Clinical value of FDG PET or PET/CT in urinary bladder cancer: A systemic review and meta-analysis☆

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ABSTRACT

Aim: The purpose of the current study was to conduct a systemic review and meta-analysis of the published literature to evaluate the diagnostic accuracy of FDG PET or PET/CT in urinary bladder cancer.
Materials and methods: The authors conducted a systematic MEDLINE search of articles published between January 2000 and December 2010. Two reviewers independently assessed the methodological quality of each study. We conducted a meta-analysis of pooled sensitivity and specificity in detecting primary and metastatic lesions of bladder cancer.
Results: Six studies met the inclusion criteria. The pooled sensitivity and specificity of PET/CT for primary lesion detection of bladder cancer were 0.90 (95% CI: 0.70–0.99) and 1.00 (95% CI: 0.74–1.00), respectively. The pooled sensitivity and specificity of FDG PET or PET/CT for staging or restaging (metastatic lesions) of bladder cancer were 0.82 (95% CI: 0.72–0.89) and 0.89 (95% CI: 0.81–0.95), respectively.
Conclusion: The diagnostic accuracy of FDG PET or PET/CT is good in metastatic lesions of urinary bladder cancer. Due to the small number of patients and limited number of studies analyzed, the diagnostic capability of FDG PET or PET/CT in detection of primary bladder wall lesions could not be assessed.

Bladder carcinoma is the most frequent type of tumor of the urinary tract and is most prevalent in the fifth to seventh decade of life [1]. More than 90% of bladder cancers are transitional cell (urothelial) carcinomas, 5% are squamous cell carcinomas, and less than 2% are adenocarcinomas. Approximately 70% of bladder cancers present as superficial tumors, which tend to recur, and 30% present as muscle-invasive disease associated with a high risk of death from distant metastases [2]. Optimal therapy planning is dependent on accurate staging of the bladder tumor. For identification of patients with metastatic disease, current imaging techniques including sonography, computed tomography (CT) and magnetic resonance imaging (MRI) have not proven to be highly accurate [3–5].

Fluorine-18 2-fluoro-2-deoxy-D-glucose (F-18 FDG) positron emission tomography (PET) has become an important noninvasive imaging modality for many malignancies because of its unique capability to image metabolically active lesions [6–9].

However, there have been a limited number of reports on the utilization of FDG PET to image bladder cancer, mainly because the urinary excretion of FDG interferes with visualization of the primary bladder tumor and regional nodes. Furthermore, only a relatively small population of bladder cancer patients can be obtained for study. Thus, the purpose of the current study was to conduct a meta-analysis of the published literature to evaluate the diagnostic accuracy of FDG PET in urinary bladder cancer.

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Table 1
Criteria list used to assess the methodological quality of the studies.

Criteria of validity	Positive score
Internal validity	
Valid reference test	Pathology from biopsy or surgery
Blind measurement of FDG PET without knowledge of reference test	
Blind measurement of reference test without knowledge of FDG PET	
Avoidance of verification bias	Assessment by reference test independent of FDG PET results
FDG PET interpreted independently of all clinical information	Mentioned in publication
Prospective study	Mentioned in publication
External validity	
Spectrum of disease	All stage of disease
Demographic information	Age and sex information given
Inclusion criteria	Mentioned in publication
Exclusion criteria	Mentioned in publication
Avoidance of selection bias	Consecutive series of patients
Standard execution of FDG PET	Type of camera, dose FDG, time interval, reconstruction

FDG: F-18-fluorodeoxyglucose; and PET: positron emission tomography.

1. Materials and methods

1.1. Data search

A comprehensive computer search for relevant articles was conducted using the PubMed/MEDLINE and EBM Review search engines. The search strategy was based on the combination of the terms (1) PET, positron emission tomography; (2) FDG, fluorodeoxyglucose; and (3) bladder cancer. Searches were limited to the period between January 2000 and December 2010. Although no language restrictions were used initially, the full-text review and final analysis was limited to articles published in the English language. A manual search of additional studies was conducted using the references of the retrieved articles. Unpublished data and conference proceedings were not included. A total of 126 studies were retrieved from these searches for potential inclusion in the meta-analysis.

1.2. Data selection

Studies were eligible for inclusion based on the following criteria: (1) they evaluated bladder cancer for local detection/recurrence and/or staging/restaging and used (2) FDG PET and/or PET/CT imaging. Studies were excluded based on the following criteria: (1) included other types of urological cancer, (2) totals of true positives, false positives, true negatives, and false negatives were not provided, and (3) no data from a sub-analysis were provided. Unpublished data and conference proceedings were not included. Based on these criteria, 6 studies were eligible for inclusion in this meta-analysis.

1.3. Data extraction

Two reviewers independently assessed the methodological quality of the eligible studies. The criteria list recommended by the Cochrane Methods Working Group on Systematic Review of Screening and Diagnostic Tests was used [10]. Some items on the list were modified for this specific review. The complete criteria list used is presented in Table 1. Internal validity criteria (IV) were scored as "positive" (adequate methods), "negative" (inadequate methods, potential bias), or "unclear" if insufficient information had been provided on a specific item. External validity criteria (EV) were assessed to evaluate generalizability. Standard performance of FDG PET or PET/CT was scored as positive when the type of PET or PET/CT camera, the dose of FDG, the time between injection and scanning, and the method of reconstruction were described. The criteria for external validity were scored as positive if sufficient information was provided to judge generalizability of findings. After the consensus meeting, we decided to score unclear scores as negative. Disagreements were resolved by consensus. Quality scores were expressed as a percentage of the maximum score. Subtotals were calculated for internal (maximum 6) and external (maximum 6) validity separately.

1.4. Statistical analysis

Data on sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FDG PET or PET/CT in the detecting and/or staging/restaging of urinary bladder cancer were calculated from the original numbers given in the publications. We calculated the pooled and individual sensitivity, the specificity, and the 95% confidence interval for pooled estimators in forest plots. The pooled sensitivity and specificity estimators were weighted average in which the weight of each study is individual sample size. The sources of heterogeneity were included the pattern of observed study results and variation introduced by diagnostic threshold. If there is any evidence which was the diagnostic threshold varies between the studies, we should consider the summary receiver operating characteristic (SROC) curve. Testing of diagnostic threshold was Spearman's correlation test. In this study, the threshold effect did not exist but we also showed the SROC curve in figures which included values of Q^* index and AUC. There were two main areas of meta-analysis: detecting bladder cancer and staging/restaging of bladder cancer. However, there were not enough studies about detection of bladder cancer to make a meta-analysis. We report this result for reference only. The meta-analysis was conducted using free software Meta-DiSc (version 1.4).

2. Results

2.1. Literature search

A total of 126 studies about primary tumor detection, staging, tumor recurrence or restaging of bladder cancer with FDG PET or PET/CT were identified. After reviewing the titles and abstracts, 119 studies were excluded based on the criteria listed in Section 1.2. Of the remaining 7 studies, one was excluded after a full review because of differentiation from other types of urological tumor and bladder cancer [11]. Six studies met the inclusion criteria [12–17]. The characteristics of the included studies are presented in Table 2.

2.2. Methodological quality assessment

Methodological quality was assessed by 12 items for each of the 6 selected studies. The scores for internal and external validity of the 6 selected studies are presented in Table 3. All studies included