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Platinum Priority – Prostate Cancer

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18F-Fluoroethylcholine PET/CT Identifies Lymph Node Metastasis in Patients with Prostate-Specific Antigen Failure After Radical Prostatectomy but Underestimates Its Extent

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Abstract

Background: The detection of lymph node metastases (LNMs) is one of the biggest challenges in imaging in urology.
Objective: To evaluate the accuracy of combined 18F–fluoroethylcholine (FEC) positron emission tomography (PET)/computed tomography (CT) in the detection of LNMs in prostate cancer (PCa) patients with rising prostate-specific antigen (PSA) level after radical prostatectomy.
Design, settings, and participants: From June 2005 until November 2011, 56 PCa patients with biochemical recurrence after radical prostatectomy underwent bilateral pelvic and/or retroperitoneal lymphadenectomy based on a positive 18F-FEC PET/CT scan.
Outcome measurements and statistical analysis: The findings of PET/CT were compared with the histologic results.
Results and limitations: Median PSA value at the time of 18F-FEC PET/CT analysis was 6.0 ng/ml (interquartile range: 1.7–9.4 ng/ml). In 48 of 56 (85.7%) patients with positive 18F-FEC PET/CT findings, histologic examination confirmed the presence of PCa LNMs. Of 1149 lymph nodes that were removed and histologically evaluated, 282 (24.5%) harbored metastasis. The mean number of lymph nodes removed per surgical procedure was 21 (standard deviation: ±18.3). A lesion-based analysis yielded 18F-FEC PET/CT sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 39.7%, 95.8%, 75.7%, and 83.0%, respectively.

A site-based analysis yielded sensitivity, specificity, PPV, and NPV of 68.4%, 73.3%, 81.3%, and 57.9%, respectively. Patients with negative PET/CT did not undergo surgery, thus sensitivity, specificity, and negative predictive value on a patient basis could not be calculated.
Conclusions: A positive 18F-FEC PET/CT result correctly predicted the presence of LNM in the majority of PCa patients with biochemical failure after radical prostatectomy but did not allow for localization of all metastatic lymph nodes and therefore was not adequately accurate for the precise estimation of extent of nodal recurrence in these patients.

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1. Introduction

Radical prostatectomy (RP) provides excellent long-term outcomes for clinically localized prostate cancer (PCa) [1–3]. However, prostate-specific antigen (PSA) failure after RP occurs in about 40% of patients and is a clinical dilemma [1–3]. Undetected lymph node involvement at the time of first diagnosis of PCa is one reason for recurrence [4].

At present, no imaging modality can reliably detect lymph node metastasis (LNM). Generally, computed tomography (CT) shows disappointing results in the identification of metastatic lymph nodes [5,6]. Hybrid positron emission tomography (PET)/CT enables the visualization of metabolic to anatomic abnormalities and may help improve detection of LNMs. 11C-Choline PET/CT has shown promising results for restaging PCa [7–9]; however, it does not allow accurate detection of metastatic spread to small lymph nodes or micrometastases to normal size nodes. 11C-Choline has a short half-life of only 20 min, which limits its availability, and it needs to be synthesized onsite using a cyclotron [10]. Poulsen et al. studied the value of 18F–fluoroethylcholine (FEC) PET/CT for lymph node staging of PCa patients before curative treatment and reported superior results [11]. To our knowledge, the value of 18F-FEC PET/CT in detection of positive lymph nodes in radically treated PCa patients with PSA relapse has not been systematically assessed.

The aim of our study was to evaluate the accuracy of 18F-FEC PET/CT in detection of LNMs in these patients. To address this question, we compared the results from 18F-FEC PET/CT with the histologic data from secondary lymphadenectomy in 56 patients with a positive 18F-FEC PET/CT result.

2. Patients and methods

2.1. Patient selection and data collection

This study was approved by our institutional review board. The records of 56 patients with biochemical recurrence after RP and positive 18F-FEC PET/CT scan and who were treated with secondary, extended-field, bilateral pelvic lymphadenectomy or both pelvic and retroperitoneal lymphadenectomy between June 2005 and November 2011 were reviewed retrospectively. All patients were initially treated for localized PCa by RP and pelvic lymphadenectomy with curative intent. PSA failure after RP was defined as an increase in PSA level to >0.2 ng/ml. Included patients discontinued androgen deprivation therapy at least 4 wk before PET/CT scan. Salvage surgery was not offered as first-choice therapy but was regarded only as an experimental option for patients who refused medication treatment. Selection for salvage lymphadenectomy was based on fitness for surgery, biological age, and desire of the patient. None of the patients had bone metastases (verified by bone scan) or local recurrence.

2.2. Surgical procedure and histologic evaluation

The surgical field for pelvic lymphadenectomy included lymph nodes along the internal and external iliac vessels, the common iliac vessels, the presacral region, the aortocaval region up to the inferior mesenteric artery, and, if positive in PET/CT scan, the pararectal region. The lateral border of lymphadenectomy was the genitofemoral nerve. Retroperitoneal lymphadenectomy included removal of all lymphatic tissue along the abdominal great vessels from the origin of the iliac vessels to the cranial border of the upper renal pole. After lymphadenectomy, surgical specimens were processed according to standard pathology protocols. Lymph node analysis was performed by step sections (200-μm-thick slices) to detect micrometastases. Sections were stained with hematoxylin and eosin for histologic evaluation.

2.3. Integrated 18F-FEC PET/CT imaging

Whole-body PET scans extending from the base of the skull to the proximal femurs were acquired in three-dimensional mode (3 min per bed position) using a state-of-the-art PET/CT scanner (Philips Gemini; Koninklijke Philips Electronics N.V., Hamburg, Germany; and Biograph 64 TruePoint PET/CT; Siemens AG, Forchheim, Germany). Prior to the CT scan, 1.5 ml/kg body weight of iodiated contrast agent (Iopromide, Imeron 300; Bracco Diagnostics Inc, Milan, Italy) was intravenously administered at a flow rate of 2.5 ml/s. The acquisition of the CT scan (200–250 mA, 120 kV, 64 × 0.6 mm collimation, pitch 0.6) was initiated 50 s after the intravenous injection of contrast in the portalvenous phase. The emission sequence was initiated 60 min after intravenous injection of 18F-FEC. The mean radiochemical dose was 300 MBq, normalized to the patients' body weight. Directly prior to the PET/CT scan, patients were asked to empty their bladder to minimize tracer accumulation. Emission data were reconstructed with attenuation correction derived from the CT scan. Two board-certified nuclear medicine physicians and one board-certified radiologist trained in PET/CT interpretation, working side by side, evaluated the PET/CT images together using a dedicated software package (Syngo TrueD; Siemens AG, Forchheim, Germany). Significant choline uptake was not noted in nodes <5 mm in our patient population. The number of positive nodes on PET/CT was determined by reinterpretation of the PET/CT examinations, focusing on lymph nodes that were either >10 mm along the short axis or positive on PET. The number of nodes fulfilling one or both of these criteria was recorded and correlated with the number of lymph nodes resected in each individual patient, as well as in the entire patient cohort.

2.4. Statistical analysis

Means, medians, ranges, and frequencies were recorded as descriptive statistical parameters. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and number of correctly recognized cases of PET/CT in the detection of PCa LNMs were calculated in a patient-, lesion-, and site-based analysis. All statistical analyses were performed with SPSS v.17.0 (IBM Corp., Armonk, NY, USA).

3. Results

Patient characteristics are summarized in Table 1. Median PSA value at 18F-FEC PET/CT was 6.0 ng/ml (interquartile range [IQR]: 1.7–9.4 ng/ml). All 56 patients had a positive 18F-FEC PET/CT analysis after a history of RP for PCa and subsequently underwent secondary lymphadenectomy.

3.1. Patient-based analysis

In 48 of 56 (85.7%) patients with positive 18F-FEC PET/CT findings, histologic examination confirmed the presence of LNMs of PCa (Table 2). Six of the eight patients with