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Original Article

Clinical impact of ^{18}F-FDG PET in management of patients with renal cell carcinoma

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ABSTRACT

We performed a retrospective study to evaluate the accuracy, diagnostic validity, and clinical impact of ^{18}F-FDG PET in the management of recurrent and metastatic disease in patients with Renal Cell Carcinoma (RCC) from our database. ^{18}F-FDG PET studies were identified from 58 patients that matched our criteria for inclusion in the study. Results were confirmed with histopathological findings, clinical follow-up time (at least 12 months), and/ or conventional imaging methods (CIM).

A sensitivity of 80.56%, specificity 86.36%, diagnostic accuracy 58.7%, positive predictive value 90.63%, and a negative predictive value of 73.08% were observed.

The clinical impact was high in 25 cases (43%) and we found no impact in only 10 studies (17.2%). We concluded that ^{18}F-FDG PET was useful and had a high clinical impact in the management of recurrent and metastatic RCC. From our data, it seemed that a positive PET study was more helpful to the physician than a negative study.

Impacto clínico de la ^{18}F-FDG PET en el manejo de pacientes con carcinoma de células renales

Palabras clave:
Cáncer renal
Carcinoma de células renales
Impacto clínico
PET
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^{18}F-FDG PET

RESUMEN

Llevamos a cabo un estudio retrospectivo para evaluar la exactitud, validez diagnóstica e impacto clínico de la ^{18}F-FDG PET en el manejo de enfermedad metastásica y recurrente en pacientes con carcinoma de células renales (CCR) de nuestra base de datos. Se identificaron estudios ^{18}F-FDG PET de 58 pacientes que cumplían con nuestros criterios de inclusión en el estudio. Se confirmaron los resultados con los hallazgos histopatológicos, seguimiento clínico (al menos 12 meses) y/o métodos convencionales de imagen (MCI).

Se obtuvo una sensibilidad de 80,56%, especificidad 86,36%, exactitud dignóstica 58,7%, valor predictivo positivo 90,63%, y valor predictivo negativo 73.08%.

El impacto clínico fue elevado en 25 casos (43%) y no hubo impacto en sólo 10 estudios (17,2%). Concluimos que la ^{18}F-FDG PET es útil y que tiene elevado impacto clínico en el manejo de CCR metastático y recurrente. Basado en nuestros resultados, un estudio PET positivo fue de más ayuda al clínico que un estudio negativo en el manejo de estos pacientes.

Introduction

The prognosis of renal cell carcinoma (RCC) is generally good, with high survival rates.[1] After definitive (surgical) treatment, follow up is based on conventional imaging methods (CIM), predominantly on Computerized Tomography (CT) scan, which may at times be inconclusive. But, when we assess recurrent disease, CIM may have limitations due to post-treatment changes (inflammation, fibrosis, and other post-surgical changes).[2,3] ^{18}F-FDG PET (FDG PET) has been shown to be an efficient non-invasive technique in the initial diagnosis, staging, restaging, monitoring response to therapy, and in the early detection of disease in most cancer patients.[4–6] Currently, FDG PET is not considered the initial diagnostic imaging modality of choice in renal cell carcinoma patients, nor in the detection of recurrent disease in these patients.[7–9] A paucity of data makes it difficult to objectively evaluate the usefullness of this technique; however studies point at a likely complementary use of FDG PET in patients with RCC, specially in detection of metastases. Due to its limitations in detecting small sized lesions and those alterations that may be masked by urinary excretion, it seems to be less precise than other imaging procedures in the diagnosis of primary renal tumor. It may be possible to correct these limitations with the new PET/CT scanners.[10]

The aim of the study was to evaluate the accuracy, diagnostic validity, and clinical impact of ^{18}F-FDG PET in the management of recurrent and metastatic disease in patients with RCC.

Materials and methods

A transversal study was applied. Data collection was performed retrospectively from the database at Focuscan PET Institute, Madrid, Spain, from March 1997 to December 2005 to identify all patients with renal cell carcinoma (clear cell subtype)

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referred to our centre. Patients were identified retrospectively, finding the information during a review of patient charts, after their FDG PET studies were performed. The procedure was observational, not experimental.

Inclusion criteria were: (a) patients with a pathological diagnosis of renal cell carcinoma (clear cell subtype) and (b) FDG PET studies were confirmed with histopahtological findings with a clinical follow up time of at least 12 months or with conventional imaging methods (CIMs). Exclusion criteria were: (a) different histological subtype, (b) history of another type of primary cancer, and (c) non-diagnostic FDG PET studies.

Whole body ^{18}F-FDG PET studies, from skull base to thighs, were perfomed utilizing a dedicated PET camera (ADAC C-PET™ 250, Philips Medical Systems, Amsterdam, Netherlands).

Data were reconstructed with attenuation correction and iterative reconstruction to image format change group pictures. Guidelines published by the Society of Nuclear Medicine[11] were used as a reference for the assessment of these studies.

Patients fasted for at least 6 h before intravenous administration of 2.5 MBq/kg ^{18}F-FDG. They were routinely administered a dose of 10 mg diazepam (Valium, Roche, Seoul, Korea) orally to reduce uptake of skeletal muscles.

Patients were asked to drink at least 0.5 l of water to reduce artifacts. Blood glucose levels were lower than 120 mg/dl in all patients. After injection the patients were in mental and physical rest (supine and semi-darkness) for at least 45 min. Images of full body emission and transmission between 45 and 90 min after administration of ^{18}F-FDG were adquired.

Two investigators evaluated all the scans nuclear medicine specialists, experts in PET, and not blinded to the clinical information of the patients or to the results of the complementary diagnostic methods. They discussed the results of the ^{18}F-FDG PET studies when non-congruent, to come to a consensous on the case. Images were inspected visually with semiquantitative evaluations of the regions of interest, measuring the SUVmax (standardized uptake value).

In our study, focal FDG uptake that did not correspond to normal physiological uptake or physiologic elimination of FDG was suggestive of malignancy when the SUVmax was higher than approximately 2.5–3.0. This finding is consistent with published literature in differentiating benign from malignant lesions, where an SUV cut-off of 2.5–3.0 was best seen to correlate with malignancy.[12,13]

Clinical histories and disease course of the patients was obtained from referring physicians. A scan was considered true—positive (TP) when FDG PET suggested the location of malignacy and was subsequently confirmed. Whereas false—positive (FP) was considered when a PET positive location was not confirmed subsequently. The sites suggested by FDG PET were confirmed with histopathologic analysis of tissue obtained by biopsy or surgery, considered as the gold standard; however, imaging procedures or clinical follow-up of 12 months were accepted if no histopathologic confirmation could be obtained. If other lesions were not detected in the absence of an FDG PET localization of malignacy, it was considered to be true -negative (TN). It was considered false -negative (FN) if the malignancy was identified subsequently with a negative FDG PET study.

For the evaluation of the clinical impact in the management of these patients, a questionnaire was sent to referring doctors (Fig. 1). questionnaire was administered by: 1) direct personal contact with doctors, 2) via a phone conversation 3) e-mail or mail, and 4) via clinical histories. Data was collected and tabulated into an Excel (Office XP) spreadsheet.

FDG PET scans' ability to differentiate patients with or without disease was determined: sensitivity, specificity, and likelihood ratio. We also calculated prevalence, pre- and post-test odds, positive and negative post-test probabilities, and recurrent disease dectection proportion.[14–16]

The clinical impact of FDG PET was evaluated utilizing Hicks et al.[17,18] criteria—high, moderate, low, and no impact (Table 1).

Finally, the contribution of FDG PET to the patient management process was assessed according to the model described by Fryback and Thornbury[19,20](Fig. 2), utilizing the data from the questionnaires administered to the referring doctors. This model consists of a hierarchic model of efficacy with 6 levels of efficacy: technical efficacy (level 1), diagnostic accuracy efficacy (level 2), diagnostic thinking efficacy (level 3), therapeutic efficacy (level 4), patient outcome efficacy (level 5), and social efficacy (level 6). Reaching a higher level in the hierarchy means that its efficacy is demonstrated at lower levels, but the reverse is not true.

From March 1999 until December 2005, 91 patients from hospitals throughout Spain were referred for an ^{18}F-FDG PET study at the Institute PET-Focuscan of Madrid, for detection of the management of recurrent or metastatic disease; 33 patients were excluded from the study, with 29 of 33 for presenting with a histological subtype different from RCC (clear cell type) and 4 for impossibilty of confirmation of PET results (not enough information on the clinical notes). Finally, we ended up with 58 patients in our study. All remitted for detection of recurrent or metastasic disease after total nephrectomy (Fig. 3).

FDG PET studies were performed in 58 patients, 42 males (74.6%) and 16 females (25.4%), with ages ranging from 20 to 79 years, with an average age of 62.8 years.

FDG PET findings were confirmed with histophatological results, clinical follow-up time (at least 12 months), and conventional imaging methods (CIM), utilizing CT scans in the vast majority of cases. Follow-up time was considered from the FDG PET study to last medical revision/contact or patient death.

Histophatological confirmation was obtained in 17 cases (29.3%). In one case, we confirmed the PET findings with a clinical follow-up time of 15 months (October 2004–January 2006). And in 40 cases (69.0%), we confirmed the FDG PET results with multiple conventional imaging methods: CT scan, MRI, and bone scan (Fig. 4a).

Results

Thirty-two FDG PET studies, of a total of 58 studies, had a positive result (55.2%), and the 26 remaining studies were negative (44.8%). FDG PET scans showed possible tumor involvement in the following locations: 12 cases of recurrences in the osseous structures, 8 presented lymph node involvement, and 7 cases of pulmonary disease; 6 cases presented with recurrence in the post-nephrectomy bed, 5 studies demonstrated liver involvement, 2 cases of cerebral cortical disease were detected, 1 case of colonic disease, and one case of adrenal gland involvement was seen.

After confirmation on histopathology, 1 year clinical follow-up, or imaging, FDG PET results were TP (true positive) in 29 patients, and FP (false positive) findings in 3 patients. The results were TN in 19 patients and FN in 7 patients (Table 2a). False positive results were confirmed with conventional imaging methods (CIM), mainly on CT scan, and one of them with histopathological findings on colonoscopic biopsy (second tumor). All 7 false negative results were confirmed with conventional imaging methods, and in 3 of these 7 cases, also with histopathological findings. FDG PET was not sensitive for the detection of lymph node, bone, and post-surgical renal bed disease (one patient had lymph node and post-surgical renal bed involvement). In a patient with suspicion of multiple