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Original Article

^{18}F-FDG PET/CT and sentinel lymph node biopsy in the staging of patients with cervical and endometrial cancer. Role of dual-time-point imaging☆

M. Mayoral[a,*,1], P. Paredes[a,b,1], B. Domènech[a], P. Fusté[c], S. Vidal-Sicart[a,b], A. Tapias[a], A. Torné[b,c], J. Pahisa[b,c], J. Ordi[d,e], F. Pons[a,b], F. Lomeña[a,b]

[a] *Nuclear Medicine Department, Hospital Clínic, Barcelona, Spain*
[b] *Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain*
[c] *Clinic Institute of Gynaecology, Obstetrics and Neonatology, Hospital Clinic, Barcelona, Spain*
[d] *Pathology Department, Hospital Clinic, Barcelona, Spain*
[e] *CRESIB (Centre de Recerca en Salut Internacional de Barcelona), Hospital Clinic, Barcelona, Spain*

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ABSTRACT

Objective: Definitive staging for cervical (CC) and endometrial cancer (EC) takes place once surgery is performed. The aim of this study was to evaluate the role of PET/CT in detecting lymphatic metastasis in patients with CC and EC using dual-time-point imaging (DPI), taking the histopathological results of sentinel lymph node (SLN) and lymphadenectomy as the reference.
Material and methods: A prospective study was conducted on 17 patients with early CC, and 13 patients with high-risk EC. The patients had a pre-operative PET/CT, MRI, SLN detection, and lymphadenectomy, when indicated. PET/CT findings were compared with histopathological results.
Results: In the pathology study, 4 patients with CC and 4 patients with EC had lymphatic metastasis. PET/CT showed hypermetabolic nodes in 1 patient with CC, and 5 with EC. Four of these had metastasis, one detected in the SLN biopsy. Four patients who had negative PET/CT had micrometastasis in the SLN biopsy, 1 patient with additional lymph nodes involvement. The overall patient-based sensitivity, specificity, positive and negative predictive values, and accuracy of PET/CT to detect lymphatic metastasis was 20.0%, 100.0%, 100.0%, 87.9%, and 88.2%, respectively, in CC, and 57.1%, 88.9%, 66.7%, 84.2% and 80.0%, respectively, in EC. DPI showed higher retention index in malignant than in inflammatory nodes, although no statistically significant differences were found.
Conclusions: PET/CT has low sensitivity in lymph node staging of CC and EC, owing to the lack of detection of micrometastasis. Thus, PET/CT cannot replace SLN biopsy. Although no statistically significant differences were found, DPI may help to differentiate between inflammatory and malignant nodes.

PET/TC con ^{18}F-FDG y biopsia del ganglio centinela en la estadificación de pacientes con cáncer de cérvix y endometrio. Utilidad de la imagen dual-time-point

Palabras clave:
Cáncer de cérvix
Cáncer de endometrio
PET/TC
Ganglio centinela
Imagen dual-time-point

RESUMEN

Objetivo: La estadificación definitiva del cáncer de cérvix (CC) y de endometrio (CE) tiene lugar tras la cirugía. Nuestro objetivo fue evaluar la utilidad de la PET/TC para la detección de metástasis ganglionares en el CC y en el CE con imagen *dual-time-point* (DPI), considerando como *gold standard* la histopatología del ganglio centinela (GC) y la linfadenectomía.
Material y métodos: Diecisiete pacientes con CC inicial y 13 con CE de alto riesgo fueron incluidas prospectivamente. Preoperatoriamente se realizó una PET/TC, RM, detección del GC y linfadenectomía en los casos indicados. Se comparó la PET/TC con la histopatología.
Resultados: En el estudio anatomopatológico, 4 pacientes con CC y 4 con CE tuvieron metástasis ganglionares. La PET/TC mostró ganglios hipermetabólicos en una paciente con CC y en 5 con CE. Cuatro de ellas tenían metástasis, una detectada en el GC. Cuatro pacientes con PET/TC negativa presentaron

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* Corresponding author.
E-mail address: mmayoral@clinic.ub.es (M. Mayoral).
[1] These authors contributed equally to this work.

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micrometástasis en el GC, una paciente con ganglios adicionales infiltrados. La sensibilidad, especificidad, valor predictivo positivo y negativo y la exactitud diagnóstica de la PET/TC para detectar metástasis ganglionares fueron 20,0; 100,0; 100,0; 87,9 y 88,2% para el CC, y 57,1; 88,9; 66,7; 84,2 y 80,0% para el CE. La DPI mostró un índice de retención superior en ganglios infiltrados respecto a los inflamatorios, sin hallar diferencias estadísticamente significativas.

Conclusiones: La PET/TC tiene baja sensibilidad para estadificar el CC y CE por la incapacidad de detectar micrometástasis y, por tanto, no sustituye la detección del GC. Aunque no hubo diferencias estadísticamente significativas, la DPI podría ayudar a diferenciar ganglios inflamatorios de tumorales.

Introduction

Cervical (CC) and endometrial cancer (EC) are the leading gynaecological malignancies after breast cancer. CC is the fourth most common and death-related female cancer worldwide.[1] The main prognostic factor in early stages is the presence of pelvic lymph node metastasis[2] and the state of para-aortical lymph nodes is an important predictor of relapse.[3] The five-year survival rates for patients with no lymph node involvement is 90–95% whereas in patients with pelvic and para-aortical metastatic lymph nodes is 50% and 20–30%, respectively.[4,5] EC is the most common female genital malignancy in developed countries.[1] The main prognostic factors include grade III tumour, deep myometrial invasion, cervical stromal involvement, as well as lymph node metastasis.[6,7] The presence of pathological pelvic and para-aortical lymph nodes entails a worse prognosis, with a five-year survival rate between 44% and 52%.[8]

Surgical staging of lymph nodes is the gold standard to determine lymphatic involvement in CC and high-risk EC. Minimally invasive surgery offers the possibility to perform surgical staging by laparoscopic approach. Treatment strategies may vary in the case of lymph nodes metastasis in both types of cancer. In stage IA1 CC without lymphovascular invasion it is indicated to perform a hysterectomy without lymphadenectomy. In stages IA2-IB1, it is recommended to perform a pelvic lymphadenectomy. Chemoradiotherapy is indicated in the case of lymph node involvement. In high-risk EC the mainstay of treatment is radical hysterectomy and bilateral anexectomy. The histopathological study of the lymphadenectomy specimen enables adjuvant treatment planning with chemotherapy and/or radiotherapy.[9]

However, the benefit of lymphadenectomy is controversial since 80% of women with early CC and EC turn out to have negative lymph nodes.[10,11] The sentinel lymph node (SLN) biopsy has the potential of limiting lymphadenectomy and thus, its morbidity, only to the reduced group of patients with metastatic lymph nodes. This technique is widely used in CC although it is still in the validation phase in some centres for EC.

In this scenario, different imaging modalities have been used to study the presence of lymph node metastasis by non-invasive approach. Magnetic resonance imaging (MRI) is the imaging modality used in the initial work-up to study the primary tumour and pelvic lymph node involvement.[12] The main criterion to consider a lymph node as metastatic by anatomical imaging is the short-axis size.[13] However, this approach is of limited value considering that metabolic changes precede morphologic changes in metastatic lesions. In the recent years, functional imaging has developed in an attempt to detect metastatic disease in early stages. Diffusion weighted imaging sequences has increased the sensitivity of MRI for metastatic lesions in gynaecological malignancies.[14] Some studies have also evaluated the role of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computed tomography (CT) in this group of patients.[15–18] PET/CT has proven to be superior to conventional imaging modalities to detect lymph node metastasis in CC and EC.[19] Furthermore, the diagnostic accuracy of PET/CT can be increased by performing dual-point imaging (DPI).[20,21] However, there is scarce evidence of its usefulness in female genital cancers.[15,22,23]

Taking into account the above conditions, the aim of this study was to evaluate the diagnostic performance of PET/CT in the detection of lymph node metastasis in patients with early CC and high-risk EC, with the additional information of DPI, considering as gold standard the histopathological results of SLN biopsy or lymphadenectomy, when performed.

Materials and methods

Patient population

This prospective study was approved by the hospital Ethics Committee and written informed consent was obtained from all patients. Patients with early CC and high-grade EC eligible for SLN detection at our centre during the time period comprised between June 2011 and January 2013 were consecutively enrolled.

The inclusion criteria for patients with CC were International Federation of Gynecology and Obstetrics (FIGO) stage IA1 with lymphovascular invasion, IA2 and IB1. The inclusion criteria for patients with EC were high risk tumours defined as myometrial invasion greater than 50%, histological subtypes serous papillary, clear cell or carcinosarcoma, and high nuclear grade (G3).

The exclusion criteria were: (1) patients with suspected extrauterine involvement, (2) pathological pelvic or para-aortic lymph nodes on other imaging modalities, (3) previous history of surgery or radiotherapy to nodal areas under study, and (4) contraindication for surgical treatment (due to age or comorbidities).

Patients underwent preoperative PET/CT, MRI and lymphoscintigraphy, SLN detection, the standardized surgical procedure and adjuvant treatment when indicated.

PET/CT technique and image interpretation

Patients were required to fast for 6 h prior to PET/CT scanning to achieve blood glucose concentrations below 140 mg/dL. Images were obtained from the skull base to the proximal third thigh 1 h after ^{18}F-FDG intravenous administration of about 4 MBq/kg, using PET/CT Biograph equipment (Siemens, Erlangen, Germany). A iodine-based oral contrast agent was used. DPI was also acquired 3 h after radiopharmaceutical injection. Time per bed was 5 min for both early images and DPI. The mean time interval between the PET/CT date and the surgery date was 4.4 days (standard deviation 5.7 days).

PET/CT images were assessed by two experienced nuclear medicine physicians using a commercial workstation (syngo.PET&CT Oncology VA20A, Siemens). Any discrepancy in observer assessment was resolved by consensus. Spherical regions of interest were placed over the pathological uptakes on PET/CT images to obtain the maximum Standardized Uptake Value (SUV_{max}). In the early images, lymph nodes were considered