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Use of ^{18}F-FDG PET/CT in the preoperative evaluation of patients diagnosed with peritoneal carcinomatosis of ovarian origin, candidates to cytoreduction and hipec. A pending issue

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ABSTRACT

Purpose: To evaluate the clinical usefulness of the results obtained with ^{18}F-FDG PET/CT in relation to CT in the preoperative staging of patients with peritoneal carcinomatosis secondary to primary or recurrent ovarian cancer candidates to cytoreductive surgery and hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC).
Material and methods: A retrospective study comparing the results obtained with CT and ^{18}F-FDG PET/CT in the preoperative evaluation of a series of 59 patients was performed. In all patients the peritoneal carcinomatosis index (PCI) was determined by preoperative radiological CT and 18F-FDG PET/CT and compared with surgical PCI, which was considered as reference.
Results: Of the 59 patients studied, in 55 peritoneal carcinomatosis presences were confirmed (4 patients had complete responses to neoadjuvant chemotherapy). The mean surgical, CT and 18F-FDG PET/CT PCI was 9.46 ± 7.70, 3.69 ± 3.96 and 2.25 ± 1.02, respectively. In the global disease detection, CT showed a higher positive likelihood ratio (LR+) than ^{18}F-FDG PET/CT (15.3, 95% CI 8.35–28.04 vs. 3.47, 95% CI 3.36–5.11) and a lower negative likelihood ratio (LR-) than 18F-FDG PET/CT (0.67, 95% CI 0.61–0.73 vs. 0.82, 95% CI 0.76–0.88). In every region of the abdomen the CT showed a greater LR+ than 18F-FDG PET/CT and a lower LR- than 18F-FDG PET/CT.
Conclusions: CT showed the best diagnostic results compared to ^{18}F-FDG PET/CT to confirme the presence of peritoneal disease. The lower performance of the ^{18}F-FDG PET/CT suggests that the main utility of ^{18}F-FDG PET/CT is to evaluate a possible metastatic extraperitoneal spread of the disease.

1. Introduction

Ovarian cancer (OC) is the fifth leading cause of cancer death in women worldwide and the leading cause of gynecologic cancer mortality [1]. Unfortunately, most patients are diagnosed at an advanced stage of the disease (stages III–IV of the International Federation of Gynecology and Obstetrics, FIGO) with peritoneal carcinomatosis (PC) [2], and the percentage of recurrence in these patients during follow up is higher than 50%.

The extent and volume of the PC is one of the most significant prognostic indicators [3] and the preoperative detection and quantification of PC is crucial in planning the treatment algorithm, especially for the design of the surgical approach. The gold standard for quantification of the PC is surgical exploration and the laparoscopy is a less invasive procedure than laparotomy [4].

To date, no non-invasive diagnostic test shown to be superior to exploratory laparoscopy-laparotomy [5]. Several imaging techniques have been used for the preoperative detection and evaluation in these patients [6]. Computed tomography scan (CT) is able to give accurate clinical information about the peritoneal implants and it is currently considered the imaging modality of choice in the detection of PC [7]. In recent years the development of positron emission tomography with 18-fluorodeoxyglucose tracer (^{18}F-FDG PET) has revolutionized the diagnostic imaging of cancer. The evalu-

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ation of the peritoneal disease, although it is very sensitive in terms of tracer uptake, the interpretation may be hampered by the very physiologic uptake and intestinal activity, in addition to the characteristics of the disease. The combination of ^{18}F FDG PET and CT (^{18}F-FDG PET/CT) allows an improvement in the anatomical localization of intra- and extra-pelvic structures and their relationship with ^{18}F FDG uptake can provide more reliable data regarding the nature of the pathological findings.

The objective of this study is to evaluate the clinical usefulness of the results obtained with ^{18}F FDG PET/CT in relation to CT in the preoperative evaluation of the peritoneal disease in patients with suspected PC of ovarian origin candidates to cytoreduction and hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC).

2. Material and methods

2.1. Patient selection

This study included a series of patients with diagnosis of primary (FIGO stages III-C/IV) or recurrent (platinum-sensitive) OC intervened between January 2008 and May 2014. Only those patients who had an ^{18}F FDG PET/CT in addition to preoperative CT staging were selected. The time interval between the completion of the imaging testing and surgery was less than 6 weeks. A written informed consent for the realization of ^{18}F FDG PET/CT, CT and surgery was obtained in all cases. The surgery performed consisted of a radical surgery with peritonectomy procedures and HIPEC administration [8,9].

2.2. Evaluation of peritoneal disease (Peritoneal carcinomatosis index)

Peritoneal carcinomatosis index (PCI), obtained during surgery, was used as a reference parameter for comparison of the preoperative findings described in both imaging tests. The PCI classifies the distribution of the disease according to lesion size and location, after the division of the abdominal cavity in 13 regions. In each region the size of the largest tumor implant was considered: LSS-0, no macroscopic disease; LSS-1 disease <0.5 cm; LSS-2 disease between 0.5–5 cm; LSS-3 disease >5 cm or confluent implants. The sum of the scores in each region (ranging between 1 and 39) determines the final PCI value [10].

2.3. CT images protocol

CT was performed following standard procedure. Contrast-enhanced scans were obtained from the base of the lungs to the pubic symphysis at 120 kV (peak), 140 mA, and 0.3 s for a tube rotation and a pitch of 0.8. Contrast-enhanced images were performed after IV administration of 130 mL of contrast medium at a flow rate of 3 mL/s, 30 min after introduction of 450 mL of oral contrast. The thickness of the reconstruction was 3 mm. The exploration of the neck, chest, abdomen and pelvis was initiated at 45 s, 75 s and 90 s, respectively, after the injection.

2.4. ^{18}F-FDG PET/CT images protocol

Imaging acquisitions were performed on an integrated PET/CT system (Gemini GXL-Philips), which includes a 3D PET and a 16-slice CT for attenuation correction and anatomical localization. All patients had fasted for at least 6 h and their blood glucose levels were within the normal range, prior to intravenous injection of 370 MBq of ^{18}F FDG. Data acquisition was performed within 60–90 min after injection, with patients maintaining their arms above their head to reduce beam-hardening artifacts. The procedure for data acquisition was as follows: CT scanning was performed first, without using oral or intravenous contrast agents, from the base of the skull to the upper thighs, with 120 kV, 100 mA and a 5 mm section thickness. Immediately after CT scanning, a PET emission scan that covered the identical transverse field of view was obtained, with 3 min acquisition time per bed position. PET image data sets were reconstructed iteratively by applying the CT data, and the reconstructed PET, CT and fused images were displayed on a multimodality workstation. Images interpretation was carried out through qualitative (visual) and semi-quantitative analysis using the Standardized Uptake Value (SUV), and mean ± SD of maximum-pixel SUV (SUVmax) of the lesions were calculated.

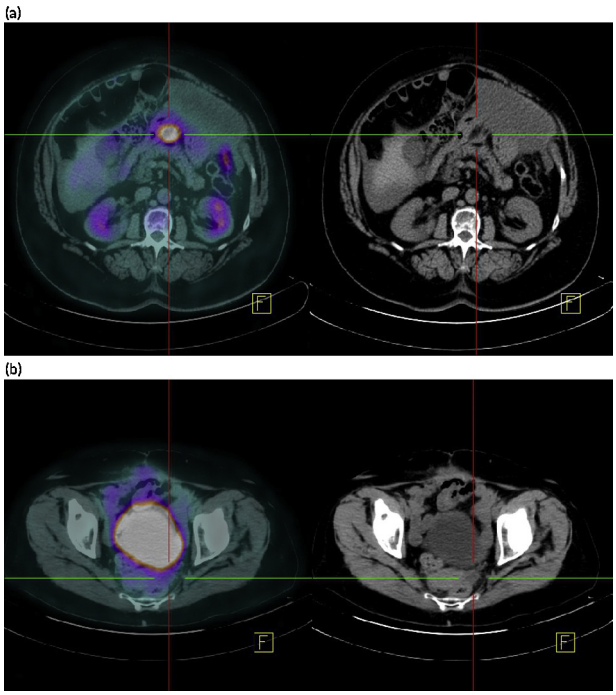

Fig. 1. Image suggestive of malignancy in ^{18}F FDG PET/CT that is not correlated with malignancy in CT (a). Image suggestive of malignancy in CT that is not correlated with malignancy in ^{18}F FDG PET/CT (b).

Peritoneal tumor was suspected on ^{18}F FDG PET/TC if they demonstrated a peritoneal nodular focal uptake, an irregularly distributed spotty uptake in the abdomen or pelvis, uniform diffuse ^{18}F FDG uptake in the greater omentum or mesenteric surface obscuring visceral outlines, and nodular or curvilinear uptake along the liver or in the left subphrenic space.

Abnormalities on CT with high suspicion of malignancy even in the absence of pathological uptake of ^{18}F FDG, and increased abnormal uptake of 18F-FDG with a high suspicion of malignancy even in the absence of a corresponding abnormality on CT were also described as peritoneal disease.

2.5. Image analysis and calculation of the radiological PCI

The images of ^{18}F FDG PET/CT and CT were reevaluated by a second independant nuclear medicine specialist and a second radiologist, both with over 15 years of experience, and different from those who carried out the initial assessment. These evaluators were unaware of the intraoperative findings as well as the description of the images previously performed by surgeons who treated the disease. In a second stage a stratified analysis was performed, considering four anatomical regions: upper region (1-3 areas), middle region (8-0-4 areas), lower region (5-6-7 areas) and small intestine (9-12 areas) (Fig. 1).