

Original Article

¹⁸F-FDG PET/CT, cytoreductive surgery and intraperitoneal chemohyperthermia for the therapeutic management in peritoneal carcinomatosis: A pilot study

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ARTICLE INFO

Article history:

Received 9 October 2015

Accepted 3 January 2016

Available online 19 February 2016

Keywords:

Peritoneal carcinomatosis
[(18)F]fluoro-2-deoxy-D-glucose Positron Emission Tomography/Computed Tomography
Cytoreductive surgery
Hyperthermic antitumoral peritoneal perfusion
Intraperitoneal chemohyperthermia

ABSTRACT

Aim: Peritoneal carcinomatosis is a common evolution of neoplasms and the terminal stage of disease. A new therapeutic technique, based on the total surgical removal of peritoneal lesions (peritonectomy procedure – PP) combined with the intraperitoneal chemohyperthermia (IPCH), has been developed. Proper patient selection is mandatory for optimizing the results of treatment. The aim of this study was to investigate the role of [(18)F]fluoro-2-deoxy-D-glucose Positron Emission Tomography/Computed Tomography (¹⁸F-FDG PET/CT) in patients with peritoneal carcinomatosis selected to undergo PP and IPCH. Furthermore, we aimed to identify characteristic patterns of abdominal ¹⁸F-FDG uptake and to correlate these patterns with available anatomic findings after surgery.

Methods: Patients with either histologically confirmed peritoneal carcinomatosis or suspected upon clinical follow-up and/or imaging findings were prospectively submitted to pre-surgery ¹⁸F-FDG PET/CT scan. Only those patients without evidence of extra-peritoneal metastases at PET/CT scan were treated with PP and IPCH.

Results: 11 patients with peritoneal carcinomatosis (5 colorectal, 4 ovarian, 1 pancreatic) and 1 unknown primitive cancer, were eligible for the study. In all cases PET/CT scan showed multiple peritoneal implants. In 6 out of 11 cases (54%) metastases were evidenced by ¹⁸F-FDG PET/CT: 2 cases with liver metastases; 1 case with bone metastases; 3 patients with lymph-node lesions. Two distinct imaging patterns, with focal or diffuse increased ¹⁸F-FDG uptake, were recognized.

Conclusions: PP + IPCH of patients selected by ¹⁸F-FDG PET/CT seems to be safe and feasible. PET/CT scan appears as a reliable tool for the detection, characterization of peritoneal implants with potential impact in the therapeutic management of these patients.

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¹⁸F-FDG PET/CT, cirugía citoreductora y quimiohipertermia intraperitoneal para el tratamiento terapéutico de la carcinomatosis peritoneal: estudio piloto

RESUMEN

Palabras clave:

Carcinomatosis peritoneal
Tomografía computarizada/tomografía de emisión de positrones con [(18)F]fluoro-2-deoxy-D-glucosa (¹⁸F-FDG PET/CT)
Cirugía citoreductora
Perfusión hipérmica antitumoral peritoneal
Quimiohipertermia intraperitoneal

Objetivo: La carcinomatosis peritoneal es una evolución común de las neoplasias y constituye el estadio terminal de la enfermedad. Se ha desarrollado una nueva técnica, basada en la extirpación quirúrgica de las lesiones peritoneales (procedimiento de peritonectomía – PP), combinada con quimiohipertermia intraperitoneal (IPCH). La adecuada selección de los pacientes es primordial, a fin de optimizar los resultados del tratamiento. El objetivo de este estudio fue investigar el papel de la tomografía de emisión de positrones con [(18)F]fluoro-2-deoxy-D-glucosa/tomografía computarizada (¹⁸F-FDG PET/CT) en pacientes con carcinomatosis peritoneal, seleccionados para someterse a PP e IPCH. Además, tratamos de identificar los patrones característicos de la captación abdominal de ¹⁸F-FDG y correlacionar dichos patrones con los hallazgos anatómicos disponibles tras la cirugía.

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Métodos: Se realizaron exámenes ^{18}F -FDG PET/TC de manera prospectiva, y previamente a la cirugía, a los pacientes con carcinomatosis peritoneal histológicamente confirmada, o sospechada mediante seguimiento clínico y/o hallazgos de imagen. Solo puede tratarse con PP y IPCH a aquellos pacientes que no reflejen evidencia de metástasis extraperitoneales en los exámenes PET/TC.

Resultados: Se seleccionó para el estudio a 11 pacientes con carcinomatosis peritoneal (5 colorrectales, 4 ováricas, una pancreática) y un cáncer primitivo desconocido. En todos los casos, el examen PET/TC reflejó múltiples implantes peritoneales. En 6 de los 11 casos (54%) las metástasis fueron evidenciadas mediante ^{18}F -FDG PET/TC: 2 casos con metástasis hepáticas, un caso con metástasis óseas, y 3 pacientes con lesiones ganglionares. Se reconocieron 2 patrones de imagen distintos, con aumento de captación focal o difusa de ^{18}F -FDG.

Conclusiones: La combinación PP + IPCH de los pacientes seleccionados mediante ^{18}F -FDG PET/TC parece ser una técnica segura y factible. La PET/TC se revela como una herramienta fiable para la detección y caracterización de los implantes peritoneales, con un impacto potencial sobre el tratamiento terapéutico de dichos pacientes.

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Introduction

Peritoneal carcinomatosis is a common evolution of many abdominal or extra-abdominal malignancies and represents the terminal stage of disease, as most patients die within 6 months.¹ It has a high rate of lymph nodes involvement and/or distant metastases to multiple sites, that may remain unknown on structural imaging at the time of diagnosis.² Cytoreductive surgery (CRS), whenever possible, followed by systemic intravenous chemotherapy is the current standard treatment for disease confined to peritoneal cavity.³

Multiple drug combinations are typically highly toxic,⁴ and have yielded little consistent demonstrable benefit with major studies reporting median survival rate of 12 months. Intraperitoneal administration of agents is attractive, but drug distribution, response rates and durability are variable and multiple treatments are required.⁵ A combined surgical technique aiming for the total removal of parietal and visceral peritoneal lesions (peritonectomy procedure, PP) and to the administration of peritoneal cavity with chemo-drugs in hyperthermia (intraperitoneal chemotherapy hyperthermia – IPCH) has been developed and seems to be a promising treatment. This ultraradical locoregional therapy combines complete cytoreduction of macroscopic peritoneal disease and perioperative intraperitoneal perfusion with a chemotherapeutic drug heated from 42 to 44 °C to treat microscopic residual disease.⁶ In order to achieve a successful management, combining the diagnostic effort with a rational treatment, it is mandatory to select favorable subsets of malignancies that may benefit from locoregional treatment, in patients with a good performance status.⁵ Assessment for valid clinical judgments include cancer histopathology (invasive vs expansive progression), total-body imaging excluding the presence of distant disease, preoperative abdominal and pelvic computed tomography (CT), the peritoneal cancer index (PCI) and the completeness of cytoreduction score.¹ Peritoneal carcinomatosis can be difficult to diagnose, because of the limited sensitivity and specificity of conventional tools such as CT or magnetic resonance imaging (MRI) in detecting the peritoneal implants.⁷ Moreover peritoneal biopsy and lavage are often subject to problems of sampling error, thus a reliable diagnosis may remain elusive in some patients. Furthermore, due to the insensitiveness of morphologic imaging, all neoplasms with peritoneal dissemination are typically understaged by current radiologic tests (CT, MRI).⁸ Positron emission tomography with [(18)F]fluoro-2-deoxy-D-glucose/computed tomography (^{18}F -FDG PET/CT) has remarkably improved the management of cancer patients and is increasingly applied in the staging and restaging of tumors.^{9–11} The CT component of this combined system may offer an approach improving the correct localization and characterization of ^{18}F -FDG uptakes.

The purpose of this prospective study was to investigate the potential value of ^{18}F -FDG PET/CT in the management of patients with peritoneal carcinomatosis eligible for PP associated with IPCH. Our secondary aim was to identify characteristic patterns of abdominal ^{18}F -FDG uptake in peritoneal disease and to correlate these patterns with available anatomic findings after surgery.

Materials and methods

Study protocol

Consecutive patients, with either histologically confirmed peritoneal carcinomatosis (by peritoneal biopsy) or suspected upon clinical follow-up (including a detailed physical examination and serum tumoral markers, as CEA, GICA, CA-125) and/or imaging findings (ultrasound, CT, MRI) if histology was negative or unavailable, were enrolled in this prospective study.

All patients staged by conventional workup, who were candidates for innovative locoregional treatment by cytoreductive surgery, peritonectomy procedure and hypertermic antitubercular peritoneal perfusion, had a whole-body ^{18}F -FDG PET/CT scan; stage and clinical management was changed according to the PET/CT findings.

We also assessed serum neoplastic markers, at baseline study and after treatment, being aware of the poor predictive value for effective staging in malignant serous peritoneal or pleural effusion.

The protocol of treatment was directly related to PET/CT results: only those patients without evidence of extra-peritoneal metastases at PET/CT scan were treated with cytoreductive surgery and IPCH, while in case of distant metastases clinical benefit by palliation was aimed.

Patient population

Potential participants were selected according to the following inclusion criteria: (1) age <75 years; (2) biopsy proven peritoneal carcinomatosis or histologically confirmed intraoperative peritoneal tumor nodules or a previous histologically or cytologically confirmed diagnosis of ovarian epithelial cancer with peritoneal involvement; (3) no evidence of disease outside the peritoneum; (4) Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2 ; (5) expected survival longer than 12 weeks; (6) adequate bone marrow function (white blood cell count $\geq 3000/\text{mm}^3$, platelet count $\geq 120,000/\text{mm}^3$); (7) adequate renal function (blood urea nitrogen ≤ 25 mg/dl, creatinine ≤ 1.5 mg/dl); (8) normal liver function (bilirubin ≤ 2 mg/dl); (9) no prior cancer other than cutaneous basal cell carcinoma; (10) normal blood coagulation tests.

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