Original article

Role of $^{18}$F-FDG PET/CT in diagnosing peritoneal carcinomatosis in the restaging of patient with ovarian cancer as compared to contrast enhanced CT and tumor marker Ca-125

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A R T I C L E   I N F O

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Contrast enhanced CT
Ca-125

A B S T R A C T

Objectives: To investigate the role of whole-body fluorine-18-2-deoxy-2-fluoro-D-glucose positron emission tomography/computed tomography ($^{18}$F-FDG PET/CT) in the identification of peritoneal carcinomatosis in patients with ovarian cancer (OC).

Material and methods: Seventy-nine patients with histologically proven stages III–IV OC who underwent $^{18}$F-FDG PET/CT were studied retrospectively. We considered group A as 51 patients who also underwent computed-tomography with contrast-enhancement (CECT), and group B as 35 patients who had also been tested for biomarker Ca-125. Sensitivity, specificity, accuracy, positive predictive values (PPV) and negative predictive values (NPV) of $^{18}$F-FDG PET/CT as compared to CECT and to Ca-125 were evaluated.

Results: $^{18}$F-FDG PET/CT sensitivity, specificity, accuracy, PPV and NPV for all 79 patients were: 85%, 92.31%, 88.61%, 91.89% and 85.71%, respectively. $^{18}$F-FDG PET/CT sensitivity in group A was 78.6%, while it was 53.6% for CECT. $^{18}$F-FDG PET/CT specificity, calculated in the same group, was 91.3%, while that of CECT was 60.9% (statistically significant difference, McNemar 4, P = 0.039). Accuracy was 84.3% and 56.9%, respectively. $^{18}$F-FDG PET/CT sensitivity in group B was 86.4%, while that of Ca-125 was 81.8% (no statistical difference, McNemar 0, P = 1). $^{18}$F-FDG PET/CT specificity in group B was 84.6% while that of Ca-125 was 38.5% (clear but not statistically significant difference, McNemar 3.12, P = 0.070). Accuracy calculated in the same group was 85.7% for $^{18}$F-FDG PET/CT and 65.7% for Ca-125.

Conclusion: $^{18}$F-FDG PET/CT is a useful diagnostic tool when peritoneal biopsy cannot be performed and it can better select those who are candidates for adjuvant chemotherapy.

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Papel del $^{18}$F-FDG PET/CT en el diagnóstico de carcinomatosis peritoneal en la reclasificación de los pacientes con cáncer de ovario en comparación con el TC con contraste y con el marcador tumoral Ca-125

R E S U M E N

Objetivos: Investigar el papel de fluor-18-2-desoxi-2-fluoro-D-glucosa tomografía por emisión de positrones/tomografía computarizada ($^{18}$F-FDG PET/CT) en la identificación de la carcinomatosis peritoneal en pacientes con cáncer de ovario (CO).

Material y métodos: Setenta y nueva pacientes con CO en estadio III-IV que se sometieron a $^{18}$F-FDG PET/CT fueron estudiadas retrospectivamente. Consideramos el grupo A de 51 pacientes que también realizaron la tomografía computarizada con contraste (CECT) y el grupo B de 35 pacientes que tenían cuantificación del Ca-125. Se evaluó sensibilidad, especificidad, exactitud, valor predictivo positivo (VPP) y valores predictivos negativos (VPN) de $^{18}$F-FDG PET/CT en comparación con CECT y Ca-125.

Resultados: La sensibilidad, especificidad, exactitud, VPN y VPN de $^{18}$F-FDG PET/CT en los 79 pacientes fueron: 85, 92,31, 88,61, 91,89 y 85,71% respectivamente. La sensibilidad de $^{18}$F-FDG PET/CT en el grupo A fue de 78,6% y de 53,6% por CECT. La especificidad de $^{18}$F-FDG PET/CT en el mismo grupo fue de 91,3%, mientras la de CECT del 60,9% (diferencia estadísticamente significativa, McNemar = 4, P = 0,039); la exactitud fue respectivamente de 84,3 y 56,9%. La sensibilidad de la $^{18}$F-FDG PET/CT en el grupo B fue de 86,4%, mientras que la del Ca-125 fue de 81,8% (sin diferencia estadística, McNemar = 0, P = 1). La especificidad $^{18}$F-FDG PET/CT en el grupo B fue de 84,6%, mientras que la del Ca-125 fue de 38,5% (diferencia evidente, no estadísticamente significativa, McNemar = 3,12, P = 0,070). La exactitud en el mismo grupo fue 85,7% para el $^{18}$F-FDG PET/CT y 65,7% para Ca-125.

Conclusión: El $^{18}$F-FDG PET/CT es un instrumento de diagnóstico útil cuando la biopsia peritoneal no se puede realizar y puede seleccionar de manera mejor las candidatas a quimioterapia adyuvante.

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**Introduction**

Carcinomas are 85–90% of all ovarian malignancies and arise from surface epithelium or inclusion cysts. Ovarian carcinomas by 90–95% arise after 50 years of age, are the 5th cause of cancer in women, although their incidence is only 3% and are also the main cause of death among all gynecological cancers.

Peritoneal carcinomatosis is one of the most significant prognostic indicators in ovarian carcinomas and their detection is critical in planning patients’ management algorithm.\(^3\,4\)

Approximately 89% of patients are diagnosed at an advanced stage, when tumor cells have already metastasized in particular to peritoneum.\(^3\) Therapy and the prognosis vary depending on the stage at diagnosis, which is often delayed because symptoms did not develop until the disease reached advanced stages; symptoms in early stages are often not specific and also attributable to many diseases (including irritable bowel syndrome, gastritis and depression).\(^5\)

Imaging plays an important role in tumor size evaluation and in diagnosing peritoneal ovarian carcinomatosis, supporting initial diagnosis and planning of surgical treatment.\(^6\,7\)

Integrated 18-fluorine-labeled 2-deoxy-2-fluoro-D-glucose positron emission tomography/computed tomography (\(^18\)F-FDG PET/CT) has been used successfully for the diagnosis, staging, restaging, therapy monitoring and prognostic prediction of ovarian cancer.\(^8\)

Peritoneum, however, is difficult to study using routine US, CECT or MRI, and few such papers have been published related to its involvement from ovarian cancer.\(^9\) \(^18\)F-FDG PET/CT today is performed widely in neoplastic diseases, demonstrating its validity even in comparison with other imaging modalities.\(^10\,11\) It is also particularly useful in differential diagnosis between neoplastic and benign diseases, and in the staging of them both localized and systemic.\(^12\,13\)

The serum marker Ca-125 is the most intensively studied ovarian cancer biomarker, used clinically to monitor the treatment response of ovarian carcinomas or disease recurrences. Ca-125 has not proved as useful as a screening test because of low sensitivity and specificity.\(^7\)

Our aim was to study retrospectively whether \(^18\)F-FDG PET/CT scan is useful in restaging patients with ovarian cancer by the detection of peritoneal carcinomatosis. \(^18\)F-FDG PET/CT performance has been also evaluated in comparison with CECT and the serum marker Ca-125.

**Material and methods**

**Patients**

We retrospectively studied 79 patients who underwent \(^18\)F-FDG PET/CT scans.

Inclusion criteria were: women older than 18 years, with histologically proven ovarian cancer, patients at stage III or IV at the moment of diagnosis and having undergone surgery for excision of the primary ovarian cancer at least 1 month before \(^18\)F-FDG PET/CT. All patients had a clinical and instrumental follow-up of at least 12 months (maximum 5 years) following the \(^18\)F-FDG PET/CT scan. During follow up, 37 of them had an histological proof for suspected peritoneal carcinomatosis from a peritoneal specimen, while the remnant 42 performed clinical, ultrasonographic, and laboratory evaluations.

The age of our patients was 59.86 ± 11.64 years (range 30–83 years). Sixty-eight of the 79 patients had also undergone adjuvant chemotherapy. Patients’ clinical characteristics, histology and surgical findings are described in Table 1.

**Table 1**

<table>
<thead>
<tr>
<th>Grading</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6/79 (7.6%)</td>
<td>14/79 (17.7%)</td>
<td>59/79 (74.7%)</td>
</tr>
</tbody>
</table>

**International Federation of Gynecology and Obstetrics (FIGO) staging at diagnosis**

<table>
<thead>
<tr>
<th></th>
<th>III</th>
<th>IIIa</th>
<th>IIIb</th>
<th>IIIc</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>69/79 (87.4%)</td>
<td>25/79 (36.3%)</td>
<td>16/79 (23.2%)</td>
<td>28/79 (40.5%)</td>
<td>10/79 (12.6%)</td>
</tr>
</tbody>
</table>

**Histology**

<table>
<thead>
<tr>
<th></th>
<th>Serous</th>
<th>Serous-papillary</th>
<th>Papillary</th>
<th>Mucinous cystadenocarcinoma</th>
<th>Borderline cystadenoma</th>
<th>Endometrioid</th>
<th>Epithelioid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>28/79 (35.4%)</td>
<td>22/79 (27.8%)</td>
<td>10/79 (12.7%)</td>
<td>8/79 (10.2%)</td>
<td>5/79 (6.3%)</td>
<td>3/79 (3.8%)</td>
<td>3/79 (3.8%)</td>
</tr>
</tbody>
</table>

**Surgery**

<table>
<thead>
<tr>
<th></th>
<th>Bilateral hysteroannexiectomy</th>
<th>Hysteroannexiectomy + peritoneal excision</th>
<th>Annexiectomy</th>
<th>LIAB</th>
<th>Hysteroannexiectomy + peritoneal excision + relapses excision</th>
<th>Several surgery for relapses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45/79 (57%)</td>
<td>17/79 (21.5%)</td>
<td>5/79 (6.3%)</td>
<td>6/79 (7.6%)</td>
<td>5/79 (6.3%)</td>
<td>1/79 (1.3%)</td>
</tr>
</tbody>
</table>

**\(^{18}\)F-FDG PET/CT**

<table>
<thead>
<tr>
<th></th>
<th>Restaging</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A: 40/51 (78.43%)</td>
<td>Group A: 26/35 (74.28%)</td>
</tr>
<tr>
<td></td>
<td>Group B: 20/79 (25.3%)</td>
<td>Group B: 11/51 (21.56%)</td>
</tr>
<tr>
<td></td>
<td>Group B: 9/35 (25.72%)</td>
<td></td>
</tr>
</tbody>
</table>

Two groups of patients were selected from the cohort of 79 patients: group A, consisting of 51 patients who performed CECT about 4 weeks before \(^{18}\)F-FDG PET/CT and group B, of 35 patients, who besides \(^{18}\)F-FDG PET/CT scan were tested for the biomarker Ca-125 levels about 4 weeks before the scan. Twenty-three of the 79 patients have been included in both the groups.

**CECT technique**

Computerized tomography examinations were performed with equipment CTMD to 16 layers (TSX-101\(^\dagger\), Aquilion\(^\dagger\) TM, Toshiba Medical Systems, Tokyo, Japan), using the following acquisition parameters: slice thickness 1 mm, pitch 1.75; increment 0.6 mm, rotation time 0.5 s, kV/mAs 120/250. All examinations were performed after injecting contrast medium.

**\(^{18}\)F-FDG PET/CT technique**

Positron emission tomography/CT images were acquired with combined modality PET/CT (GE Discovery LSA, Wi) that integrates a PET scanner (advance nxi) to a 16-slice CT (light speed plus). Prior to administration of \(^{18}\)F-FDG all patients fasted for at least 8 h, had a capillary blood glucose of <160 mg/mL, and to avoid artifacts caused by muscles, were instructed not to have any physical activity in the waiting time before the image acquisition. Image acquisition was obtained 50 min after the intravenous injection of 4.6 MBq/kg of \(^{18}\)F-FDG.

Patients were hydrated by drinking 500 mL of tap water and asked to urinate before the test. No muscle relaxant was administered.

The scan was carried out from the external acoustic meatus to the root of the thigh while patients laid on their back with hands above their head. The CT acquisition parameters were:
Results were consistent, performed immediately after the acquisition of CT images. The CT scans were obtained without administration of contrast medium. The PET acquisition was obtained in cranial-caudal direction: PET was reconstructed with a matrix of 128 × 128, ordered subset expectation maximum iterative reconstruction algorithm (two interations, 28 subsets), 8 mm Gaussian filter, and 50 cm field of view.

An experienced physician interviewed each patient for collection of anamnestic data and informed consent was obtained for the whole examination procedure.

Image analysis

Two Nuclear Medicine experienced physicians and two experienced radiologists, blindly and independently reviewed the 18F-FDG PET/CT and CECT.

The 18F-FDG uptake patterns indicative of peritoneal carcinomatosis were: (a) focal nodular 18F-FDG uptake detected on peritoneal surfaces, excluding lymph nodes; (b) diffuse 18F-FDG uptake in the superficial abdominal planes which appeared thickened; (c) diffuse 18F-FDG uptake in the ascitic fluid.

Irregular regions of interest (ROI) were semiautomatically drawn on images using a dedicated workstation and software (Xeleris™ Workstation, GE, Waukesha, WI, USA).

In all patterns the intensity of 18F-FDG uptake was measured by Standardized Uptake Value (SUV). SUV was calculated as follows: SUV = measured activity concentration in Bq/mL/injected activity in Bq per kg body weight × 1000. SUVmax was considered as the maximum value measured on the visualized lesions.

Indicative CECT patterns for peritoneal carcinomatosis were: (a) peritoneal nodules with well-defined margins of any size in direct continuity with the peritoneal planes, excluding lymph nodes; (b) focal wall thickening in organs of gastrointestinal and urogenital tracts in direct contact with peritoneum; (c) presence of ascites.

Statistical analysis

We evaluated sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of 18F-FDG PET/CT for all 79 patients in identifying peritoneal carcinomatosis (using as gold standard the recent histological examination of a peritoneal specimen performed during clinical and instrumental follow-up of at least 12 months).

Sensitivity, specificity and accuracy of 18F-FDG PET/CT and CECT were also calculated in group A, and the first two values were compared by the McNemar test. In group B sensitivity, specificity and accuracy of 18F-FDG PET/CT and biomarker Ca-125 levels (evaluated in the dichotomous way as normal or abnormal if > or ≤35 U/mL) were also calculated and the first two values compared by the McNemar test.

Cohen’s K test was used to calculate the degree of agreement between 18F-FDG PET/CT and CECT results in group A, and between 18F-FDG PET/CT and biomarker Ca-125 levels (evaluated as normal or abnormal if > or ≤35 U/mL) in group B.

Statistical analysis was performed using SPSS 20.0.0 for Mac OS X. p-Value of <0.05 was considered statistically significant.

Results

The overall sensitivity, specificity, accuracy, PPV and NPV for identifying peritoneal carcinomatosis using 18F-FDG PET/CT are reported in Table 2. Patterns of peritoneal carcinomatosis observed by 18F-FDG PET/CT are reported in Table 3. SUVmax calculated on peritoneal lesions was on average 7.7 (range: 3.0–17.6). Sensitivity and specificity of 18F-FDG PET/CT and of CECT calculated by McNemar formula and accuracy of the two techniques are reported in Table 4.

In group A the agreement between 18F-FDG PET/CT and CECT, calculated using Cohen’s K, was quite low (K = 0.134, P = 0.338).

Normal values for serum Ca-125 biomarker were less than 35 U/mL. In 9/35 patients serum Ca-125 was normal and in 26/35 (74.3%) patients was elevated. The average value observed was 298.45 U/mL (range: 18–2619 U/mL). Results for group B are shown in Table 5.

In group B the agreement between 18F-FDG PET/CT and Ca-125 as calculated using Cohen’s K was very low (K = 0.051, P = 0.752).

Discussion

The importance of 18F-FDG PET/CT in detecting abdominal recurrences of ovarian cancer is well established, even if its role in the study of peritoneal involvement is still in discussion. Up to date laparotomy is the most accurate but invasive way to determine peritoneal spread.8,9

Recently in literature have been reported studies about diagnostic accuracy of 18F-FDG PET/CT and CECT in evaluation of peritoneal carcinomatosis using histological exams and clinical instrumental follow up as gold standard, but including groups of few and heterogeneous patients. Suzuki et al. studied 35 heterogeneous patients and found 18F-FDG PET/CT accuracy of 78%.14

We analyzed 79 18F-FDG PET/CT scans performed in 79 patients all with ovarian cancer, observing 18F-FDG PET/CT diagnostic accuracy of 88.6%, in agreement with results reported by other researchers.15

In our homogeneous cohort of 79 patients with suspected peritoneal carcinomatosis from ovarian cancer, 18F-FDG PET/CT overall sensitivity was 85%, while specificity was 92.3%. To date no similar results are reported in literature.

We found true positive results for peritoneal carcinomatosis in 43% of them and true negative results in 45.6%; other 3.8% of patients were false positive and 7.6% were false negative.

Six of the 79 patients (7.6%) were false negative at 18F-FDG PET/CT, due to the small size of the peritoneal lesions in 2/6, the presence of few ascites in other 2, and the mucinous histotype in the last 2. Other 3/79 patients (3.8%) had a false positive 18F-FDG PET/CT scan, due to intestinal activity.

A recent study analyzed 48 18F-FDG PET/CT scans demonstrating true positive results for 77% of them and true negative results in 23%15.

Table 2

<table>
<thead>
<tr>
<th>PET/CT</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>18F-FDG</td>
<td>85% (95%CI: 73.93–96%)</td>
<td>92.31% (95%CI: 83.9–100%)</td>
<td>88.61% (95%CI: 81.6–95.6%)</td>
</tr>
<tr>
<td>PPV</td>
<td>91.89% (95%CI: 83.1–100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>85.71% (95%CI: 75.1–96%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: positive predictive value.

Table 3

<table>
<thead>
<tr>
<th>PET/CT</th>
<th>Scan findings in all patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No peritoneal involvement</td>
<td>42</td>
</tr>
<tr>
<td>Peritoneal nodules</td>
<td>22</td>
</tr>
<tr>
<td>Peritoneal masses</td>
<td>4</td>
</tr>
<tr>
<td>Peritoneal thickening</td>
<td>8</td>
</tr>
<tr>
<td>Ascites</td>
<td>2</td>
</tr>
<tr>
<td>More than one pattern</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 4

18F-FDG PET/CT statistical results for identifying peritoneal carcinomatosis in 79 patients.
The sensitivity of F-FDG PET/CT for detecting peritoneal carcinomatosis was 78.57%, with a 95% confidence interval (95%CI) of 63.37–93.77%. Specificity was 91.30%, with a 95%CI of 79.79–100%. Accuracy was 84.31%, with a 95%CI of 74.33–94.29%. Positive predictive value (PPV) was 91.67%, with a 95%CI of 80.61–100%. Negative predictive value (NPV) was 77.78%, with a 95%CI of 62.10–93.46%.

Sensitivity, specificity, accuracy, and other statistical measures for F-FDG PET/CT compared to CECT are provided in Table 4.

Table 4: Sensitivity, specificity, accuracy, PPV and NPV for detecting peritoneal carcinomatosis in group A.

<table>
<thead>
<tr>
<th>Test</th>
<th>F-FDG PET/CT</th>
<th>CECT</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>78.57%</td>
<td>95%CI: 63.37–93.77%</td>
<td>McNemar 2.77, P = 0.092 (difference evident but not statistically significant)</td>
</tr>
<tr>
<td>Specificity</td>
<td>91.30%</td>
<td>95%CI: 79.79–100%</td>
<td>McNemar 4, P = 0.039 (difference statistically significant)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>84.31%</td>
<td>95%CI: 74.33–94.29%</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>91.67%</td>
<td>95%CI: 80.61–100%</td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>77.78%</td>
<td>95%CI: 62.10–93.46%</td>
<td></td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.

Some researchers have compared 18F-FDG PET/CT with CECT. Dromain et al. analyzed 28 patients for peritoneal carcinomatosis from gastrointestinal cancer and found that 18F-FDG PET/CT sensitivity was 57% while CECT sensitivity was 82%. Neoplastic spread in peritoneal cavity can cause intestinal obstruction, but frequently causes ascites. The presence of ascites allows differentiation of neoplastic implants over the visceral or the parietal peritoneum.

Identification of peritoneal metastases depends on their size, so macroscopic nodules can be easily identified (Fig. 1), and on the presence of ascites, that can be carcinomatous too (Fig. 2).

CET C sensitivity is influenced by the size of the peritoneal nodules and ranges from 25% for lesions less than 0.5 cm to 90% for lesions larger than 5 cm. In a large study by Temppany et al. CECT showed a sensitivity of 92%, but the greater part of the patients (88%) had peritoneal lesions bigger than 2 cm.

Literature reports that detection of smaller peritoneal lesions is more difficult. In a study by Coakley et al. sensitivity of CECT for the detection of peritoneal metastases less than 1 cm was only of 25%. The 18F-FDG PET/CT in the assessment of peritoneal carcinomatosis can detect lesions not identified at CECT because of their site or size.

False-negatives at 18F-FDG PET/CT may be related to the presence of cystic lesions, small size lesions or histotypes characterized by low 18F-FDG uptake (e.g. mucinous histotype). To date, the major difficulty of 18F-FDG PET/CT is the spatial resolution because the majority of the peritoneal implants are smaller than 5 mm (resolving power of PET) or microscopic infiltration. In a study of Pannu et al., 18F-FDG PET/CT identified 13% peritoneal lesions ≤1 cm and 50% >1 cm. Furthermore, some signs suggestive of peritoneal involvement at 18F-FDG PET/CT, such as the widespread and uniform low-grade 18F-FDG uptake, are ambiguous and associated with low probability of the real presence of carcinomatosis.

False positives are mainly related to intestinal activity and 18F-FDG retentions in ureters and bladder, these errors more likely occurs in cases of misalignment of PET and CT images caused by respiratory and intestinal movements.

In the group A of our study we found sensitivity, specificity, accuracy, PPV and NPV of 18F-FDG PET/CT about 78.57%, 91.30%, 84.31%, 91.67% and 77.78% and sensitivity, specificity, accuracy, PPV and NPV of CECT about 53.57%, 60.87%, 56.86%, 62.50% and 51.85%.

In our study 18F-FDG PET/CT and CECT correctly determined peritoneal carcinomatosis in 43/51 (84.31%) patients and 15/51 patients (29.4%) patients, respectively.

In 11/51 patients 18F-FDG PET/CT was positive while CECT was negative. The subsequent histological proof and follow-up confirmed the positive results of 18F-FDG PET/CT in 10/11 cases, while in a patient 18F-FDG PET/CT misinterpreted intestinal activity. In other 11/51 patients 18F-FDG PET/CT was negative while CECT was positive. In 8/11 the sequel follow-up confirmed the 18F-FDG PET/CT negative results, while in 3/11 patients 18F-FDG PET/CT did not recognize peritoneal lesions due to the mucinous histotype in 2 patients and the presence of few ascites in the other one. In 13 patients the two methods were concordant in identifying the peritoneal involvement. At the end of the follow-up period 12/13 patients were true positive, while only one patient as examined by both techniques was false positive. In 16/51 patients 18F-FDG PET/CT and CECT were both negative in identifying peritoneal lesions. In 13/16 patients the follow up confirmed the absence of the disease, while the remnant 3/16 were false negative because the small size in 2 patients and the microscopic involvement of peritoneum in another one in whom the disease evolved rapidly in the follow 6 months. Four of 51 (7.8%) cases with lesions larger than 2 cm were highlighted at CECT. Three of them showed elevated 18F-FDG uptake while one had a negative 18F-FDG PET/CT scan.

Fifteen of 51 patients (29.4%) were positive at 18F-FDG PET/CT for lesions smaller than 2 cm, 3/51 patients (5.9%) were positive at CECT for the same type of lesions.

The analysis of SUVmax may help the differentiation of 18F-FDG uptake in peritoneal carcinomatosis from that in normal intestine. A study of Suzuki et al. showed that 18F-FDG PET/CT diagnostic

Table 5: Sensitivity and specificity, accuracy, PPV and NPV for detecting peritoneal carcinomatosis in group B.

<table>
<thead>
<tr>
<th>Test</th>
<th>18F-FDG PET/CT</th>
<th>Ca-125</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>86.36%</td>
<td>95%CI: 72.02–100%</td>
<td>McNemar 0, P = 1 (no statistical difference)</td>
</tr>
<tr>
<td>Specificity</td>
<td>84.62%</td>
<td>95%CI: 65.70–97.94%</td>
<td>Specificity McNemar 3.12, P = 0.070 (evident but not significant)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>85.71%</td>
<td>95%CI: 74.12–97.31%</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>90.48%</td>
<td>95%CI: 49.99–81.44%</td>
<td></td>
</tr>
<tr>
<td>NPV</td>
<td>78.57%</td>
<td>95%CI: 51.49–86.97%</td>
<td></td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.
accuracy was 78% using a SUVmax threshold value equal to 5.1. The same study reported that SUVmax was higher in peritoneal metastatic lesions (5.79 ± 2.34) than that one related to physiological bowel uptake in healthy subjects (3.65 ± 0.71) and in patients with ovarian cancer but without peritoneal involvement (3.13 ± 1.03); anyway the difference was not statistically significant.14

In our study, the SUVmax was on average 7.7 (range: 2.8–17.6). SUVmax was on average 5.3 (range: 2.8–9.2) in the 3/37 patients false positive at 18F-FDG PET/CT otherwise it was on average 8.0 (range: 2.8–17.6) in the 34/37 true positive patients.

SUVmax is higher in patients with peritoneal carcinomatosis, but the comparison is not possible for the numerical difference of the two groups. SUVmax can provide a further aid in the interpretation of images 18F-FDG PET/CT, although it is not possible to define a threshold value.

The literature reports studies on the value of Ca-125 in recurrence and metastasis from ovarian cancer. High levels of Ca-125 may suggest metastatic ovarian cancer, but not specifically peritoneal carcinomatosis. Elevated Ca-125 serum levels have been observed in only 50% of symptomatic stage-I cases and in 80% of advanced-stage cases.21 Moreover, Ca-125 is relatively nonspecific for ovarian cancer. Altogether, Ca-125 serum levels above the threshold of 35 U/mL may be found in 1% of the normal population, in 6% of patients with benign disease, and in 28% of patients with a nongynecologic malignancy.21 In a study of Thrall et al. the increase of Ca-125 is a very sensitive indicator of disease recurrence.22 In another study conducted by Simcock et al., 18F-FDG PET/CT was performed in 56 women with elevated levels of Ca-125, and resulted positive in all patients except one.24 These studies did not consider only peritoneal carcinomatosis, but all possible sites of recurrences. In our previous study of preliminary results of a group of 24 patients with the same characteristics of the group B, sensitivity and specificity of Ca-125 were, respectively, 93.3% and 33.3%.25

In our study we selected the homogeneous group B of patients that performed Ca-125 serum level dosage at least 4 weeks before 18F-FDG PET/CT. The sensitivity of 18F-FDG PET/CT resulted higher than that of Ca-125, but not statistically significant, while specificity resulted much higher for 18F-FDG PET/CT (Table 5). In the group B, in patients with Ca-125 elevated, 18F-FDG PET/CT was false positive in one patient and false negative in three patients. In one patient with normal Ca-125 value 18F-FDG PET/CT was falsely positive.

This study, being a retrospective one, presents some limitations; not all patients dosed Ca-125 at the time of the 18F-FDG PET/CT. The number of patients included is influenced by how many patients performed CECT within 8 weeks before the 18F-FDG PET/CT, although this is still in line with other studies in literature. The histological exam was not performed for all patients because guidelines consider the clinical assessment instrument sufficient for diagnosis in patients already treated for recurrent ovarian cancer.

Conclusions

Whole body 18F-FDG PET/CT is better than CECT in restaging patients with peritoneal carcinomatosis from ovarian cancer. 18F-FDG PET/CT can evaluate all districts in the same moment, including peritoneal sheets, and also better exploits the ascites as
well as for distinguishing nodular peritoneal lesions from the gut, and for identifying its metabolic characteristics. 18F-FDG PET/CT can be helpful in reducing the number of laparotomies and better select patients who are candidates for adjuvant chemotherapy. It is a useful diagnostic tool when peritoneal biopsy is either unavailable or inappropriate.

Conflict of interest

The authors declare no conflict of interest.

References