¹⁸F FDG PET/CT Evaluation of Patients with Ovarian Carcinoma

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Abstract

Purpose—The role of ^{18}F FDG PET has been studied in ovarian carcinoma, but its sensitivity and specificity calculations are based on dedicated PET acquisition, not PET/CT in the majority of the published studies. Therefore, we were prompted to review our experience with PET/CT in the management of patients with ovarian carcinoma.

Materials and methods—This is a retrospective study of 43 women with ovarian carcinoma, 27–80 years old (average: 53.9 ± 7.8), who had whole-body PET/CT at our institution from Jan 1st, 2003 to Aug 31st, 2006. We reviewed the patients' outcomes from medical records and compared them to the interpretation of the PET/CT scans. Sensitivity and specificity were calculated using a 2×2 table with pathology results (79.1% of the patients) or clinical follow-up (20.9% of the cases) as the gold standard. Confidence interval (CI) estimations were performed using the Wilson score method.

Results—All patients had advanced stage ovarian cancer and the study was requested for re-staging. A total of 60 scans were performed: 30 pts had 1 scan, 9 pts had 2 scans and 4 pts had 3 scans. The administered doses of ^{18}F FDG ranged 381.1 – 769.6 MBq (average: 569.8 ± 73.3). PET/CT had a sensitivity of 88.4% (95% CI: 75.1–95.4) and a specificity of 88.2% (95% CI: 64.4–97.9) for detection of ovarian cancer. The SUV max of the detected lesions ranged 3–27 (average: 9.4±5.9). The CA-125 tumor marker ranged 3–935 kU/ml (average: 265.2) in patients with positive scans and 4–139 kU/ml (average: 17.1) in patients with negative scans. This difference was statistically significant (*P* value: 0.0242).

Conclusion—This study confirms the good results of ^{18}F FDG PET/CT for identification of residual/recurrent ovarian cancer, as well as for distant metastases localization. PET/CT should be an integral part in evaluation of patients with high risk ovarian cancer or rising values of tumor markers (CA-125), prior to selection of the most appropriate therapy.

Keywords

ovarian; carcinoma; FDG; PET; CT

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Introduction

There are approximately 21,650 new cases of ovarian carcinoma and 15,520 deaths from ovarian carcinoma expected in 2008 in the United States (1). Epithelial ovarian cancer is usually diagnosed in an advanced stage and carries a poor prognosis. Imaging has become a significant part of the clinical management of patients with ovarian cancer. It is important for tumor detection, staging, treatment planning, and follow-up. Imaging findings assist in creating a specific treatment plan for each individual patient (2).

^{18}F Fluoro-2-Deoxyglucose (^{18}F FDG) positron emission tomography and computed tomography (PET/CT) combines the ability to detect active metabolic processes and their morphologic features in a single exam. The role of ^{18}F FDG PET is proven in a variety of cancers, including lymphoma, colorectal carcinoma, lung cancer and melanoma, entities for which it changed the practice of oncology (3). In ovarian cancer, sequential imaging with PET has been shown to predict response to neoadjuvant chemotherapy (as early as after the first cycle). PET was more accurate than clinical or histopathologic response criteria including changes in tumor marker CA-125 alone in determining the prognosis (4). It is especially beneficial in conjunction with elevated serum CA-125 (5–7) or when CT or magnetic resonance imaging (MRI) show a suspected recurrence, but biopsy is infeasible. In this paper we review our experience with PET/CT in the management of patients with ovarian cancer.

Materials and methods

This is a retrospective study of 43 consecutive women with epithelial ovarian cancer, 27–80 years old (average: 53.9 ± 7.8), who had whole-body PET/CT at our institution from Jan 1st, 2003 to Aug 31st, 2006. The study was performed with the Institutional Review Board approval. The inclusion criteria were histopathologically proven diagnosis of ovarian cancer and availability of PET/CT scans. The reports of PET/CT and pathology examinations were reviewed and their results were recorded. A joint Nuclear Medicine - Radiology readout assures the accuracy of the findings on the CT portion of the exams during routine interpretation of the PET/CT exams. Reinterpretation of the studies by board certified Nuclear Medicine physicians was performed for consistency.

The ^{18}F-FDG PET/CT scans were acquired using a Discovery LS PET/CT unit (GE Medical Systems, Milwaukee, WI). The patients fasted at least 6 hours prior to imaging and their blood glucose levels were less than 150 mg/dl at the time of the tracer injection. A standard dose of 555 MBq was prescribed for adult patients. However, due to variations in the daily clinical schedule, the administered doses of ^{18}F FDG ranged 381.1 – 769.6 MBq (average: 569.8 ± 73.3). Approximately 60 minutes after tracer administration, a CT scan (5 mm contiguous axial cuts) was obtained in four integrated multi-slice helical non-contrast CT, from the skull base to the mid-thighs. The acquisition was obtained in helical mode, using 140 kV, 40 mAs and a 512×512 matrix size, acquiring a field of view (FOV) of 867 mm in 22.5 s. The CT scan was used for attenuation correction purposes and to help in anatomic localization of FDG. Immediately after the CT, an emission PET scan was acquired in 2D mode over the same anatomical regions starting at the level of the mid-thighs. The acquisition time was 4 minutes per bed position (35 slices/bed) in 6 beds, with a one-slice overlap at the borders of the FOV. The PET emission scan was corrected using segmented attenuation data of the CT scan. The PET images were reconstructed with a standard iterative algorithm (OSEM, two iterative steps, 28 subsets) using GE software release 5.0. All images were reformatted into axial, coronal, and sagittal views and viewed with the software provided by the manufacturer (eNtegra, GE Medical Systems, Haifa, Israel).

Semi-quantitative analysis of the ^{18}F FDG uptake in the suspected lesions was based on calculation of standard uptake value (SUV), defined as the ratio of activity per milliliter of tissue to the activity in the injected dose corrected for decay and the patient's body weight. Regions of interest were placed around the areas of increased FDG uptake for SUVmax determination. The cutoff SUVmax for malignant lesions was considered ≥2.5 (8).

Sensitivity and specificity for PET/CT in detection of ovarian cancer were calculated using the pathology results (79.1% of the patients) or clinical follow-up (20.9% of the cases) as the gold standard, using a 2 × 2 contingency table. For the 79.1% of patients with PET/CT findings correlated with tissue diagnosis, histological specimens were obtained after surgical re-exploration due to abnormal imaging findings in the abdomen/pelvis or from biopsy of lesions reported outside the abdominal cavity. Sites of disease progression on anatomic imaging (CT and/or MRI) at 6–12 months after PET/CT were recorded as true positive lesions for the remaining 20.9% of patients. Confidence interval (CI) estimations were performed using the Wilson score method (9).

Results

All patients had advanced stage ovarian cancer and the study was requested for disease re-staging. A total of 60 PET/CT scans were performed: 30 patients had 1 scan, 9 patients had 2 scans and 4 patients had 3 scans. Using the pathology results (79.1% of the patients) or clinical follow-up (20.9% of the cases) as the gold standard, PET/CT had an overall per patient sensitivity of 88.4% (95% CI: 75.1–95.4) and specificity of 88.2% (95% CI: 64.4–97.9) for detection of ovarian cancer. There were 5 false negative scans and 2 false positive scans (rectal uptake and colon uptake at the site of post-surgical anastomosis).

The results were also analyzed looking at lesions detected in the pelvis vs. those in other locations. PET/CT had a sensitivity of 80.9% (95% CI: 59.4–92.9) and specificity of 93.7% (95% CI: 69.7–99.9) for pelvic disease and a sensitivity of 93.5% (95% CI: 78.2–99.9) and specificity of 93.7% (95% CI: 69.7–99.9) for extra-pelvic lesions. The extra-pelvic lesions were located in the liver, lungs, omentum/peritoneum, bones and lymph nodes and are detailed in Table 1.

SUV max ranged from 3–27 (average: 9.4±5.9). The two false positive lesions had SUVmax of 5.2 and 5.3, respectively. The CA-125 tumor marker measurements were available at the time of 55 of the 60 PET/CT scans. CA-125 values ranged 3–935 U/ml (average: 265.2) in patients with positive scans and 4–139 U/ml (average: 17.1) in patients with negative scans. This difference was statistically significant (*P* value: 0.0242). The normal value for CA-125 is <35 U/ml at our institution. A total of 16 patients had CA-125 >35 U/ml: 15 had positive PET/CT (all true positive) and 1 had negative PET/CT (false negative after pathology exam).

The sensitivities and specificities of PET/CT in ovarian cancer are presented in Figure 1, based on overall, pelvic and extra-pelvic lesion per patient analysis. In Figure 2 we present PET/CT images of recurrent disease in the pelvis (arrows), as well as liver metastases (arrowheads). Peritoneal (black arrowheads), liver (white arrowheads) and vertebral (arrows) metastases are seen in Figure 3 on the PET/CT scan of a 63-year-old woman with ovarian cancer.

Discussion

Accurate diagnosis of recurrence and re-staging in ovarian cancer is important in an effort to improve the poor prognosis. Re-staging radiologic studies are complicated by alterations to the anatomy and physiology of the abdomen/pelvis from surgery and radiation. Moreover, the ability to fully evaluate the patient in one combined imaging modality rather than multiple tests is advantageous if the performance of that test is equal to or better than the others.

There has long been interest in the role of PET in ovarian carcinoma, but the majority of studies in the current literature are primarily based on dedicated PET acquisitions (10–26). Both early (15) as well as recent studies (13) with dedicated PET have shown comparable or higher sensitivity, specificity, and diagnostic accuracy in comparison to conventional imaging or tumor markers.

However, there is evidence that PET plus CT performs better than either alone in various solid cancers including ovarian cancer (27,28). There are relatively few studies published on concurrent PET/CT in gynecologic malignancy (29–31). A recent prospective study (32) in 97 patients, evaluating the utility of PET/CT for the evaluation of a pelvic mass of unknown origin (with post-surgical histopathologic follow-up) found that the sensitivity and specificity for PET/CT in diagnosing a malignant pelvic tumor were 100% and 93%, respectively. Other studies evaluating PET/CT in recurrent ovarian cancer also show promising results. Three retrospective studies (29,33,34) evaluating PET/CT in recurrent ovarian cancer provide sensitivity and specificity values of 83–95%, and 71–100%, respectively, which are, again, superior to that reported in the literature for conventional imaging. And, another (35) showed that a change in the clinical management was observed in 44% of cases when PET/CT information was added to conventional follow-up findings.

With these considerations in mind, PET/CT shows promise in the restaging evaluation of ovarian cancer. Our study confirms this with an overall per patient sensitivity of 88% and specificity of 88% for detection of ovarian cancer at restaging. In comparison, conventional imaging has a reported sensitivity of 53–70% and specificity of 82–83% (13,29).

One group has demonstrated improved sensitivity and specificity of PET/CT for the evaluation of recurrent ovarian carcinoma when their early experience was compared to later. Sensitivity improved from78% to 93% and specificity from 75% to 100% (30,31). This indicates that as experience grows with this relatively new modality, the accuracy will increase.

The results in our study showed a lower sensitivity of 81% for lesions in the pelvis compared to 96% for disease in other sites. This difference is likely due to post-surgical and post-treatment induced inflammatory uptake within the pelvis. This hypothesis is supported by a study (32) showing that staging with PET/CT (before surgery) has sensitivity and specificity of 100%, and 92%, respectively, in comparison to subsequent histopathologic findings. Nonetheless, conventional imaging is also complicated by post-therapy changes, such that the reported sensitivity and specificity remains higher with PET/CT. Another contributing factor to these results may be to post-therapy anatomical changes accounting for challenges in interpretation of non-contrast enhanced CT images. Using i.v. contrast-enhanced pelvic CT may result in improved sensitivity in this location for patients with ovarian cancer. The specificities were equal at 94% for pelvic and extra-pelvic lesions.

Outside the pelvis, both the sensitivity and specificity are high, indicating the very good performance of PET/CT in identifying more distant lesions. Extra-pelvic lesions were located in the liver, lungs, omentum, bones, and lymph nodes. This is significant in terms of altering the management, as shown in one study which found that a change in clinical management was observed in 44% of cases when PET/CT information was added to conventional follow-up findings (35).

The limitations in this study acknowledge that patient selection in referrals for PET/CT is important for the results of the scan. However, this is difficult to overcome in any retrospective review.

Taken together, the results of this study confirm a high sensitivity and specificity of PET/CT in ovarian cancer staging both within and outside the pelvis. The values reported in this study

are in accord with those reported in the literature thus far and add to the limited number of studies on this important subject. The main advantages of PET/CT for ovarian cancer are in restaging, finding extra-pelvic lesions that can effect patient management, and in evaluation of those patients with increased CA-125 levels. The sensitivity of PET/CT is lower within the pelvis, probably due to post-operative changes and lack of i.v. contrast, but remains higher than conventional imaging. The latter, however, is established and remains important for its improved resolution. Therefore, the combined use of conventional imaging and PET/CT in the evaluation of ovarian cancer is recommended.

Conclusions

This study confirms the good results of ^{18}F FDG PET/CT for identification of residual/recurrent ovarian cancer, as well as distant metastases. PET/CT should be an integral part in evaluation of patients with high-risk ovarian cancer or rising CA-125 values.

Acknowledgements

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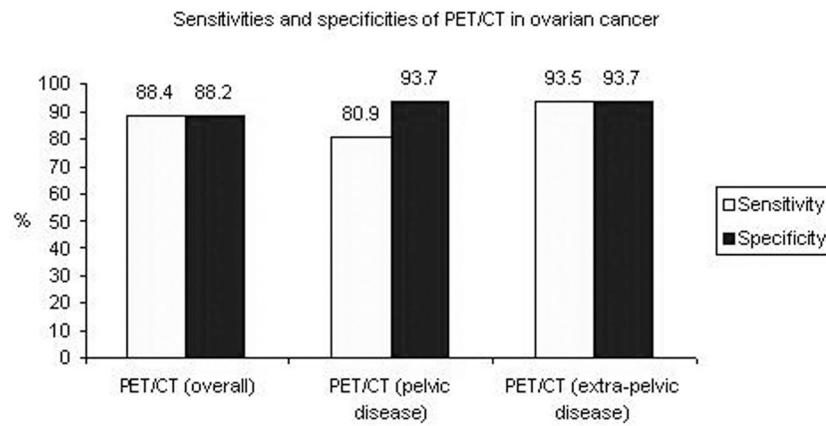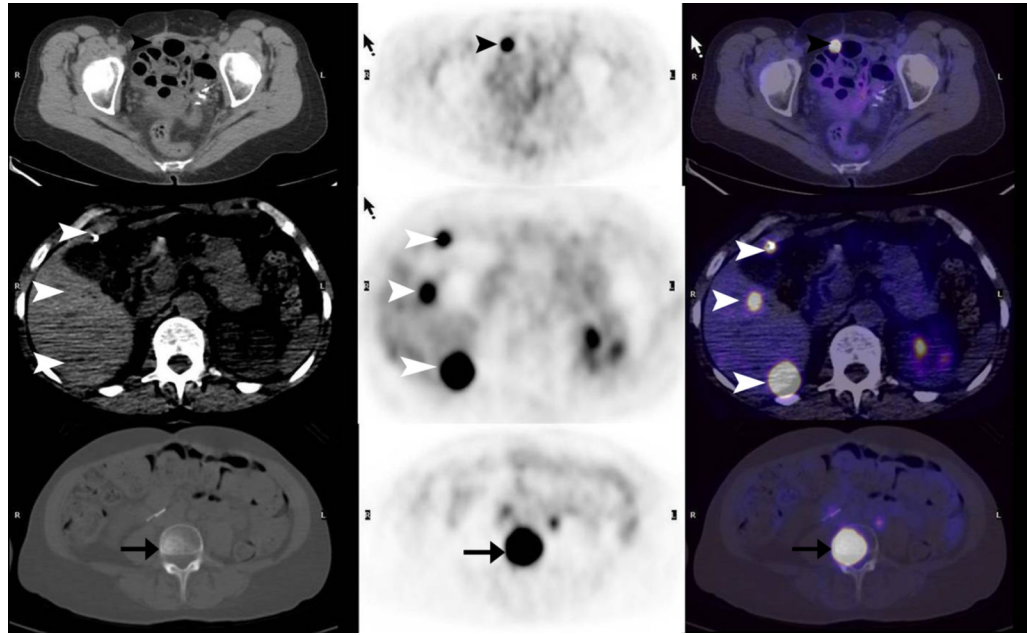
Figure 1.
The sensitivities and specificities of PET/CT in ovarian cancer, based on overall, pelvic and extra-pelvic lesion per patient analysis.
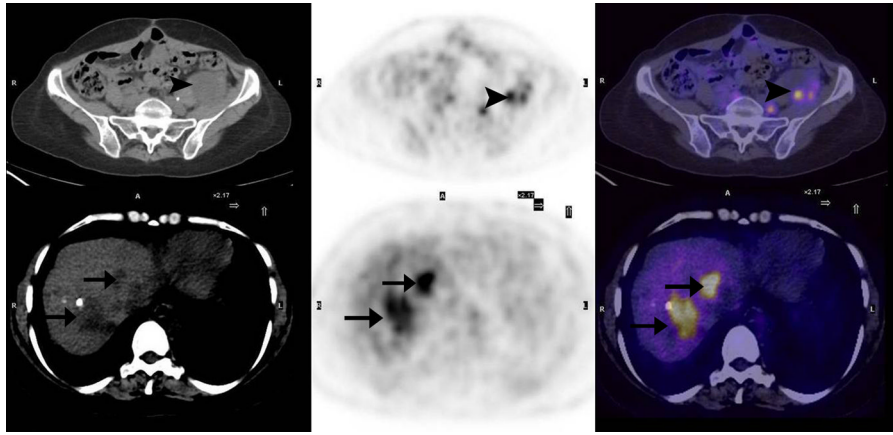
Figure 2.
40-year-old woman with ovarian cancer. Transaxial PET, CT and fused PET/CT images demonstrate metastases in the pelvis (arrowheads) and liver (arrows).

Figure 3.
63-year-old woman with ovarian cancer. Transaxial PET, CT and fused PET/CT images show peritoneal (black arrowheads), liver (white arrowheads) and vertebral (arrows) metastases.

Table 1

Summary of the extra-pelvic lesions detected in the studied population.

Patient #	Extra-pelvic lesions
2	Mediastinal lymph nodes, peritoneum
6	Falciform ligament, peritoneum
7	Mediastinal lymph nodes, liver
8	Peritoneum, omentum, liver
10	Omentum
13	Liver, retroperitoneal lymph nodes
14	Peritoneum
16	Lung, liver
18	Left supraclavicular lymph node
20	Lung
21	Liver
22	Liver, retroperitoneal lymph nodes
23	Liver, peritoneum
24	Mediastinal lymph nodes, thoracic spine
26	Peritoneum
27	Liver, peritoneum, mediastinal lymph nodes
29	Lung, peritoneum
38	Liver, retroperitoneal lymph nodes
43	Liver, peritoneum, lumbar spine