Original article

Nuclear Medicine Communications

Diagnostic performance of ^{18}F-FDG PET/contrast-enhanced CT versus contrast-enhanced CT alone for post-treatment detection of ovarian malignancy

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Objective **The aim of this study was to evaluate the diagnostic performance of combined fluorine-18 fluorodeoxyglucose (^{18}F-FDG) PET/contrast-enhanced computed tomography (Ce-CT) in comparison with Ce-CT alone for the detection of residual/recurrent tumor after initial treatment of malignant ovarian tumors.**

Patients and methods **The study prospectively recruited 111 patients with a clinical suspicion of ovarian tumor recurrence. Each patient underwent ^{18}F-FDG PET/computed tomography (CT) with low-dose CT, followed immediately by Ce-CT. Study-based analyses for a total of 136 scans were carried out. For each study, 11 subsites were assessed on a four-point score (score 0 = definitely benign, score 1 = probably benign, score 2 = probably malignant, and score 3 = definitely malignant). The subsites were collectively categorized into four groups: local tumor site, peritoneum, pelvi-abdominal lymph nodes, and other sites (e.g. liver, lung, bone, brain, etc). The final diagnosis of disease status was made on subsequent follow-up by conventional imaging (CT/MRI), ^{18}F-FDG PET/CT, or histopathology whenever possible.**

Results **Of the 136 studies evaluated, 97 (71%) studies had recurrent/residual disease and 39 (29%) studies were disease free on the basis of the final diagnosis. ^{18}F-FDG PET/Ce-CT and Ce-CT had a sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of 96 versus 84%, 92 versus 59%, 90 versus 59%, 97 versus 84%, and 95 versus 76%, respectively. ^{18}F-FDG PET/Ce-CT was significantly more sensitive, specific, and accurate compared with Ce-CT, with *P*-values of 0.002, 0.001, and less than 0.0001, respectively. Site-based analyses also showed significant differences.**

Conclusion **Combined^{18}F-FDG PET/Ce-CT significantly outperforms Ce-CT alone in the post-treatment detection of malignant ovarian tumors. *Nucl Med Commun* 37:453–460**

Nuclear Medicine Communications 2016, **37**:453–460

Keywords: contrast-enhanced computed tomography, fluorine-18 fluorodeoxyglucose PET, ovarian cancers, PET/CT

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Received 30 September 2015 **Revised** 8 December 2015
Accepted 16 December 2015

Introduction

Ovarian cancer accounts for 4% of all cancers in women worldwide, with over 190 000 new cases diagnosed each year; 70% of them will present with advanced disease. In addition, it has a high propensity for recurrence after therapy. Approximately 20–30% of patients with early-stage disease and 50–75% of patients with advanced disease who achieve a complete response after first-line chemotherapy will ultimately develop a recurrent disease. Therefore, a noninvasive detection method is essential for follow-up [1].

Although the level of CA-125 has been shown to be a sensitive marker for tumor recurrence and levels may increase 3–6 months before there is clinically apparent disease, it does not provide information on the size distribution of the lesions. Levels may also increase in a number of benign conditions, not being a specific marker for ovarian cancer, and a number of patients, with relapse of disease, present with normal CA-125 levels [2].

Contrast-enhanced computed tomography (Ce-CT) is the current recommended method for imaging ovarian cancer after therapy if the tumor markers are elevated [3]. However, computed tomography (CT) uses morphologic criteria to detect the disease. Therefore, accurate detection of intra-abdominal tumor recurrences may be limited because of difficulties in identifying small tumor deposits and in separating bowel structures from adjacent tumor tissue. Also, CT cannot differentiate residual viable tumor from post-treatment fibrosis. For the detection of metastatic lymph nodes (LNs), CT depends on the size criteria. However, sometimes, normal-sized LNs may contain tumor cells, whereas enlarged nodes could be because of inflammation [4].

0143-3636 DOI: 10.1097/MNM.0000000000000477

Also, metastases from ovarian cancer are primarily peritoneal rather than parenchymal in location. Therefore, they usually occur on the surfaces of the viscera rather than as masses within the viscera. These tumor implants can be miliary and isoattenuating relative to the viscera at CT, which makes their detection challenging [5].

Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) PET imaging for ovarian cancer surveillance has proven useful for detecting early recurrences and, depending on the clinical circumstances, has a diagnostic accuracy of ~80% [6]. Recognized limitations include failure to detect small lesions with all three modalities and misinterpretation of normal physiological abdominal activity on PET. However, lesion conspicuity is high on PET owing to low background activity. Therefore, there is interest in using PET especially in patients with clinically suspected recurrence, but with negative or equivocal anatomical imaging findings.

Integrated PET/CT offers the combined benefits of anatomical and functional imaging, and has been used to localize areas of increased ^{18}F-FDG uptake with improved sensitivity and specificity. The usefulness of concurrent ^{18}F-FDG PET/CT for post-treatment surveillance of patients with ovarian cancer has been investigated in several studies, with reported sensitivity, specificity, and accuracy of patient-based analyses of 73–100%, 40–100%, and 63–100%, respectively [7–17].

The aim of this prospective study was to compare the diagnostic performance of whole-body diagnostic Ce-CT and ^{18}F-FDG PET/CT using Ce-CT in post-treatment detection of ovarian cancer.

Methods

Patients

This prospective study was carried out in Alfa Scan Radiology Center, Cairo, Egypt, during the period from January 2010 to November 2012. The inclusion criteria were patients with pathologically proven ovarian cancer who were treated with initial standard treatments, referred for post-treatment detection of residual or recurrent disease.

Patients who were referred for initial staging or with synchronous or a history of other malignancies were excluded. Also, patients who were lost to follow-up were excluded.

The study was approved by the Institutional Review Board and each patient signed a written informed consent form.

PET/CT imaging protocol

The ^{18}F-FDG PET/CT scans were acquired using a Philips Gemini time-of-flight PET/CT machine equipped with LYSO crystals (Philips, Amsterdam, the Netherlands). The patients were instructed to fast for at least 6 h before imaging and their blood glucose level was measured at the time of the tracer injection and was less than 200 mg/dl. A dose of 3.7–5.2 MBq/kg was injected intravenously and adjusted according to the patient's weight. For the optimal delineation of bowel structures, 400–600 ml of diluted mannitol solution was administered 1 h before CT imaging.

Approximately 60 min after tracer administration, a low-dose CT scan (5 mm contiguous axial cuts) was obtained in a 64 integrated multislice CT machine from the skull base to the mid-thigh. The acquisition was obtained in a helical mode, using 120 kV, 60 mAs, and a 512×512 matrix size, acquiring a field of view (FOV) of 700 mm in 22.5 s. The first CT scan was used for attenuation correction.

Immediately after the low-dose CT, an emission PET scan was acquired in a three-dimensional mode over the same anatomical regions starting from the skull vertex to the level of the mid-thigh. The acquisition time was 2 min per bed position in nine bed positions, with a one slice overlap at the borders of the FOV. The generated PET and low-dose CT slices were 5 mm in thickness.

Immediately after completing PET acquisition, a diagnostic CT was acquired using 120 kV, 300 mAs, and a 512×512 matrix size. The acquired FOV was 500 mm using dose automatic modulation in the Z direction. Nonionic contrast media were used at a dose of 1–2 ml/kg (maximum 150 ml). Slice thickness was 1.5 mm. The radiation exposure dose from low-dose CT was on average 3.37 mGy, whereas that for diagnostic CT was 11.48 mGy.

After completion of acquisition, the images were reconstructed with a standard iterative algorithm and then the reconstructed CT attenuation-corrected PET images, low-dose CT images, and Ce-CT images were transferred to the viewing stations for reviewing in axial, coronal, and sagittal planes and in a maximum-intensity projection three-dimensional cine mode using the manufacturer's review station (Brilliance; Philips).

Data interpretation

The fused PET/CT and Ce-CT images were interpreted separately by a team of one nuclear medicine physician and one radiologist who was aware of the aim of the study.

For each study, 11 sites were evaluated for the presence or absence of abnormality. The sites were local tumor site, peritoneum, pelvic LNs, abdominal LNs, mediastinal LNs, cervical LNs, liver, lung, bone, brain, and other sites (pleura, muscles, adrenal glands).

First PET/CT images using low-dose CT were reviewed for any abnormal ^{18}F-FDG uptake other than the known normal physiologic biodistribution. Any abnormality was noted and recorded on a four-point scale according to the

possibility of being benign or malignant as follows: score 0 = definitely benign uptake (e.g. bowel, endometrial uptake), score 1 = probably benign (e.g. reactive LNs), score 2 = probably malignant (e.g. abnormal focal uptake related to bowel but not sure of being definite peritoneal metastases), and score 3 = definitely malignant (e.g. pathologic LN with high ^{18}F-FDG uptake).

Ce-CT images were reviewed for any abnormality and scaled according to the same four-point scale. Score 0 = definitely benign (e.g. hepatic cyst, adrenal adenoma with low HFU), score 1 = probably benign (e.g. 1 cm lymph node with preserved fatty hilum), score 2 = probably malignant (e.g. 1 cm or less lymph node with lost fatty hilum, peritoneal fat stranding and ascites with no nodules), and score 3 = definitely malignant (e.g. the presence of enhancing solid or cystic nodules or masses of soft tissue/low attenuation, focal, multifocal or diffuse peritoneal thickening, fat stranding, and ascites if associated with peritoneal lesion/lesions).

Combined PET/CT images were reviewed thereafter and a consensus was reached for any discrepancy in the readings between the radiologist and the nuclear medicine physician, and the final decision was recorded using the same four-point score as well.

Reference standard

The final diagnosis of the presence or absence of recurrent/residual disease was made on the basis of subsequent follow-up by conventional imaging (CT/MRI), tumor markers, PET/CT, and/or clinical follow-up of at least 6 months or histopathological findings obtained during surgery or biopsy whenever possible.

Clinical recurrence was defined as the detection of recurrent disease by Ce-CT or a continuously increasing CA-125 level to a value greater than twice the nadir within 6 months of the ^{18}F-FDG PET/CT scan. Recurrent disease detected more than 6 months after the ^{18}F-FDG PET/CT scan was interpreted as a new recurrence.

Statistical analysis

Study-based and site-based analyses were carried out. True-positive, true-negative, false-positive (FP), and false-negative (FN) readings were identified on the basis of subsequent clinical/imaging/histopathological validation. Diagnostic performance parameters were calculated in the form of sensitivity, specificity, accuracy, positive predictive value, and negative predictive value. The nonparametric McNemar test was used to evaluate the statistical significance of the differences in sensitivity and specificity (a two-sided $P < 0.05$ was considered significant), whereas receiver-operating characteristic analysis was used to compare the accuracy of the two modalities.

Quantitative data were summarized and expressed as mean ± SD and median (range), whereas qualitative data were expressed as frequencies and percentages. The analyses were carried out using the SPSS, 21.0 (SPSS Inc., Chicago, Illinois, USA), MedCalc 11.0 (MedCalc, Ostend, Belgium), and Microsoft Excel 2003 (Microsoft, Redmond, Washington, USA).

Results

Patients

A total of 111 patients were eligible for this study. The general characteristics of the 111 patients enrolled in this study are summarized in Table 1.

Study-based analyses

Of the 136 studies evaluated, 97 (71%) had recurrent/residual disease and 39 (29%) were free of disease on the basis of the final clinical diagnosis. PET/CT excluded recurrent/residual disease in 36/39 and confirmed recurrent disease in 93/97, yielding a specificity of 92% and a sensitivity of 96%, respectively, compared with 59 and 84% for Ce-CT.

Ce-CT and PET/CT were concordantly true-negative in 22 studies. PET/CT successfully excluded disease in 14 out of 16 FP studies in Ce-CT. Both modalities were true-positive in 80 studies. In addition, PET/CT diagnosed disease in 13 out of 16 FN results by Ce-CT. The difference in the overall accuracy was statistically highly significant ($P < 0.001$; Table 2).

Site-based analyses

A total of 1496 sites were available for analyses from 136 studies. Of these, 236 were positive according to the final follow-up data. The peritoneum was the most frequent site of disease relapse (32%), followed by the primary tumor site, and pelvic and abdominal LNs (14% each). Mediastinal LNs were found in 11% of the lesions. Other

Table 1 General characteristics of 111 patients with ovarian cancer enrolled in this work

Parameters	*n* (%)
Patients	111 (100)
Age	
Median (range)	54 (13–76)[a]
Pathologic subtype	
Epithelial	99 (89.1)
Nonepithelial	12 (10.9)
Number of studies	136
Timing of PET/CT after therapy (months)	4 (0.25–40)[a]
Treatment modality	
Surgery alone	27 (20)
Surgery + chemotherapy	102 (75)
Chemotherapy alone	7 (5)
Tumor markers	
Elevated	64 (47)
Normal	54 (40)
Unknown results	18 (13)

CT, computed tomography.
[a]The numbers in parentheses indicate the range of the data.

Table 2 Diagnostic performances of Ce-CT and combined PET/Ce-CT from 136 studies in patients with ovarian cancer (study-based and site-based analysis)

	Modality	FN	TP	TN	FP	Sensitivity 95% CI	*P*	Specificity 95% CI	*P*	Accuracy 95% CI	*P*
Study-based analysis	Ce-CT	16	81	23	16	84% (77–90)	0.002*	59% (51–67)	0.001*	76% (69–84)	<0.001*
	PET/CT	4	93	36	3	96% (93–99)		92% (88–97)		95% (91–99)	
Peritoneum	Ce-CT	23	52	52	9	69% (62–77)	<0.001*	85% (79–91)	0.004*	76% (69–84)	<0.001*
	PET/CT	3	72	61	0	96% (93–99)		100%		98% (95–100)	
Primary tumor site	Ce-CT	7	27	96	6	79% (73–86)	0.06	94% (90–98)	0.21	90% (85–95)	0.004
	PET/CT	0	34	100	2	100%		98% (96–100)		99% (97–100)	
Pelvi-abdominal LNs	Ce-CT	20	28	87	1	58% (50–67)	<0.001*	99% (97–101)	1.0	85% (78–91)	<0.001*
	PET/CT	0	48	88	0	100%		100%		100%	
Other distant sites[a]	Ce-CT	13	26	84	13	67% (59–75)	0.01*	87% (81–92)	<0.001*	81% (74–87)	<0.001*
	PET/CT	3	36	97	0	92% (88–97)		100%		98% (95–100)	

Ce-CT, contrast-enhanced computed tomography; CI, confidence interval; FN, false negative; FP, false positive; TN, true negative; TP, true positive.
[a]Other distant sites include: mediastinal LNs, liver, lung, brain, and bone metastases.
*Statistically significant.

distant sites of metastases included cervical LNs (3%), liver (2%), lung (1%), bone (1%), brain (1%), and other rare sites such as pleura, spleen, adrenal glands, and anterior abdominal wall muscles (6%).

Peritoneum

PET/CT detected peritoneal metastases in 72/75 and excluded metastases in all negative cases of peritoneal metastases, yielding a sensitivity of 96% and a specificity of 100% compared with 69 and 85% for Ce-CT. The difference was statistically significant.

The overall accuracy for PET/CT according to receiver-operating characteristic analysis was 98% compared with 76% for Ce-CT ($P < 0.0001$; Table 2).

Primary tumor site

PET/CT detected local tumor recurrence/residue in all positive cases ($n = 34$) and excluded disease in 100/102, yielding a sensitivity of 100% and a specificity of 98% compared with 79 and 94% for Ce-CT (Table 2). No statistical difference was noted.

Pelvi-abdominal lymph nodes

For statistical purposes, pelvic and abdominal lymph nodal sites were summed together. PET/CT detected pelvi-abdominal nodal metastases in all positive cases ($n = 48$) and excluded disease in all negative cases ($n = 88$), yielding a sensitivity of 100% and a specificity of 100%, respectively, compared with 58 and 99% for Ce-CT (Table 2), with a statistically significant difference in sensitivity.

Other sites

PET/CT detected lesions in other subsites in 36/39 and excluded disease in all negative cases ($n = 97$), yielding a sensitivity of 92% and a specificity of 100% compared with 67 and 87% for Ce-CT, with a statistically significant difference (Table 2).

Mediastinal LNs were found in 25/136 cases (18%) and cervical LNs in 7/136 cases (5%). PET/CT detected 24/25 mediastinal lesions. Six patients were scored 2 'probably malignant' and 18 were scored 3 'definitely malignant'. Among 18 patients with definitely malignant mediastinal lesions, 17 showed peritoneal involvement. There was a statistically significant association between peritoneal and mediastinal involvement ($P < 0.001$).

Discussion

In the current work, combined ^{18}F-FDG PET/CT with Ce-CT showed consistently higher diagnostic performance indices compared with Ce-CT alone. On the basis of the study, we reported a sensitivity, specificity, and accuracy for PET/CT and Ce-CT of 96 versus 84%, 92 versus 59%, and 95 versus 76%, respectively. The PET/CT results were generally comparable with those reported in the literature, with sensitivities ranging from 73 to 100%, specificity ranging from 40 to 100%, and accuracy varying between 63 and 100% [13,17–23].

Four FN results were found with ^{18}F-FDG PET/CT. One of them did not show any significant metabolic activity, but was proven to have peritoneal metastases on subsequent follow-up within 4 months. PET/CT is known to be inherently less sensitive to peritoneal micrometastases [6,24]. Another patient had non-^{18}F-FDG-avid mucinous cystadenocarcinoma. Misregistration of ^{18}F-FDG activity to the normal bowel loop uptake was responsible for missing a peritoneal lesion in another patient. The last FN result had a 7 mm pulmonary nodule showing no pathologic ^{18}F-FDG uptake, but progressed on subsequent follow-up. Only the latter patient was categorized correctly by Ce-CT.

The FP PET/CT studies in this setting ($n = 3$) were attributed to the presence of postoperative inflammatory changes at the operative bed/peritoneum ($n = 2$) or reactive pelvic LNs ($n = 1$). All of them resolved spontaneously on subsequent follow-up PET/CT with no interval treatments. FP PET/CT interpretation secondary to inflammatory changes has been reported [25,26]. It is worth noting that Ce-CT correctly excluded disease in one patient with FP inflammatory ^{18}F-FDG uptake at the primary tumor site.

PET/CT correctly excluded disease in 14/16 FP Ce-CT (Table 2). These patients remained free of disease for a median of 12 months (range = 7–27 months), a finding that confirms the previously reported prognostic impact of negative PET/CT [27]. However, this analysis is beyond the scope of this work.

A site-based analysis was also carried out. Peritoneal metastases were found in 55% of patients showing evidence of disease recurrence. ^{18}F-FDG PET is very sensitive to the hypermetabolic activity of peritoneal tumors, but it has low specificity because of lack of anatomical localization [28]. The combined PET/CT detected significantly more peritoneal lesions than Ce-CT alone with a sensitivity, specificity, and accuracy of 96 versus 69%, 100 versus 85%, and 98 versus 76%, respectively. Only three FN cases were encountered in PET/CT mainly because of mismatch of the ^{18}F-FDG activity to bowel activity secondary to bowel movement between PET and Ce-CT parts of the study [29]. The other case was assumed to have peritoneal micrometastases that were beyond the PET/CT resolution. No FP cases were identified in our series.

These results are in agreement with those reported in the literature [30,31]. In contrast, Funicelli *et al.* [32] reported that enhanced abdominal CT had a higher detection rate than that of ^{18}F-FDG PET/CT. However, they carried out a two-arm study with a PET/CT study population different from those of Ce-CT. In addition, their diagnostic CT criteria were more subjective, nonspecific, and broad, which might have led to over estimation of their reported sensitivity.

The identification of local tumor recurrence is not always straightforward and differentiation from peritoneal involvement may not be feasible. PET/CT showed a sensitivity of 100% with no FN results (Fig. 1) and a specificity of 98% with only two FP lesions. One was in a patient with low-grade serous adenocarcinoma who underwent fertility preserving surgery. PET/CT showed a contralateral ^{18}F-FDG-avid cystic mass that was misinterpreted as a tumor and proved to be a functional ovarian cyst. The other FP lesion was attributed to metabolic activity within operative bed inflammatory changes.

Ce-CT showed a sensitivity of 79% and a specificity of 94% with seven FN and six FP results. This can be attributed to the inability of CT to differentiate between residual viable postoperative pelvic bed soft tissue masses/sheets and granulation tissue (Fig. 1). Also, the presence of small residual tumor tissue on serosa of pelvic bowel loops may be easily missed. Moreover, in cases with fertility preserving surgery, the presence of contralateral functional cystic mass may be equivocal.

For lymph nodal detection, PET/CT outperformed Ce-CT in the number of nodal lesions detection (sensitivity 100 vs. 58% for Ce-CT). PET/CT could detect recurrence in normal-sized LNs in a large series of cases ($n = 20$). In this setting, no false results were identified by PET/CT (Fig. 1). These results are in agreement with the previously reported results [33,34].

One of the advantages of PET/CT is whole-body scanning, which may aid the detection of additional remote sites of disease [35,36]. Both PET/CT and Ce-CT correctly diagnosed three cases with brain metastases and one case with bone metastases.

PET/CT detected more lesions than Ce-CT in normal-sized mediastinal and cervical LNs. Positive supradiaphragmatic LNs were found in 23% of the studies, which was slightly more frequent than described previously in the literature [16,37]. The detection of mediastinal LNs was associated with the presence of peritoneal involvement. Transdiaphragmatic metastatic spread from peritoneal to thoracic cavity may explain this association [38].

PET/CT detected metastases in abdominal muscles and subcutaneous nodules in four studies. Also, metastases were observed in the spleen ($n = 3$), adrenal ($n = 5$), and pleura ($n = 2$). Only three FN results were found (one thyroidal and two lung nodules). No PET/CT FP results were obtained.

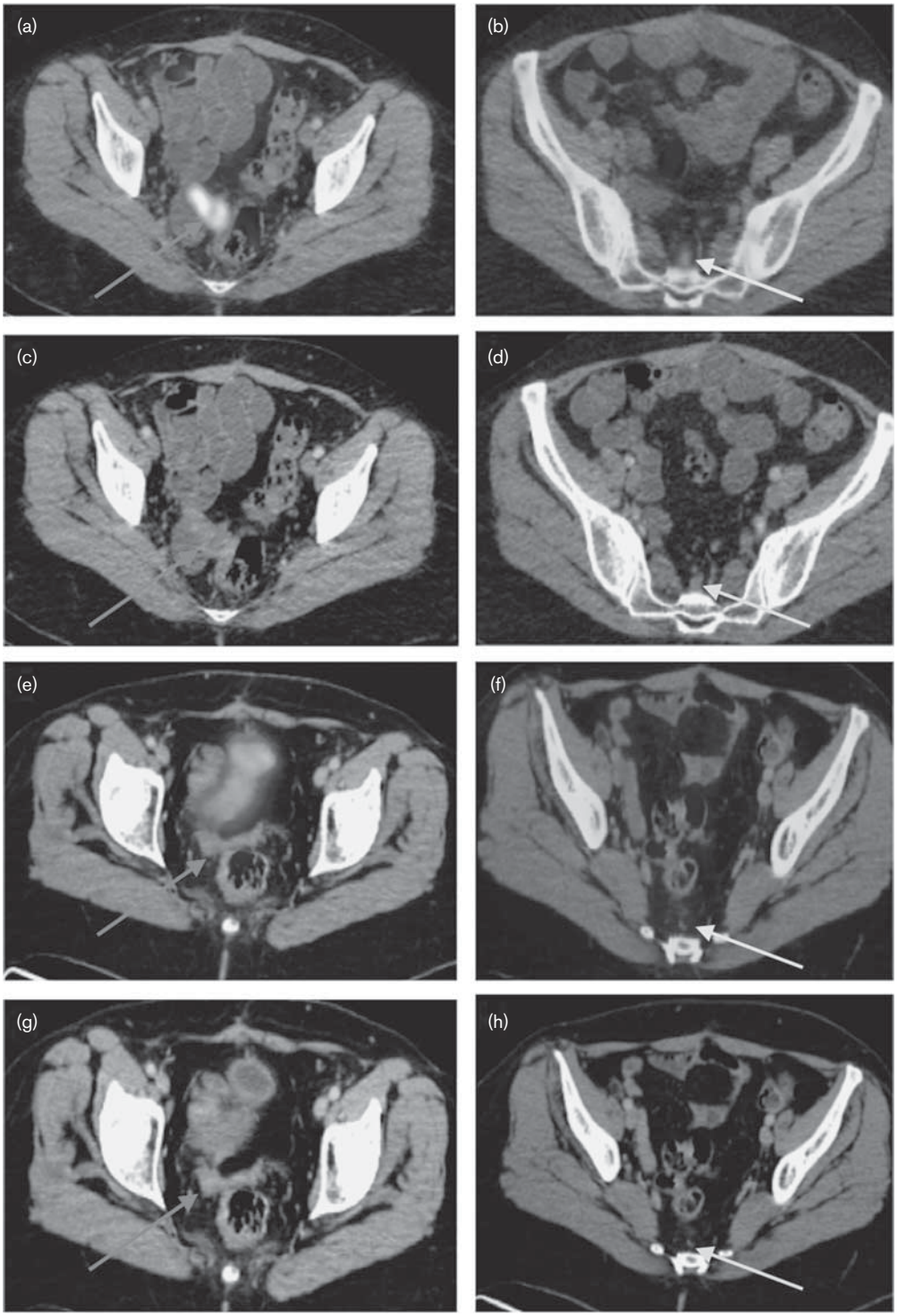
However, Ce-CT showed 13 FN and 13 FP results. The FN results were found in supradiaphragmatic LNs (normal-sized by CT criteria), adrenal nodules (misinterpreted as adenomas), and splenic focal lesions (interpreted as probably benign). Also, small lower anterior abdominal muscles nodules were missed in Ce-CT and identified by PET/CT because of higher contrast resolution of the latter modality.

Given the consistently higher diagnostic yield from combined PET/CT, we would recommend PET/CT with contrast enhancement as a one-stop restaging modality in patients with suspected OC recurrence. Despite the lack of multiple conventional treatment options for recurrent disease, novel target therapies are evolving and early diagnosis of disease relapse could potentially alter the disease outcome.

There has been rapid progress in combined modality imaging. We believe that combined reading between well-trained nuclear medicine physicians and radiologists does not only add information pertinent to functional and anatomical imaging, respectively, but also combines the cumulative experience of both physicians. With this synergy in mind, the role of PET/MR should be investigated thoroughly in many diseases, including gynecological cancers [39].

This work has some limitations: the lack of a histopathologic correlation of all the sites of abnormal ^{18}F-FDG uptake. The confirmation of all the sites is not

Fig. 1



A 58-year-old female patient with treated papillary serous adenocarcinoma in January 2010. Tumor marker (CA-125) values were normal. Combined PET/CT (a) and Ce-CT (c) showed pelvic recurrence. In addition, PET/CT showed a small ^{18}F-FDG-avid presacral lymph node (b) that was considered benign on the basis of Ce-CT criteria (d). The patient received six cycles of chemotherapy and was referred for reassessment. PET/CT showed complete metabolic resolution of the FDG uptake within the pelvic soft tissue thickening (e) and presacral LN (f). Ce-CT showed residual soft tissue thickening at the pelvic operative bed, still suggesting residual disease (g) with no abnormality in the presacral region (h). Subsequent follow-up with a stable appearance on follow-up Ce-CT (not shown), confirming its benign nature (granulation tissue). The patient remained disease free for 13 months. Arrows point to the lesion(s) described. Ce-CT, contrast-enhanced computed tomography; CT, computed tomography; ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; LN, lymph node.

ethically acceptable solely for the purpose of validation of PET/CT findings. Also, an accurate surgical assessment of pelvic and retroperitoneal LNs is difficult. The impact of PET/CT on change of management, quality of life, or survival was not addressed. Also, quantification of SUV and metabolic tumor volume that may have prognostic significance was beyond the scope of this work. However, the study has some advantages; it has a prospective design with relatively large number of patients. Also, the Ce-CT and PET/CT studies were carried out simultaneously and interpreted using uniform criteria.

Conclusion

This study showed that ^{18}F-FDG PET/CT outperforms Ce-CT for the detection of residual/recurrent tumor in patients with ovarian cancer after therapy, on the basis of both patient and lesion sites.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Gadducci A, Cosio S, Zola P, Landoni F, Maggino T, Sartori E. Surveillance procedures for patients treated for epithelial ovarian cancer: a review of the literature. *Int J Gynecol Cancer* 2007; **17**:21–31.

2 Goonewardene TI, Hall MR, Rustin GJ. Management of asymptomatic patients on follow-up for ovarian cancer with rising CA-125 concentrations. *Lancet Oncol* 2007; **8**:813–821.

3 Forstner R, Sala E, Kinkel K, Spencer JA. ESUR guidelines: ovarian cancer staging and follow-up. *Eur Radiol* 2010; **20**:2773–2780.

4 Forstner R. CT and MRI in ovarian carcinoma. In: Hamm B, editor. *CT and MRI of the female pelvis*. Berlin, Heidelberg, New York: Springer Verlag; 2006. pp. 231–261.

5 Bharwani N, Reznek RH, Rockall AG. Ovarian cancer management: the role of imaging and diagnostic challenges. *Eur J Radiol* 2011; **78**:41–51.

6 Nakamoto Y, Saga T, Ishimori T, Mamede M, Togashi K, Higuchi T, *et al.* Clinical value of positron emission tomography with FDG for recurrent ovarian cancer. *Am J Roentgenol* 2001; **176**:1449–1454.

7 Sironi S, Messa C, Mangili G, Zangheri B, Aletti G, Garavaglia E, *et al.* Integrated FDG PET/CT in patients with persistent ovarian cancer: correlation with histologic findings. *Radiology* 2004; **233**:433–440.

8 Pannu HK, Bristow RE, Cohade C, Fishman EK, Wahl RL. PET-CT in recurrent ovarian cancer: initial observations. *Radiographics* 2004; **24**:209–223.

9 Hauth EA, Antoch G, Stattaus J, Kuehl H, Veit P, Bockisch A, *et al.* Evaluation of integrated whole-body PET/CT in the detection of recurrent ovarian cancer. *Eur J Radiol* 2005; **56**:263–268.

10 Bristow RE, Giuntoli RL, Pannu HK, Schulick RD, Fishman EK, Wahl RL. Combined PET/CT for detecting recurrent ovarian cancer limited to retroperitoneal lymph nodes. *Gynecol Oncol* 2005; **99**:294–300.

11 Mangili G, Picchio M, Sironi S, Viganò R, Rabaiotti E, Bornaghi D, *et al.* Integrated PET/CT as a first-line re-staging modality in patients with suspected recurrence of ovarian cancer. *Eur J Nucl Med Mol Imaging* 2007; **34**:658–666.

12 Thrall MM, DeLoia JA, Gallion H, Avril N. Clinical use of combined positron emission tomography and computed tomography (FDG-PET/CT) in recurrent ovarian cancer. *Gynecol Oncol* 2007; **105**:17–22.

13 Chung HH, Kang WJ, Kim JW, Park NH, Song YS, Chung JK, *et al.* Role of [^{18}F]FDG PET/CT in the assessment of suspected recurrent ovarian cancer: correlation with clinical or histological findings. *Eur J Nucl Med Mol Imaging* 2007; **34**:480–486.

14 Sebastian S, Lee SI, Horowitz NS, Scott JA, Fischman AJ, Simeone JF, *et al.* PET-CT vs. CT alone in ovarian cancer recurrence. *Abdom Imaging* 2008; **33**:112–118.

15 Picchio M, Sironi S, Messa C, Mangili G, Landoni C, Gianolli L, *et al.* Advanced ovarian carcinoma: usefulness of [(18)F]FDG-PET in combination with CT for lesion detection after primary treatment. *Q J Nucl Med* 2003; **47**:77–84.

16 Iagaru AH, Mittra ES, McDougall IR, Quon A, Gambhir SS. ^{18}F-FDG PET/CT evaluation of patients with ovarian carcinoma. *Nucl Med Commun* 2008; **29**:1046–1051.

17 Kitajima K, Murakami K, Yamasaki E, Domeki Y, Kaji Y, Fukasawa I, *et al.* Performance of integrated FDG-PET/contrast-enhanced CT in the diagnosis of recurrent ovarian cancer: comparison with integrated FDG-PET/non-contrast-enhanced CT and enhanced CT. *Eur J Nucl Med Mol Imaging* 2008; **35**:1439–1448.

18 Bilici A, Ustaalioglu BB, Seker M, Canpolat N, Tekinsoy B, Salepci T, Gumus M. Clinical value of FDG PET/CT in the diagnosis of suspected recurrent ovarian cancer: is there an impact of FDG PET/CT on patient management? *Eur J Nucl Med Mol Imaging* 2010; **37**:1259–1269.

19 Bhosale P, Peungjesada S, Wei W, Levenback CF, Schmeler K, Rohren E, *et al.* Clinical utility of positron emission tomography/computed tomography in the evaluation of suspected recurrent ovarian cancer in the setting of normal CA-125 levels. *Int J Gynecol Cancer* 2010; **20**:936–944.

20 Sari O, Kaya B, Kara PO, Gedik GK, Celik C, Ozbek O, *et al.* The role of FDG-PET/CT in ovarian cancer patients with high tumor markers or suspicious lesion on contrast-enhanced CT in evaluation of recurrence and/or in determination of intra-abdominal metastases. *Rev Esp Med Nucl Imagen Mol* 2012; **31**:3–8.

21 Dragosavac S, Derchain S, Caserta NM, De Souza G. Staging recurrent ovarian cancer with (18)FDG PET/CT. *Oncol Lett* 2013; **5**:593–597.

22 Antunovic L, Cimitan M, Borsatti E, Baresic T, Sorio R, Giorda G, *et al.* Revisiting the clinical value of ^{18}F-FDG PET/CT in detection of recurrent epithelial ovarian carcinomas: correlation with histology, serum CA-125 assay, and conventional radiological modalities. *Clin Nucl Med* 2012; **37**:e184–e188.

23 Pan HS, Lee SL, Huang LW, Chen YK. Combined positron emission tomography-computed tomography and tumor markers for detecting recurrent ovarian cancer. *Arch Gynecol Obstet* 2011; **283**:335–341.

24 Rose PG, Faulhaber P, Miraldi F, Abdul-Karim FW. Positive emission tomography for evaluating a complete clinical response in patients with ovarian or peritoneal carcinoma: correlation with second-look laparotomy. *Gynecol Oncol* 2001; **82**:17–21.

25 Nanni C, Rubello D, Farsad M, De Iaco P, Sansovini M, Erba P, *et al.* (18)F-FDG PET/CT in the evaluation of recurrent ovarian cancer: a prospective study on forty-one patients. *Eur J Surg Oncol* 2005; **31**:792–797.

26 De Iaco P, Musto A, Orazi L, Zamagni C, Rosati M, Allegri V, *et al.* FDG-PET/CT in advanced ovarian cancer staging: value and pitfalls in detecting lesions in different abdominal and pelvic quadrants compared with laparoscopy. *Eur J Radiol* 2011; **80**:e98–e103.

27 García-Velloso MJ, Jurado M, Ceamanos C, Aramendía JM, Garrastachu MP, López-García G, Richter JA. Diagnostic accuracy of FDG PET in the follow-up of platinum-sensitive epithelial ovarian carcinoma. *Eur J Nucl Med Mol Imaging* 2007; **34**:1396–1405.

28 Coleman RE, Delbeke D, Guiberteau MJ, Conti PS, Royal HD, Weinreb JC, *et al.* Concurrent PET/CT with an integrated imaging system: intersociety dialogue from the joint working group of the American College of Radiology, the Society of Nuclear Medicine, and the Society of Computed Body Tomography and Magnetic Resonance. *J Nucl Med* 2005; **46**:1225–1239.

29 Liu Y. Benign ovarian and endometrial uptake on FDG PET-CT: patterns and pitfalls. *Ann Nucl Med* 2009; **23**:107–112.

30 Kim HW, Won KS, Zeon SK, Ahn BC, Gayed IW. Peritoneal carcinomatosis in patients with ovarian cancer: enhanced CT versus ^{18}F-FDG PET/CT. *Clin Nucl Med* 2013; **38**:93–97.

31 Dirisamer A, Schima W, Heinisch M, Weber M, Lehner HP, Haller J, Langsteger W. Detection of histologically proven peritoneal carcinomatosis with fused ^{18}F-FDG-PET/MDCT. *Eur J Radiol* 2009; **69**:536–541.

32 Funicelli L, Travaini LL, Landoni F, Trifiro G, Bonello L, Bellomi M. Peritoneal carcinomatosis from ovarian cancer: the role of CT and [(18)F]FDG-PET/CT. *Abdom Imaging* 2010; **35**:701–707.

33 Kitajima K, Murakami K, Yamasaki E, Kaji Y, Fukasawa I, Inaba N, Sugimura K. Diagnostic accuracy of integrated FDG-PET/contrast-enhanced CT in staging ovarian cancer: comparison with enhanced CT. *Eur J Nucl Med Mol Imaging* 2008; **35**:1912–1920.

34 Yuan Y, Gu ZX, Tao XF, Liu SY. Computer tomography, magnetic resonance imaging, and positron emission tomography or positron emission tomography/computer tomography for detection of metastatic lymph nodes in patients with ovarian cancer: a meta-analysis. *Eur J Radiol* 2012; **81**:1002–1006.

35 Avril N, Gourtsoyianni S, Reznek R. Gynecological cancers. *Methods Mol Biol* 2011; **727**:171–189.

36 Grassetto G, Groheux D, Marzola MC, Hindié E, Al-Nahhas A, Rubello D. FDG PET/CT in ovarian cancer: what about treatment response and prognosis? *Clin Nucl Med* 2012; **37**:54–56.
37 Fulham MJ, Carter J, Baldey A, Hicks RJ, Ramshaw JE, Gibson M. The impact of PET-CT in suspected recurrent ovarian cancer: a prospective multi-centre study as part of the Australian PET Data Collection Project. *Gynecol Oncol* 2009; **112**:462–468.
38 Hynninen J, Auranen A, Carpén O, Dean K, Seppänen M, Kemppainen J, *et al*. FDG PET/CT in staging of advanced epithelial ovarian cancer: frequency of supradiaphragmatic lymph node metastasis challenges the traditional pattern of disease spread. *Gynecol Oncol* 2012; **126**:64–68.
39 Bagade S, Fowler KJ, Schwarz JK, Grigsby PW, Dehdashti F. PET/MRI evaluation of gynecologic malignancies and prostate cancer. *Semin Nucl Med* 2015; **45**:293–303.