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REVIEW ARTICLE

Diagnostic accuracy of integrated FDG-PET/contrast-enhanced CT in staging ovarian cancer: comparison with enhanced CT

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Abstract
Purpose The purpose of the study is to evaluate the accuracy of integrated positron emission tomography and computed tomography (PET/CT) with ^{18}F-fluorodeoxyglucose (FDG) with IV contrast for preoperative staging of ovarian cancer, in comparison with enhanced CT, using surgical and histopathological findings as the reference standard.
Materials and methods Forty patients with ovarian cancer underwent FDG-PET/contrast-enhanced CT scans for staging before primary debulking surgery. PET/CT and the CT component separately, were interpreted by two experienced radiologists by consensus for each investigation. Status with regard to lesion inside and outside the pelvis was determined on the basis of histopathology. The significance of differences between the two imaging modalities was determined using the McNemar test.
Results Staging revealed stage I in 18 patients (IA, n=9; IB, n=3; IC, n=6), stage II in seven (IIA, n=2; IIB, n=3; IIC, n=2), stage III in 14 (IIIA, n=1; IIIB, n=3; IIIC, n=10), and stage IV in one. The results of CT and PET/CT were concordant with the final pathological staging in 22 out of 40 (55%) and 30 out of 40 (75%) cases, respectively. The overall lesion-based sensitivity improved from 37.6% (32 out of 85) to 69.4% (59 out of 85), specificity from 97.1% (578 out of 595) to 97.5% (580 out of 595), and accuracy from 89.7% (610 out of 680) to 94.0% (639 out of 680) between CT and PET/CT. There were significant differences in sensitivity and accuracy, with p values of 5.6×10^{-7} and 1.2×10^{-7}, respectively.
Conclusion Integrated FDG-PET/contrast-enhanced CT is a more accurate imaging modality for staging ovarian cancer and useful for selecting appropriate treatment than enhanced CT.

Keywords Ovarian cancer · Staging · ^{18}F-FDG · PET/CT

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Introduction

Ovarian cancer is the second most common cancer of the female genital tract, but accounts for over half of all deaths related to gynecologic neoplasms [1]. The stage is determined after exploratory laparotomy and through evaluation of all specific lesions at risk in accordance with the recommendations of the International Federation of Gynecology and Obsterics (FIGO) [2]. The tumor stage at the time of diagnosis is generally considered as the most

important prognostic factor. The 5-year survival rate is 93% for stage I disease, 70% for stage II, 37% for stage III, and 25% for stage IV [3]. Primary therapy of ovarian cancer usually consists of surgical cytoreduction followed by chemotherapy, and successful cytoreductive surgery, in particular, can improve a patient's chances for long-term survival [4,5]. Hence, in the past few years, increasingly radical surgery has been used with the intention of increasing the percentage of macroscopically tumor-free patients. Patients with stage I disease would benefit from appropriate surgical treatment, as intraoperative rupture of the lesion capsule may worsen the prognosis [6]. However, patients with distant metastases, extra-abdominal spread and/or liver and peritoneal spread at presurgical staging (stage IIIC or IV) are more suitable for neoadjuvant chemotherapy before considering surgical intervention [7]. Therefore, accurate staging of patients with ovarian cancer before treatment is important for determining the most appropriate therapy.

Conventional morphological imaging modalities including TVUS, radiography, computed tomography (CT), and magnetic resonance (MR) imaging have been widely used to stage ovarian cancer [8–20]. Especially, multidetector CT (MDCT) allows the routine acquisition of sections 0.5- to 2-mm thick over large volumes, and the data can then be manipulated on an interactive display in multiple planes [15,16]. Small lesions can be detected more easily in coronal or sagittal reformatted images, which have fewer artifacts at MDCT.

In contrast to these morphological imaging modalities, positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG), which exploits the increased utilization of glucose by malignant cells and thereby their high glucose uptake, has opened a new field in clinical imaging and is widely used for staging, restaging, therapeutic response monitoring, and prognostication in patients with various cancers. Integrated PET/CT, in which a full-ring-detector clinical PET scanner and MDCT scanner are combined, makes it possible to acquire both metabolic and anatomic imaging data using a single device in a single diagnostic session and provides precise anatomic localization of suspicious areas of increased FDG uptake [21,22]. Although many reports have described the usefulness of integrated PET/CT for assessing recurrence of ovarian cancer [23–28], to our knowledge, only one study of PET [29] and one study of integrated PET/CT [30] for staging of ovarian cancer have been reported. Castellucci et al. [30] did not involve the use of intravenous contrast material for the CT component of PET/CT scan. The purpose of the present study was to assess the role of PET/contrast-enhanced CT for staging ovarian cancer prior to surgery, compared with enhanced CT, using histopathological results as reference standards.

Materials and methods

Patients

Between April 2006 and April 2008, 65 women with suspicion of ovarian cancer who had not received any therapy underwent FDG-PET/contrast-enhanced CT examinations for cancer staging in our PET center. Twenty-five women who had not received primary debulking surgery in our institute because of having distant metastasis or receiving some therapy at another hospital were excluded in this study. The remaining 40 patients (age range 38–77 years; mean 55.4 years) with ovarian cancer received primary cytoreductive surgery without neoadjuvant chemotherapy after PET/CT examinations, and they were enrolled in this study with the approval of the institutional review board. Informed consent was obtained from each patient after the nature of the procedures had been fully explained.

FDG-PET/CT study

Whole-body imaging was performed using a combined PET/CT scanner (Biograph, Sensation 16 PET/CT, Siemens AG, Erlangen, Germany). CT covered a region ranging from the meatus of the ear to the mid-thigh. The technical parameters of the 16-detector row helical CT scanner were a gantry rotation speed of 0.5 s, a table speed of 24 mm per gantry rotation. The PET component of the combined imaging system had an axial view of 16.2 cm (per bed position) with an interslice spacing of 3.75 mm in one bed position and provided an image from the meatus of the ear to the mid-thigh with six to seven bed positions. The transaxial field of view and pixel size of the PET images reconstructed for fusion were 58.5 cm and 4.57 mm, respectively, with a matrix size of 128×128. To avoid artifacts caused by the urinary tract, patients were asked to drink 1,000 ml of water 1–2 h prior to image acquisition, and to void just before the start of acquisition. No urinary bladder catheterization was used. After at least 4 h of fasting, patients received an intravenous injection of 4.0 MBq/kg body weight of FDG. The blood glucose levels were checked in all patients before FDG injection, and no patients showed a blood glucose level of more than 160 mg/dl.

About 50 min later, initially unenhanced low-dose CT was performed at 140 kV and 40 mA for attenuation correction of PET image. A whole-body emission PET scan was performed immediately after the low-dose CT, with a 3-min acquisition per bed position using a three-dimensional acquisition mode. Attenuation-corrected PET images were reconstructed with an ordered-subset expectation maximization iterative reconstruction algorithm (eight subsets, three iterations). Finally, diagnostic contrast-

enhanced full-dose CT was performed for the same axial coverage at 140 kV and 230 mA, with 2-mm slice thickness. Intravenous administration of a total volume of 150 mL (maximum) or 2 mL/kg of iodinated contrast material (Iomeprole 300, Eisai, Tokyo, Japan) containing 300 mg of iodine per milliliter via power injection at a rate of 2.5 mL/s was performed, and the scan of neck~thorax, upper~middle abdomen, and lower abdomen~pelvis was started at 45, 75, and 90 s, respectively, after injection. Oral contrast agent was not administered. PET, CT, and fused PET/CT images were generated for review on a computer workstation (AZE Virtual Place Version 3.0035).

Image analysis

Ovarian cancer is surgically staged primarily on the basis of 17 specific sites, which have been detailed by Bristow et al. [1] and Forstner et al. [9] and are also important for ovarian cancer staging in accordance with the modified recommendations of the FIGO criteria. These 17 specific sites include the contralateral ovary, uterus, pelvic sidewall, rectosigmoid colon, urinary bladder, pelvic peritoneum (cul-de-sac), peritoneum of the anterior abdomen, paracolic gutter, diaphragm, omentum, mesentery, serous membrane of the small and large bowel, liver surface, pelvic LN, paraaortic LN, liver, and lung.

Enhanced full-dose CT component images were retrospectively evaluated in consensus by two experienced radiologists (readers A and B with 8 and 20 years of experience in CT, respectively) who had knowledge of neither the other imaging results nor the clinical data. CT images were viewed in coronal, axial, and sagittal sections and inspected, and appropriate windowings were applied. The criteria for the spread of cancer as determined by CT were modified from those described by Forstner et al. [9] and Coakley et al. [12]. In brief, tumor presence was defined as unilateral or bilateral. Uterine invasion was diagnosed when there was localized distortion of the uterine contour or an irregular interface between the tumor and the myometrium. Invasion of the rectosigmoid colon or urinary bladder was diagnosed when there was subtle nodule linear contrast enhancement. Invasion of the pelvic side wall included direct invasion of the muscular pelvic side wall or of pelvic side wall vessels. Imaging criteria for pelvic side wall invasion were presence of a tumor less then 3 mm away from the pelvic side wall or iliac vessels that were surrounded or distorted by the tumor. Peritoneal implantation was diagnosed when nodular, plaque-like, or infiltrative soft tissue lesions with abnormal enhancement were seen in the peritoneal fat or on the peritoneal surface. Omental invasion was diagnosed when there was an infiltrative (feathery pattern), nodular, or cake-like appearance of enhanced soft tissue in the omentum. Invasion of the small or large bowel was diagnosed when irregular thickening or distortion with abnormal enhancement was evident in the bowel wall. LNs with a short-axis diameter greater than 10 mm were defined as malignant. Furthermore, the presence of a central unenhanced area suggesting central necrosis was considered a sign of malignancy, and the presence of peripheral low attenuation suggesting a fatty hilum within a LN was considered a benign sign, regardless of node size [31,32].

Integrated FDG-PET/contrast-enhanced CT images were retrospectively interpreted in consensus by two experienced radiologists (readers C and D with 3 and 5 years of experience in PET/CT, respectively) who had knowledge of neither the other imaging results nor the clinical data. Attenuation-corrected PET images, contrast-enhanced full-dose CT images and co-registered fused images were displayed together on the monitor. An involved lesion was diagnosed when abnormal focal FDG uptake observed on PET images corresponded to an abnormal mass on CT. LNs with increased glucose uptake were deemed positive for metastatic spread, even if they were smaller than 1 cm in short-axis diameter. Conversely, LNs with no detectable tracer uptake were deemed negative for metastatic spread, even if they were larger than 1 cm in short-axis diameter. Semiquantitative analysis was not done in this study. This method of PET/CT image analysis was based on previous studies [31–33].

Operative procedures and histopathological evaluation

All patients underwent surgical staging within 2 weeks of the PET/CT examination. Laparotomy staging involved total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and lymphadenectomy. In all patients, resection or cytoreduction or biopsy of peritoneal implants was performed throughout the abdomen and pelvis; the sites were the pelvis (cul-de-sac), the anterior abdomen, paracolic gutter, the small and large bowel surfaces, mesentery, diaphragm, liver, and spleen. At surgery and biopsy or cytology, the presence or absence of tumor tissue at 17 specific sites was recorded. When the patient had pleural effusion or liver metastasis, aspiration biopsy was performed to prove the existence of malignant cells. The surgical specimens were histopathologically evaluated by an experienced pathologist, who was blinded to the imaging results.

Statistical analysis

Overall staging accuracy was assessed separately for CT component and for PET/CT. We also performed site-based analyses of the 17 regions by comparing the results for CT alone with those for PET/CT based on the general consensus verdict. Sensitivity, specificity, and accuracy were

calculated using standard statistical formulae. McNemar test was used to determine the significance of differences between two imaging modalities. Differences were considered significant at P values of less than 0.05.

Results

Final histopathologic analysis of the primary ovarian tumors demonstrated papillary serous adenocarcinoma (n=11 cases), mucinous cystadenocarcinoma (n=7), clear cell carcinoma (n=7), undifferentiated adenocarcinoma (n=6), endometrioid adenocarcinoma (n=5), and serous cystadenocarcinoma (n=4). The final staging revealed stage I in 18 patients (IA, n=9; IB, n=3; IC, n=6), stage II in seven (IIA, n=2; IIB, n=3; IIC, n=2), stage III in 14 (IIIA, n=1; IIIB, n=3; IIIC, n=10), and stage IV in one, according to the FIGO criteria.

Overall staging accuracy was assessed separately for CT alone and for PET/CT using the modified FIGO criteria (Table 3). The results for CT alone were concordant with the final pathological staging in 22 out of 40 patients (55.0%), and the results for PET/CT were concordant with the final pathological staging in 30 out of 40 patients (75.0%). CT alone incorrectly up-staged five patients (one patient was staged IIA instead of IA; one was staged IIB instead of IB; one was staged IIIB instead of IIA; and two were staged IV instead of IC, IIIC) and incorrectly down-staged 13 patients (four patients were staged IA instead of IB, IC, IIA, and IIB; one was staged IB instead of IIC; three were staged IIA instead of IIC, IIIB, and IIIC; two were staged IIB instead of IIIA, IIIB; and three were staged IIIB instead of IIIC, IIIC, and IV). PET/CT incorrectly up-staged three patients (one patient was staged IIB instead of IB; and two were staged IIIB instead of IIB, IIC) and incorrectly down-staged seven patients (three patients were staged IA instead of IB,IC, and IIB; one was staged IIA instead of IIC; two were staged IIB instead of IIIA, IIIB; and one was staged IIIB instead of IIIC). Two patients who were incorrectly up-staged as IV (splenic metastasis, liver metastasis) by CT alone and correctly diagnosed by PET/CT had splenic hamartoma and liver hemangioma, respectively. One patient who was correctly staged as IV by PET/CT and incorrectly down-staged IIIB by CT alone had lung metastasis.

As shown in Table 1, when diagnostic accuracy for lesions inside the pelvis was compared between CT alone and PET/CT, the sensitivity improved from 35.1% (13 out of 37) to 62.2% (23 out of 37), specificity from 94.6% (192 out of 203) to 96.6% (196 out of 203), and accuracy from 85.4% (205 out of 240) to 91.3% (219 out of 240). Although the specificity did not differ significantly between the two imaging modalities (McNemar test; p=0.13), there were significant differences in sensitivity and accuracy, with p values of 0.0044 and 0.00051, respectively (McNemar test).

Table 1 Inside pelvic lesion-based diagnostic accuracy of CT alone and PET/CT

Site	TP	FN	TN	FP	Sensitivity (%)	Specificity (%)	Accuracy (%)
Contralateral ovary							
CT	6	4	28	2	60	93	85
PET/CT	8	2	29	1	80	97	93
Invasion of uterus							
CT	3	7	27	3	30	90	75
PET/CT	6	4	28	2	60	93	85
Pelvic sidewall invasion							
CT	1	2	35	2	33	95	90
PET/CT	2	1	35	2	67	95	93
Rectosigmoid colon							
CT	1	3	34	2	25	94	88
PET/CT	2	2	35	1	50	97	93
Urinary bladder							
CT	0	2	37	1	0	97	93
PET/CT	1	1	38	0	50	100	98
Pelvic peritoneum (cul-de-sac)							
CT	2	6	31	1	25	97	75
PET/CT	4	4	31	1	50	97	80
Total lesions							
CT	13	24	192	11	35	95	85
PET/CT	23	14	196	7	62	97	91

TP True positive, FN false negative, *TN* true negative, *FP* false positive

As shown in Table 2, when diagnostic accuracy for lesions outside the pelvis was compared between CT alone and PET/CT, the sensitivity improved from 39.6% (19 out of 48) to 75.0% (36 out of 48), and accuracy from 92.0% (405 out of 440) to 95.5% (420 out of 440), whereas specificity was reduced from 98.5% (386 out of 392) to 98.0% (384 out of 392). Although the specificity did not differ significantly between the two imaging modalities (McNemar test; p=1.0), sensitivity and accuracy differed significantly with p values of 0.0001 and 0.00018, respectively (McNemar test).

For lesions both inside and outside the pelvis, the overall sensitivity improved from 37.6% (32 out of 85) to 69.4% (59 out of 85), specificity from 97.1% (578 out of 595) to 97.5% (580 out of 595), and accuracy from 89.7% (610 out of 680) to 94.0% (639 out of 680). Although the specificity did not differ significantly between the two imaging modalities (McNemar test; p=0.07), sensitivity and accuracy differed significantly with p values of 5.6×10^{-7} and 1.2×10^{-7}, respectively (McNemar test).

The mean short-axis diameter of metastatic peritoneal lesions detected by PET/CT was 10.2±4.2 (range 4–23 mm) and that of the missed metastatic peritoneal lesions was

Table 2 Outside pelvis lesion-based diagnostic accuracy of CT alone and PET/CT

Site	TP	FN	TN	FP	Sensitivity (%)	Specificity (%)	Accuracy (%)
Peritoneum of anterior abdomen							
CT	3	3	34	0	50	100	93
PET/CT	5	1	34	0	83	100	98
Paracolic gutter							
CT	1	2	36	1	33	97	93
PET/CT	2	1	37	0	67	100	98
Diaphragm							
CT	0	1	39	0	0	100	98
PET/CT	1	0	39	0	100	100	100
Omentum							
CT	3	6	30	1	33	97	83
PET/CT	5	4	30	1	56	97	88
Mesentery							
CT	2	5	32	1	29	97	85
PET/CT	4	3	31	2	57	94	88
Serous membrane of small and/or large bowel							
CT	2	2	34	2	50	94	90
PET/CT	3	1	33	3	75	92	90
Liver surface							
CT	2	0	38	0	100	100	100
PET/CT	2	0	38	0	100	100	100
Pelvic lymph node							
CT	3	5	32	0	38	100	88
PET/CT	6	2	32	0	75	100	95
Paraaortic lymph node							
CT	3	5	32	0	38	100	88
PET/CT	7	1	30	2	88	94	93
Liver							
CT	0	0	39	1	NA	95	98
PET/CT	0	0	40	0	NA	100	100
Lung							
CT	0	1	39	0	0	100	98
PET/CT	1	0	39	0	100	100	100
Total lesions							
CT	19	29	386	6	40	98	92
PET/CT	36	12	384	8	75	98	95

TP True positive, *FN* false negative, *TN* true negative, *FP* false positive

3.8±1.4 (range 2–6 mm), respectively. The mean short-axis diameter of metastatic lymph nodes detected by PET/CT was 7.3±1.4 (range 5–9 mm) and that of the missed nodes was 3.8±0.7 (range 1–6 mm), respectively.

We illustrate three cases which PET/CT could correctly diagnose as peritoneal disseminations and metastatic LNs (Figs. 1, 2, and 3).

Discussion

Conventional morphological imaging modalities including transvaginal ultrasonography (TVUS), radiography, CT, and MR imaging have been widely used to stage ovarian cancer [8–20] (Table 3). CT has been the most common modality, and the use of intravenous and orally administered contrast agents and a thinner slice thickness are generally recommended. Several early studies found that CT had an accuracy of 70–90% for preoperative staging of ovarian cancer [9] and a sensitivity of 63–92% and specificity of 82–96% for detection of peritoneal involvement [10,12]. Ricke et al. [13] reported that MR imaging with fat-saturated gadopentetate dimeglumine-enhanced T1-weighted sequences had good accuracy for diagnosing pelvic and abdominal cancer spread in patients with ovarian cancer, showing 71–87% sensitivity and 44–87% specificity for peritoneal dissemination, and 64% sensitivity and 75% specificity for pelvic and paraaortic lymph node (LN) metastasis. Although several early studies demonstrated that MR imaging was superior to CT for staging ovarian cancer [9,14], this advantage has been largely

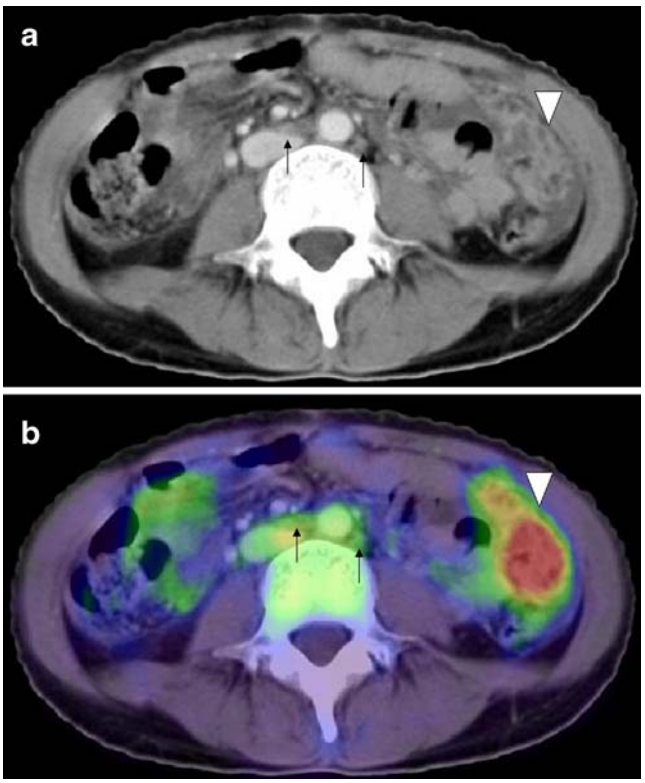

Fig. 1 A 55-year-old woman of stage IIIC with omental carcinomatosis and paraaortic LN metastasis. **a** Enhanced CT shows an infiltrative appearance of the omentum (*triangle*), suggesting omental involvement. Small paraaortic LNs measuring 7 and 8 mm are identified (*arrows*), which does not rule out LN metastasis on the basis of the size criterion for CT. **b** PET/contrast-enhanced CT shows abnormal FDG uptake corresponding to omentum cake (*triangle*) and small paraaortic LNs (*arrows*), suggesting the presence of omental carcinomatosis and nodal cancer spread. Histopathological examination of the resected specimen confirmed extensive omental and paraaortic LN involvement by cancer

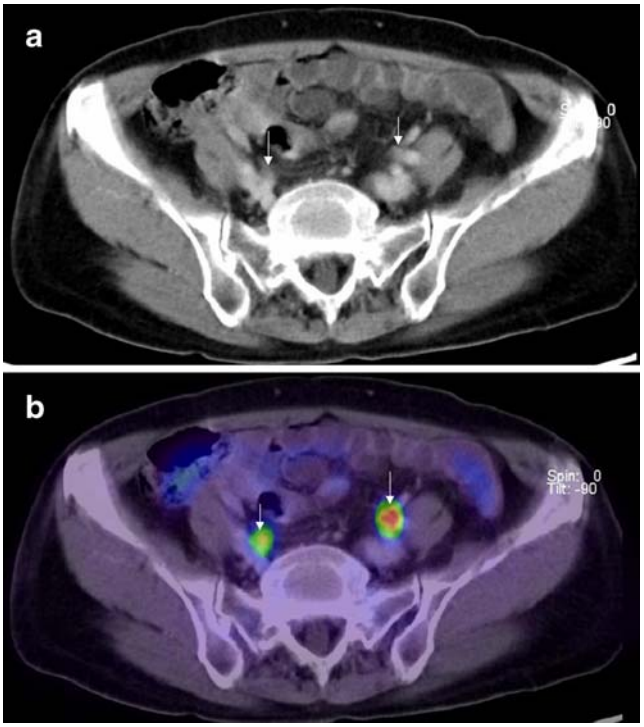

Fig. 2 A 50-year-old woman of stage IIIC with pelvic LN metastases. **a** Enhanced CT shows a small right internal iliac LN measuring 6 mm and a left internal iliac LN measuring 7 mm in short diameter (*arrows*), which does not rule out LN metastasis on the basis of the size criterion for CT. **b** PET/contrast-enhanced CT shows abnormal FDG uptake corresponding to bilateral small iliac LNs seen in (**b**; *arrows*), suggesting the presence of nodal cancer spread. Histopathological examination confirmed extensive LN cancer involvement

superseded by the advent of MDCT [15,16]. MR imaging also has the shortcomings of higher cost, problems with high-resolution imaging of the entire abdomen and pelvis, and the longer examination time required [15,18]. Moreover, peritoneal implants of ovarian serous cystadenocarcinoma may often be calcified [20], and MR imaging is unable to detect calcification. When used alone, even recent MDCT and MR imaging techniques using thin slices and contrast materials have limited usefulness for visualizing small intra-abdominal disseminated lesions and diagnosing tumor's invasion of uterus, bladder, or pelvic sidewall and LN metastases.

Although there have been several PET and PET/CT papers discriminating ovarian benign and malignant tumors [33–35], there have been two PET and PET/CT reports of discussing about staging of ovarian cancer [29,30]. Although one previous study has investigated the usefulness of integrated PET/CT [30] for the staging of ovarian cancer, it did not involve the use of intravenous contrast material for the CT component of PET/CT scan. To our knowledge, the present study is the first to have investigated the additional diagnostic value of integrated PET/contrast-enhanced CT in comparison with enhanced CT alone for staging ovarian cancer. Our results of CT and PET/CT were concordant with the final pathological staging in 55% and 75%, respectively. The overall lesion-based sensitivity improved from 37.6% to 69.4%; specificity from 97.1% to 97.5%, and accuracy from 89.7% to 94.0%. Yoshida et al. [29] reported an increase in diagnostic accuracy of PET plus separated CT in comparison to CT alone (87% vs 53%) in a small group of 15 patients with ovarian cancer. Castellucci et al. [30] reported that the diagnostic accuracy of PET/CT in comparison with enhanced CT separately was 69% vs 53% in 32 patients with ovarian cancer. The results of these two studies were similar to those of our study.

In our series, PET/CT was able to detect a higher number of malignant lesions than CT alone at 15 sites. However, even PET/CT was unable to detect tiny lesions. In our series, the minimum size of lesions detectable by PET/CT was 4 mm, and the maximum size of lesions that were not detected by PET/CT was 6 mm. In particular, the sensitivity of PET/CT for detecting cancer involvement at six sites (uterus, rectosigmoid colon, bladder, pelvic peritoneum,

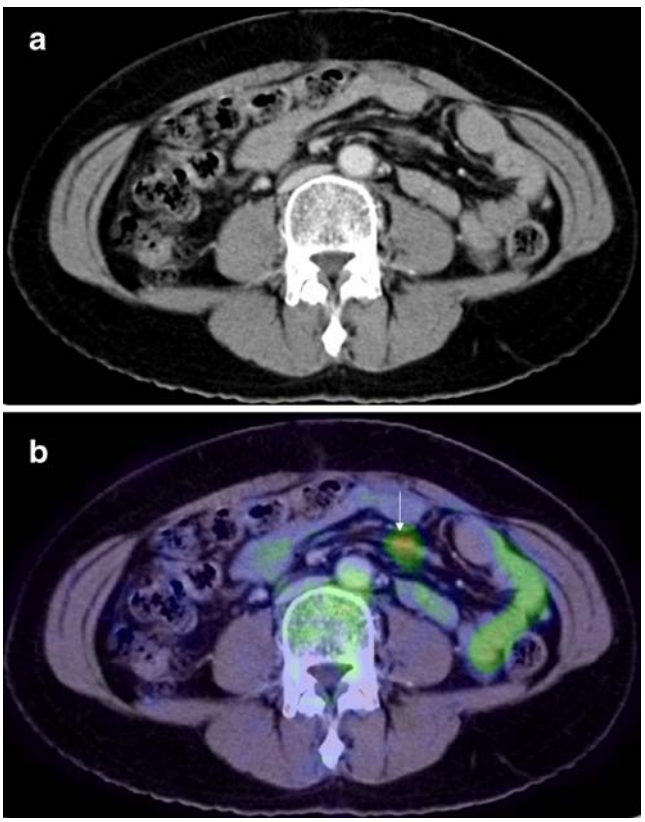

Fig. 3 A 57-year-old woman of stage IIIB with peritoneal dissemination. **a** Enhanced CT shows no abnormal findings on this slice. **b** PET/contrast-enhanced CT shows abnormal FDG uptake corresponding to a small peritoneal implant in the mesentery (*arrow*), suggesting the presence of peritoneal carcinomatosis. Histopathological examination confirmed extensive peritoneal involvement by cancer

Table 3 Diagnostic accuracy of CT alone and PET/CT for detecting clinical stage in patients with ovarian cancer

Patient	FIGO stage	CT diagnosis	PET/CT diagnosis
1	IA	IA	IA
2	IA	IA	IA
3	IA	IA	IA
4	IA	IA	IA
5	IA	IA	IA
6	IA	IA	IA
7	IA	IA	IA
8	IA	IA	IA
9	IA	IIA	IA
10	IB	IB	IB
11	IB	IA	IA
12	IB	IIB	IIB
13	IC	IC	IC
14	IC	IC	IC
15	IC	IC	IC
16	IC	IC	IC
17	IC	IA	IA
18	IC	IV	IC
19	IIA	IA	IIA
20	IIA	IIIB	IIA
21	IIB	IIB	IIB
22	IIB	IA	IA
23	IIB	IIB	IIIB
24	IIC	IB	IIA
25	IIC	IIA	IIIB
26	IIIA	IIB	IIB
27	IIIB	IIIB	IIIB
28	IIIB	IIA	IIIB
29	IIIB	IIB	IIB
30	IIIC	IIIC	IIIC
31	IIIC	IIIC	IIIC
32	IIIC	IIIC	IIIC
33	IIIC	IIIC	IIIC
34	IIIC	IIIC	IIIC
35	IIIC	IIIC	IIIC
36	IIIC	IIA	IIIC
37	IIIC	IIIB	IIIC
38	IIIC	IIIB	IIIB
39	IIIC	IV	IIIC
40	IV	IIIB	IV
Diagnostic accuracy		55% (22/40)	75% (30/40)

FIGO International Federation of Gynecology and Obsterics

omentum, and mesentery) was less than 60%. PET or PET/CT can only detect lesions with a certain volume of malignant cells sufficient to change the observed level of glucose metabolism, and neither of these modalities can detect micrometastasis [24–26,36]. Sironi et al. [24] demonstrated that PET/CT was able to diagnose 32 of 41 lesions (21 peritoneal lesions, 16 LNs, and four pelvic lesions, size range: 0.3–3.2 cm, mean size 1.7 cm; sensitivity 78%) revealed by second-look surgery in 17 patients with recurrent ovarian cancer, and a size threshold of 0.5 cm was identified for the largest missed lesion. Pannu et al. [25] demonstrated that for peritoneal lesions larger than 1 cm (n=8), 50% were detectable by PET/CT and that for peritoneal lesions no larger than 1 cm (n=23), only 13% were detectable by PET/CT in patients with recurrent ovarian cancer. Bristow et al. [26] demonstrated that PET/CT was able to diagnose only 24 of 59 retroperitoneal LN metastases (median node diameter=2.5 cm, range=0.8–5.2 cm) revealed by surgery in 11 patients with ovarian cancer recurrence (sensitivity 41%). Sironi et al. [36] demonstrated that for metastatic pelvic LNs larger than 5 mm (n=13), 100% were detected by PET/CT and that for metastatic pelvic LNs no larger than 5 mm (n=5), 0% were detected by PET/CT in 15 patients with uterine cervical cancer. With a spatial resolution of 4–6 mm with currently available PET and PET/CT systems, the detection of microscopic lesions remains challenging. Improving the spatial resolution and sensitivity of PET and PET/CT scanners and developing new, more specific radioactive tracers may help to overcome this limitation in the future.

In our series, PET/CT also showed specificity that was better than or equal to CT alone at 14 sites and worse specificity at three sites (small and large bowel surface, mesentery, and paraaortic LN). Physiological FDG uptake in the intestine and nonpathologic FDG uptake in the inflammatory nests of the intestine were overdiagnosed as peritoneal dissemination by PET/CT. Nonpathological FDG uptake in follicular hyperplasia with inflammatory granulation tissue in paraaortic LN were overdiagnosed as LN metastasis by PET/CT.

The overall node-based sensitivity, specificity, and accuracy of CT alone for detection of pelvic LN and paraaortic LN metastases were 37.5% (six out of 16), 100% (64 out of 64), and 87.5% (70 out of 80), respectively, and those of PET/CT were 81.3% (13 out of 16), 96.9% (62 out of 64), and 93.8% (75 out of 80), respectively. PET/CT was significantly more sensitive than CT alone (McNemar test; p=0.023). Because identification about metastatic LNs provided by morphological imaging modalities such as CT and MR is based on measurement of node size, with a short-axis diameter exceeding 10 or 8 mm being the most accepted criterion for diagnosis of nodal involvement, the sensitivity of CT and MR imaging for diagnosis of metastatic LNs is relatively low. Tempany et al. [10] reported that the sensitivity and specificity of CT and MR imaging for detection of LN metastasis in patients with ovarian cancer were 40% and 85–90%, respectively, using a size criterion of 1 cm. Ricke et al. [13] evaluated the performance of MR imaging for assessing pelvic and paraaortic LNs and demonstrated that the overall sensitivity and specificity for LN detection were 64% and 75%. However, PET is a functional method based on the increased glucose metabolism of cancer cells, regardless

of node size, and it seems that PET and PET/CT enable the detection and localization of tiny metastatic LNs. Although PET and PET/CT could sometimes detect metastatic LNs smaller than 1 cm, the sensitivity of these modalities is insufficient because of their low spatial resolution [26, 36]. Moreover, PET and PET/CT are not 100% specific for diagnosis of LN metatasis because follicular or sinusoidal hyperplasia with inflammatory granulation tissue in LNs often show abnormal FDG uptake, as was the case in our series.

In addition to staging, imaging can be used for selecting appropriate treatment. Although CT alone incorrectly down-staged four of 11 patients with stage IIIC–IV as stage I–IIIB, PET/CT incorrectly down-staged only one of 11 patients with stage IIIC–IV as stage I–IIIB (paraaortic LN metastasis was missed due to lack of FDG uptake in one patient by PET/CT). Although CT alone incorrectly up-staged one of 29 patients with stage I–IIIB as stage IIIC–IV (liver hemangioma was misdiagnosed as metastasis), this overdiagnosis was not observed at PET/CT. When patients are divided in stage IIIC–IV and I–IIIB, the sensitivity, specificity, and accuracy improved from 64% (seven out of 11) to 91% (ten out of 11), 97% (28 out of 29) to 100% (29 out of 29), and 88% (35 out of 40) to 98% (39 out of 40), respectively, compared between CT alone and PET/CT. PET/CT imaging can help identify that very important group of patients with stage IIIC–IV disease for whom optimal debulking is not possible and who may be more optimally treated with preoperative chemotherapy.

Because we used unenhanced low-dose CT for attenuation correction in our series to prevent overestimation of PET attenuation factors by contrast media when IV contrast-enhanced CT is used for attenuation, the problem of high radiation exposure has occurred. Recent report has demonstrated that there is an increase in standardized uptake value in normal and pathologic regions of high concentration when IV contrast-enhanced CT is used for attenuation; this increase is clinically insignificant in the evaluation of patients with cancer, and contrast-enhanced CT could be used for attenuation correction [37]. Further study in a larger patient population is needed to elucidate the efficacy, radiation exposure, and cost-effectiveness of enhanced full-dose PET/CT.

This study had certain limitations. First, the patient population was relatively small. Because we excluded some patients who had undergone neoadjuvant chemotherapy before primary debulking surgery because of apparent distant metastasis, there was a bias in the selected patients. Therefore, the proportion of patients with advanced disease (stage III and IV) in our series may have been lower than the actual trend. More studies with a larger sample size will be needed to help verify the accuracy of PET/CT. Second, no oral contrast materials were used in our series. Adding an oral contrast agent would likely help to better delineate normal bowel activity and demonstrate pathologic intra-abdominal activity (peritoneal implantation). Third, the CT images in our series were acquired as part of a PET/CT study, and we did not directly compare the diagnostic performance of PET/CT with separate CT.

In conclusion, integrated FDG-PET/contrast-enhanced CT is a more accurate imaging modality for staging of ovarian cancer than enhanced CT alone. Although PET/CT is not perfect, it can help to identify that very important group of patients who may be more appropriately treated with preoperative chemotherapy.

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