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SPECIAL SECTION: OVARIAN CANCER

Diagnostic performance of PET/CT and PET/MR in the management of ovarian carcinoma—a literature review

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Abstract

Ovarian cancer is a challenging disease. It often presents at an advanced stage with frequent recurrence despite optimal management. Accurate staging and restaging are critical for improving treatment outcomes and determining the prognosis. Imaging is an indispensable component of ovarian cancer management. Hybrid imaging modalities, including positron emission tomography/computed tomography (PET/CT) and PET/magnetic resonance imaging (MRI), are emerging as potential non-invasive imaging tools for improved management of ovarian cancer. This review article discusses the role of PET/CT and PET/MRI in ovarian cancer.

Keywords PET/CT · PET/MRI · Ovarian cancer · Imaging · FIGO

Introduction

Ovarian cancer (OC) is one of the leading causes of death from gynecologic cancer in the United States [1]. OCs are often metastatic at the time of presentation, and are associated with a high rate of recurrence and poor prognosis [2]. Ovarian neoplasms are classified histogenetically by cell subtype: epithelial, stromal, or germ cell. Epithelial OC comprises 90% of malignant ovarian tumors [3]. OC metastases may occur due to peritoneal, lymphatic, or hematogenous spread. Peritoneal implantation of cancer cells most commonly occurs along the peritoneal surfaces within the pelvis, bowel, liver surface, omentum, or diaphragm. Lymphatic drainage from the ovaries can cause external and common iliac, para-aortic, inguinal, and supraclavicular lymphadenopathy. Hematogenous spread most often affects the liver, lungs, brain, and bones [4–6].

Malignant ovarian tumors are usually first seen by imaging—transvaginal ultrasonography (TVUS) or abdominal contrast-enhanced computed tomography (CT)—and the diagnosis is supported by the finding of elevated levels of the serum biomarker CA125 [7–9]. While CT is the most common imaging test used for staging and surveillance, other modalities are being increasingly used in the management of ovarian cancer. In this review, we discuss the current clinical role of positron emission tomography (PET)/CT and PET/magnetic resonance imaging (MRI) for the identification, staging, and restaging of OC, as well as evaluation of treatment response. We also discuss our experience with PET/MRI in imaging OC, with emphasis on the advantages and challenges of this new hybrid imaging modality in gynecologic cancers.

PET/CT

Since its introduction in the 1990s, PET/CT has become an extremely useful imaging modality for staging, restaging, and assessment of treatment response in oncology [10]. In this section, we will discuss the role of PET/CT in characterization of adnexal mass, staging of ovarian cancer, evaluating treatment response and prognostication and in the management of recurrent disease.

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Role in characterization of an adnexal mass

PET/CT is not commonly used to characterize an adnexal mass, as physiologic uptake may be seen in normal ovaries, limiting its value. However, several authors have reported on the utility of PET/CT in characterization of pelvic masses (Table 1) [11]. Studies show that PET CT has 81–100% sensitivity and 93–95% specificity for diagnosing malignant ovarian tumor [12, 13].

PET/CT can also aid in distinguishing borderline ovarian tumors from OCs. In a retrospective assessment of 13 patients, PET/CT reported good sensitivity (83.3%), specificity (85.7%), and area under curve value (0.893; $p = 0.0001$) in distinguishing borderline ovarian tumors from stage I malignant ovarian tumors [16]; a cutoff maximum standard uptake value (SUV_{max}) of 3.7 differentiated borderline ovarian tumors from stage I malignant ovarian tumors. Similarly, in a prospective study of 30 patients the SUV_{max} in borderline tumors (2.0 ± 0.70) was significantly lower than that of malignant tumors (9.32 ± 4.58), but not significantly different compared with benign tumors (1.74 ± 1.44, $p = 0.005$) [22]. For detection of malignant or borderline malignant pelvic tumors, the sensitivity was 71.4% and the specificity was 81.3%, and for OC, the sensitivity was 100% and the specificity was 85.0%. In concordance with prior studies, another retrospective study of 171 ovarian cancer patients reported a strong glycolytic phenotype (average SUV_{max} 7.6) in epithelial OC [20].

Few studies have compared the diagnostic performance of PET/CT with that of TVUS, CT, and MRI. Although TVUS remains the standard initial screening method for suspicious adnexal findings [15, 18], PET/CT can provide additional value to TVUS or CT findings. Castellucci et al. reported that PET/CT, compared with TVUS, had similar sensitivity (87% vs 90%), specificity (100% vs 61%), negative predictive value (81% vs 78%), positive predictive value (100% vs 80%), and accuracy (92% vs 80%) in characterizing ovarian lesions [14]. A prospective study reported that PET/CT, compared with CT, had higher specificity (77% vs 38%) and similar sensitivity (93% vs 96%) for characterizing malignant tumors [21]. Similarly, another prospective study also reported higher accuracy for PET/CT (92.1%) compared with pelvic ultrasonography (83.0%) and abdominopelvic CT or pelvic MRI (74.9%; $p = 0.013$) in distinguishing malignant or borderline ovarian tumors from benign tumors [19].

While the above studies report the utility of PET CT in diagnosing ovarian tumors, its cost effectiveness for this purpose remains unproven. Currently, pelvic ultrasound and MR are the most commonly used imaging modality for the diagnosis and characterization of ovarian tumors.

Role in staging of OC

PET/CT an effective imaging modality for staging OC, with 75.5–83.3% sensitivity, 68.4–99.4% specificity, 87.5–95.3% positive predictive value, and 96.5–98.6% negative predictive value (Table 2) [23, 24]. PET/CT findings can lead to an alteration in FIGO stage and modifications in the treatment plan. One study reported migration of FIGO stage III to stage IV OC after PET/CT in 26% of patients [25]. Similarly, another prospective study reported upstaging to stage IV in 41% (27/66) of patients with advanced OC [26].

PET/CT has also shown better performance in staging OC compared with other modalities (CT or MRI). A meta-analysis reported that PET/CT was more accurate (sensitivity 73.2%, specificity 96.7%, odds ratio 90.32) than CT and MRI in detection of lymph node metastasis in OC [31]. In another prospective assessment, PET/CT was superior to CT for the detection of carcinomatosis in subdiaphragmatic peritoneal surfaces ($p = 0.020$) and in the bowel mesentery ($p = 0.001$) in advanced epithelial OC [29]. PET/CT also detected higher rates of extra-abdominal disease spread than did CT (78% vs 60%). Similar results were obtained in another retrospective study of 40 patients [27]. PET/CT had higher lesion-based sensitivity (69.4% vs 37.6%), specificity (97.5% vs 97.1%), and accuracy (94.0% vs 89.7%) in preoperative staging of OC, when compared to CT. There were significant differences ($p < 0.05$) in sensitivity and accuracy between the imaging modalities. In addition, Dauwen et al. reported that PET/CT was better than CT in detecting retroperitoneal lymph node metastases, but not in detecting peritoneal metastases [21]. There was no statistically significant difference between the two modalities for FIGO staging.

Role in OC treatment prognosis and response evaluation

The metabolic parameters of PET/CT, such as SUV_{max}, total lesion glycolysis (TLG), and metabolic tumor volume (MTV), can provide important prognostic information and assess response to treatment (Fig. 1; Table 3). A prospective study with 33 metastatic ovarian cancer patient reported a significant correlation between PET metabolic response after the first (SUV_{max} 4.9 ± 2.8, $p < 0.008$) and third (SUV_{max} 3.5 ± 2.8, $p < 0.005$) cycle of chemotherapy with overall survival in advanced-stage OC [32]. Liao et al. reported that in post-surgery OC patients, high whole-body TLG was associated with poor prognosis (hazard ratio 1.043, $p = 0.011$) [33]. In yet another study, higher TLG was reported as an independent prognostic factor ($p = 0.008$) for disease progression after cytoreductive surgery in OC [34].

Table 1 Studies evaluating positron emission tomography/computed tomography (PET/CT) for the characterization of benign and malignant adnexal lesions

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Castellucci et al. [14]	P	50 (32 ovarian cancer, 18 benign ovarian lesions)	Malignancy criteria of focally increased 18F-FDG uptake with $SUV_{max} > 3.0$	TVUS	PET/CT: sensitivity 87%, specificity 100%, NPV 81%, PPV 100%, accuracy 92%; TVUS: sensitivity 90%, specificity 61%, NPV 78%, PPV 80%, accuracy 80%	PET/CT provides additional value to TVUS for the differential diagnosis of benign from malignant pelvic lesions
Tanizaki et al. [13]	P	160 (67 malignant tumors, 14 borderline malignant tumors, 79 benign tumors)	Optimal cutoff SUV_{max} for detecting ovarian cancer was found to be 2.90	–	Sensitivity 80.6%, specificity 94.6%, PPV 91.5%, NPV 87.1%	PET/CT is useful for the preoperative differential diagnosis of ovarian cancer from benign tumors
Rieber et al. [15]	P	103 (12 malignant ovarian tumors and 91 benign ovarian tumors)	For PET/CT, TP: 7/12, FP: 20/91, FN: 3/5, TN: 71/91	TVUS, MRI, PET	Sensitivity: MRI 83%, TVUS 92%, PET 58%, consensus diagnosis 92%; specificity: MRI 84%, TVUS 59%, PET 78%, consensus diagnosis 84%; diagnostic accuracy: MRI 83%, TVUS 63%, PET 76%, consensus diagnosis 85%	TVUS should be the primary screening method for suspicious adnexal findings
Kim et al. [16]	R	Borderline ovarian cancer ($n=7$) and malignant ovarian cancer ($n=6$)	SUV_{max} 3.7 was the best cutoff value to differentiate borderline from malignant tumors	–	Sensitivity 83.3%, specificity 85.7%, area under the curve 0.893 ($p=0.0001$)	SUV_{max} could distinguish borderline ovarian tumors from stage I malignant ovarian tumors, with high sensitivity and specificity
Risum et al. [12]	P	97 (40 benign tumors and 57 malignant tumors)	–	–	Sensitivity 100% (57/57) and specificity 92.5% (37/40) in diagnosing a malignant pelvic tumor ($p<0.00005$)	PET/CT demonstrates high diagnostic value
Fenchel et al. [17]	P	99 (12 malignant, 87 benign)	FP PET results were obtained in five of seven	PET, MRI, ultrasound	Overall sensitivity 58% (95% CI 27.7–84.8%) and specificity 76% (95% CI 65.5–84.4%) for FDG PET	Sensitivity of ultrasound is as high as that of PET and MRI and remains the method of choice for diagnosis
Hubner et al. [18]	P	51 (15 malignant)	Mean SUV_{max} for carcinoma was 6.12 ± 3.53	–	PPV 86%, NPV 76%	Useful in identifying ovarian malignancy
Nam et al. [19]	P	133 (25 benign tumors, 13 borderline tumors, 95 malignant tumors)	Sensitivity 97.9%, specificity 73.7%, PPV 90.2%, NPV 93.3% for ovaries and adnexa	ultrasound, CT, MRI	In distinguishing malignant/borderline from benign ovarian tumors, the accuracy of PET/CT (92.1%) was higher than that of pelvic ultrasound (83.0%) and abdominopelvic CT or pelvic MRI (74.9%; $p=0.013$)	PET/CT is superior to pelvic ultrasound, abdominopelvic CT, and pelvic MRI for diagnosis of malignant ovarian tumors
Karantanis et al. [20]	R	171 (32 serous ovarian cancer, 28 grade III epithelial ovarian cancer)	SUV_{max} averaged 7.76 for grade I, 6.76 for grade II, and 7.95 for grade III	–	Ovarian cancer exhibited a strong glycolytic phenotype (average SUV_{max} 7.6)	Glycolytic phenotype in epithelial ovarian cancer, expressed as SUV_{max}, is strong

Table 1 (continued)

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Dauwen et al. [21]	P	69 (56 malignant, 13 benign)	Median SUV_{max} 3.61 (range 0.89–7.97) for borderline, 15.71 (range 0.59–32.45) for malignant, and 2.39 (range 1.07–25.39) for benign tumors	CT	PET/CT sensitivity 93% and specificity 77% for malignant tumors; for CT alone, sensitivity 96% and specificity 38%	Similar sensitivity, but higher specificity for PET/CT than for CT alone
Yamamoto et al. [22]	P	30	SUV_{max} in borderline tumors (2.0 ± 0.70) was lower than in malignant tumors (9.32 ± 4.58; $p = 0.005$)	–	FDG PET/CT: sensitivity 71.4% and specificity 81.3% to detect malignant or borderline malignant pelvic tumors; sensitivity 100% and specificity 85.0% to detect ovarian cancer	PET/CT has high diagnostic value in differentiating between malignant and benign tumors

P prospective, SUV_{max} maximum standardized uptake value, *TVUS* transvaginal ultrasonography, *PPV* positive predictive value, *NPV* negative predictive value, *TP* true positive, *FP* false positive, *FN* false negative, *TN* true negative, *MRI* magnetic resonance imaging, *R* retrospective, *CI* confidence interval

PET/CT may also be useful in predicting prognosis in OC. One study reported that larger fractional decrease in TLG after 2 weeks of systemic therapy predicted partial response after 10 weeks ($p = 0.037$) in ovarian, breast, and endometrial cancers [46]. Also, a rise in SUV between the second and sixth week predicted progression ($p = 0.034$) was associated with worse progression-free survival (hazard ratio 1.068, $p = 0.013$). Vallius et al. reported that the median omental SUV_{max} change during neoadjuvant chemotherapy (NACT) was − 64% (range − 16% to − 84%) and was associated with treatment response ($p = 0.004$) [36]. The SUVmax decrease < 57% enabled identification of non-responders to NACT. In another study by the same group, MTV reduction < 85% was associated with progressive (PD)/stable disease (SD) (70% sensitivity, 78% specificity, 0.79 AUC) and was able to identify candidates who may benefit by a change in management [35]. Similarly, poor outcome in epithelial OC was associated with higher values for MTV ($p = 0.022$, hazard ratio 5.571) and TLG ($p = 0.037$, hazard ratio 2.967) [38]. Gallicchio and colleagues compared all metabolic parameters for patients with peritoneal carcinomatosis from epithelial OC and reported that a quantitative assessment of MTV ($p = 0.01$), rather than SUV_{max} ($p = 0.48$) or TLG ($p = 0.06$), was helpful for stratifying patients [41]. MTV survival analysis showed significantly better OS in patients presenting with a high tumor burden than in those presenting with less burden ($p = 0.01$; 26 months vs 14 months); the higher the MTV, the better the response to chemotherapy [41].

Role in recurrent OC

Tumor recurrence is identified in 60–70% of OC patients and is one of the main prognostic factor in OC [47]. Hence early identification of tumor recurrence is critical in restaging and optimal management (Fig. 2; Table 4).

PET/CT is reported to have 41–97% sensitivity, 86–100% specificity, and 83–97% accuracy [49–52, 56, 60, 63–65, 67, 71, 73–75]. The quantitative metabolic parameters from PET have been associated with optimal surgery outcome and progression-free survival in recurrent OC [66, 69]. A retrospective study of 56 recurrent OC patients showed that whole-body MTV and whole-body TLG (p = 0.008 for both) were significant prognostic factors for post-relapse survival (median PRS duration for surviving patients was 35 months, range 16–90 months).[69]. Another study reported that MTV above 7.52 mL ($p = 0.0191$) and/or TLG above 35.94 g ($p = 0.0069$) were associated with significantly shorter progression-free survival (estimates at 3.5 years) in recurrent OC [66].

Fulham et al. reported that PET/CT altered management in 80% of patients, detected new lesions in 77% of patients, and was superior to other modalities in detecting nodal,

Table 2 Studies evaluating positron emission tomography/computed tomography (PET/CT) for staging of ovarian cancer

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Dauwen et al. [21]	P	68 (56 malignant tumors, 13 benign tumors)	TP 52/56; TN 10/13	CT	PET/CT correctly staged 31 of the patients and CT 32 (accuracy 55% vs 57%; difference 2%, 95% CI–13% to 16%)	PET/CT is better than CT in detecting retroperitoneal lymph node metastases, but not in detecting peritoneal metastases
De Iaco et al. [24]	P	40	Tumor < 0.5 cm, mean SUV_{max} 5.4; tumor < 5 cm, mean SUV_{max} 8.6; tumor > 5 cm, mean SUV_{max} 7.9		For PET/CT, sensitivity 78.9%, specificity 68.4%, PPV 95.3%	High rate of FP results in early-stage disease
Kitajima et al. [27]	R	40	Mean short-axis diameter of metastatic peritoneal lesions detected by PET/CT was 10.2 ± 4.2 mm (range 4–23 mm), and for metastatic lymph nodes, 7.3 ± 1.4 mm (range 5–9 mm)	CT	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% between CT and PET/CT; significant differences in sensitivity and accuracy	PET/CT is more accurate than CT for staging ovarian cancer
Michielsen et al. [28]	R	53	WB-DWI/MRI showed excellent correlation with FDG PET/CT ($\kappa = 1.00$) for detecting distant metastases	CT, 3-T WB-DWI/MRI	WB-DWI/MRI accuracy: tumor characterization 94%, peritoneal staging 71%, detecting retroperitoneal lymphadenopathies 87%	WB-DWI/MRI shows high accuracy for characterizing primary tumors and staging compared with CT and FDG PET/CT
Hynninen et al. [29]	P	41	Upper abdominal areas requiring extensive surgical procedures showed no significant differences between the two imaging methods	CT	FDG PET/CT was superior for the detection of carcinomatosis in subdiaphragmatic peritoneal surfaces ($p = 0.020$) and in the bowel mesentery ($p = 0.001$); extra-abdominal disease spread was detected by PET/CT in 78% of patients and by CT in 61% of patients	PET/CT was not superior to CT for the detection of intra-abdominal disease spread but was more effective for the detection of extra-abdominal disease than CT
Signorelli et al. [23]	P	68	TP nodes had a significantly higher median size (14 mm) than FN nodes (6 mm; $p = 0.009$); similarly, metastatic deposits in TP nodes had significantly higher median size (9 mm) than FP nodes (2 mm; $p = 0.002$)	–	Overall patient-based PET/CT: sensitivity 83.3%, specificity 98.2%, accuracy 95.6%, PPV 90.9%, NPV 96.5%; nodal lesion site-based analysis: sensitivity 75.5%, specificity 99.4%, accuracy 98.1%, PPV 87.5%, NPV 98.6%	PET/CT is an accurate tool for the detection of nodal metastases
Risum et al. [26]	P	66	FDG PET/CT indicated stage IV metastatic disease in 41% (27/66) of patients with advanced ovarian cancer and 31% (27/87) of all ovarian cancer patients	–	PET/CT stage III, complete debulking (no macroscopic residual tumor) and GOG performance status ≤ 2 were statistically significant prognostic variables	Use of diagnostic PET/CT leads to stage migration in primary advanced ovarian cancer
Fruscio et al. [25]	P	95	Detection by PET/CT of metastatic disease was significantly associated only with residual tumors	–	All FIGO stage IV patients had metastatic disease according to 18F-FDG PET, whereas 25 patients were upstaged from FIGO stage III to IV by PET/CT	PET/CT can detect distant metastases in ovarian cancer

Table 2 (continued)

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Lee et al. [30]	R	295	Median size of SdLNM was 7.65 mm	–	Patients with SdLNM diagnosed with stage IV disease according to PET/CT had significantly poorer progression-free survival ($p < 0.001$) and overall survival ($p = 0.016$) than those with PET/CT stage III disease	SdLNM detected using preoperative PET/CT is a negative prognostic factor in ovarian cancer
Yuan et al. [31]	M	18 studies	Meta-regression analyses and subgroup analyses revealed no statistical difference	CT, MRI	PET/CT was a more accurate modality (sensitivity 73.2%, specificity 96.7%, odds ratio 90.32); no significant difference was detected between CT and MRI	PET/CT is more accurate than CT and MRI in the detection of lymph node metastasis

P prospective, *TP* true positive, *TN* true negative, *CI* confidence interval, SUV_{max} maximum standardized uptake value, *PPV* positive predictive value, *FP* false positive, *R* retrospective, *WB-DWI/MRI* whole-body diffusion-weighted imaging/magnetic resonance imaging, *FN* false negative, *NPV* negative predictive value, *GOG* Gynecologic Oncology Group, *FIGO* International Federation of Gynecology and Obstetrics, *SdLNM* supradiaphragmatic lymph node metastases, *M* meta-analysis

Fig. 1 A 77-year-old woman with high-grade serous ovarian cancer with peritoneal carcinomatosis. **a** Axial contrast-enhanced computed tomography (CT) and **b** axial positron emission tomography (PET)/CT images showed FDG-avid (maximum standardized uptake value 5.9) nodularity at the left anterior lower abdomen (arrow), consistent with peritoneal carcinomatosis. At follow-up after 3 months of systemic therapy, axial non-contrast-enhanced CT **c** and axial PET/CT images **d** showed excellent response to interval therapy, with marked decrease in size and resolution of FDG avidity at peritoneal carcinomatosis. Coronal maximum intensity projection at baseline (**e**) and after 3 months of systemic therapy (**f**) showed treatment response

peritoneal, and subcapsular liver disease in recurrent OC [72]. Similarly, another study reported that PET/CT altered the known disease distribution in 64% patients and had a high impact on the management plan in 57% of patients with recurrent OC [70]. PET/CT altered the apparent disease distribution in 61%, showing lower disease burden in 9% and higher disease burden in 52%, compared to prior findings on CT, clinical examination, and pathology. In a prospective data registry involving 22,975 studies of OC, 83.7% patients underwent PET/CT for initial staging, restaging, and recurrence detection. The researchers reported that physicians changed their intended management plan in 36.5% of patients (95% confidence interval 35.9–37.2%) after reviewing PET findings [61].

PET/CT has also shown better performance in detecting recurrent OC compared to CA125 and CT. In a retrospective evaluation of 121 patients, PET/CT had superior overall sensitivity (82% vs 59% and 69%), specificity (87% vs 80% and 47%), accuracy (83% vs 63% and 66%), positive predictive value (96% vs 93% and 88%), and negative positive value (55% vs 32% and 21%) in detecting recurrent OC, compared with CA125 and CT [75]. Similarly, another study reported that PET/CT significantly outperformed CT in terms of sensitivity (96% vs 84%), specificity (92% vs 59%), negative predictive value (90% vs 59%), positive predictive value (97% vs 84%), and accuracy (95% vs 76%; $p < 0.05$) in detecting recurrent OC [49].[51]. PET CT is also reported to have better performance in detecting recurrent OC, compared to MR. Sanli et al. reported that, compared with MRI, PET/CT had superior sensitivity (97.5% vs 95%), specificity (100% vs 85.7%), positive predictive value (100% vs 97.4%), negative predictive value (87.5% vs 75%), and diagnostic accuracy (97.8% vs 93.6%) in the detection of < 2-cm peritoneal implants in recurrent OC [54]. A meta-analysis with 34 articles analyzed the diagnostic accuracy of CA125, PET alone, PET/CT, CT, and MRI in recurrent OC [52]. They reported pooled sensitivities of 69% for CA125, 79% for CT, 75% for MRI, and 91% for PET/CT; pooled specificities of 93% for CA125, 84% for CT, 78% for MRI, and 88% for PET/CT; and area under the curve values of 0.92 for CA125, 0.88 for CT, 0.78 for MRI, and 0.95 for PET/CT, and they concluded that PET/CT has a useful supplemental

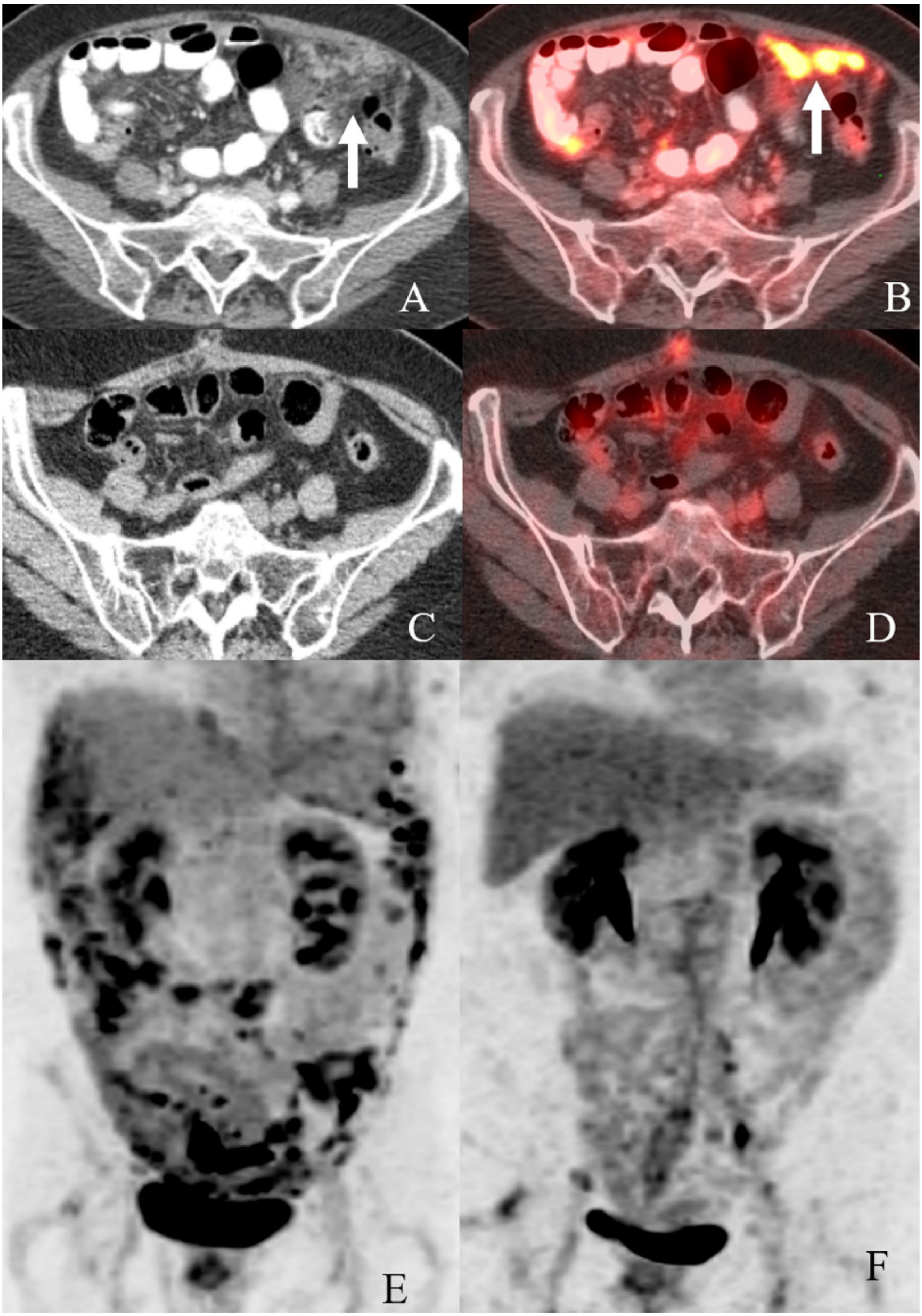
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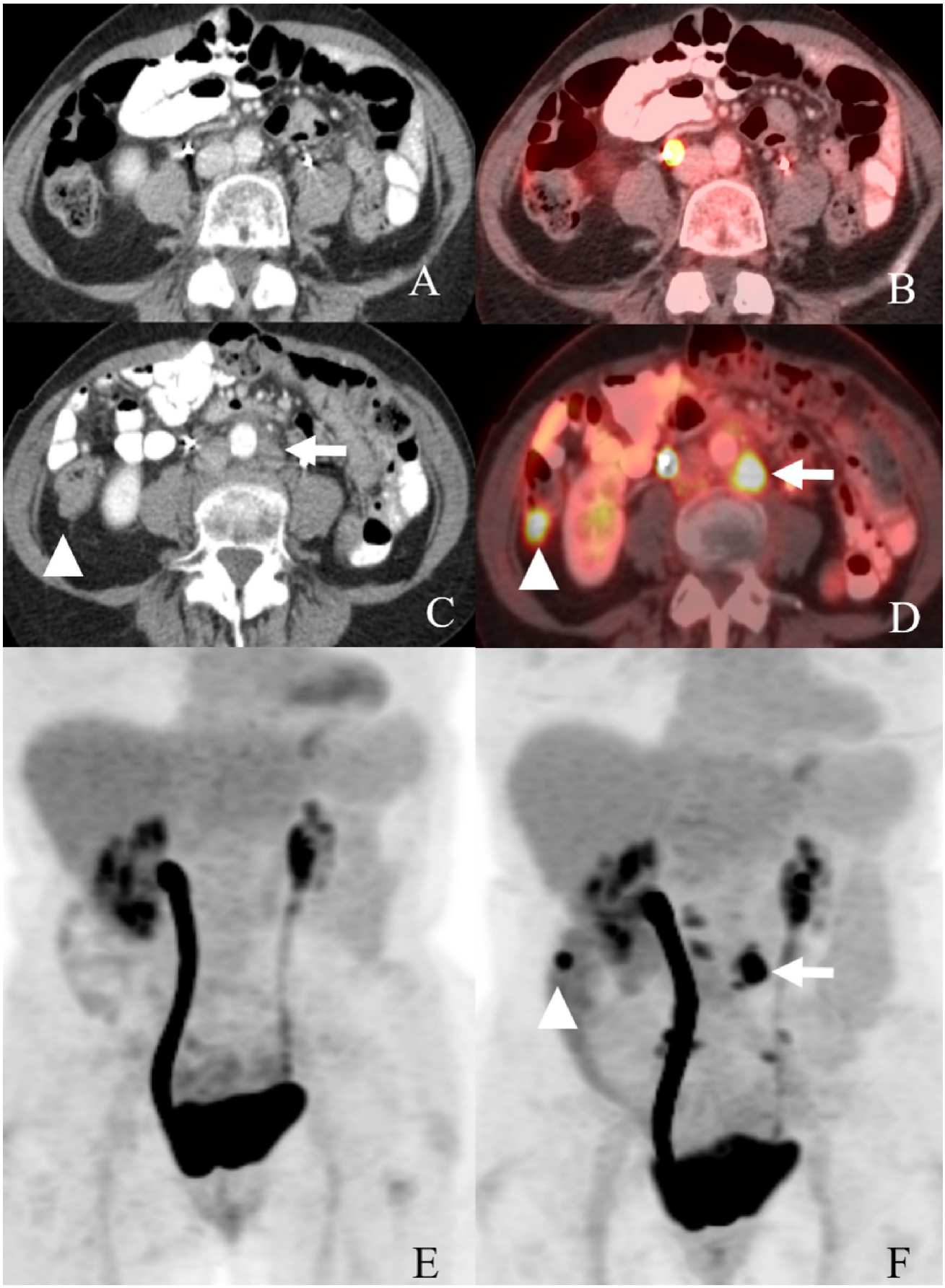
Table 3 Studies evaluating positron emission tomography/computed tomography (PET/CT) for prognosis and response to treatment in ovarian cancer

Study	Type	Patients	Pertinent PET/CT findings	Result	Conclusion
Liao et al. [33]	R	47	Detection rate of the threshold SUV 2.5 was 37.32%, and for background methods, 96.48% ($p=0.005$)	WBTLG was associated with the prognosis of patients (HR 1.043, $p=0.011$)	Background method WBTLG in post-surgery patients could be an independent prognostic factor
Vallius et al. [35]	P	29	Survival analysis, MTV change ($p=0.05$, HR 1.20, 95% CI 1.00–1.44) and target peak SUV change ($p=0.03$, HR 1.18, 95% CI 1.02–1.37) during NACT corresponded to OS	MTV reduction < 85% identified progression or stable disease (sensitivity 70%, specificity 78%, AUC 0.79)	Total MTV reduction < 85% during NACT could identify candidates for second-line systemic therapy
Vallius et al. [36]	P	26	Neither omental nor ovarian SUV_{max} decreases were associated with Ki-67	Median omental SUV_{max} change during NACT was − 64% (range − 16 to − 84%), and it was associated with histopathologic evidence of treatment response ($p=0.004$)	PET/CT was able to identify non-responders to NACT
Avril et al. [32]	P	33	Metastatic ovarian cancer showed high FDG uptake at baseline, with a mean SUV of 6.8 ± 2.1	PET metabolic response after the first (4.9 ± 2.8, $p<0.008$) and third (3.5 ± 2.8, $p<0.005$) cycle of chemotherapy associated with OS	Sequential PET predicted patient outcome and was more accurate than response criteria
Lee et al. [34]	R	175	Mean values of SUV_{max} were as follows: serous carcinoma 10.3 ± 3.7, endometrioid carcinoma 12.1 ± 6.6, clear cell carcinoma 8.8 ± 8.2, mucinous carcinoma 6.1 ± 3.5, mixed-type carcinoma 14.2 ± 7.7	Tumor stage ($p=0.0006$) and TLG ($p=0.008$) independently correlated with disease PFS	TLG is an independent prognostic factor for disease progression after cytoreductive surgery
Caobelli et al. [37]	R	168	Lymph node or distant involvement were also independently associated with an increased risk of disease progression	Higher 3-year PFS (64% vs 53%), 4-year PFS (23% vs 12%), and 4-year OS (67% vs 25%) in patients with negative restaging than in those with positive restaging after PET/CT	PET/CT has important prognostic value in assessing the risk of disease progression and mortality rate
Chung et al. [38]	R	55	The AUC was 0.654, and 70 was the cutoff value of MTV. The AUC for TLG was 0.618 and 563 was the cutoff value	Poor outcome was associated with higher values for MTV ($p=0.022$, HR 5.571) and TLG ($p=0.037$, HR 2.967)	MTV and TLG showed statistically significant association with recurrence
Konishi et al. [39]	R	80	Median SUV_{max} was lower in mucinous adenocarcinoma (AC + 2.76) and clear cell AC (4.9) than in serous AC (11.4) or endometrioid AC (11.4)	Median SUV_{max} was lower in clinical stage I (5.37) than in clinical stage ≥ II (10.3)	Preoperative PET/CT SUV_{max} differs according to histologic type
Risum et al. [40]	P	153	Only statistically significant independent predictor of OS was incomplete debulking (HR 1.7, $p=0.01$)	Incomplete debulking ($p=0.0001$), pleural exudates ($p=0.001$), postmenopausal state ($p=0.01$), WHO performance status > 2 ($p=0.01$), PET/CT stage IV ($p=0.01$), and large bowel mesentery implants ($p=0.02$) were significant prognostic variables	PET/CT stage IV, pleural exudates, and large bowel mesentery implants are criteria for referral of patients with advanced OC for NACT
Gallicchio et al. [41]	R	31	SUV_{max} ($p=0.48$) and TLG ($p=0.06$) did not reveal significant differences in OS	MTV survival analysis showed significantly higher OS in patients presenting with a high tumor burden than in those with less burden ($p=0.01$, 26 months vs 14 months)	Quantitative assessment by MTV rather than by SUV_{max} and TLG on PET/CT may be helpful for stratifying patients with peritoneal carcinomatosis

Table 3 (continued)

Study	Type	Patients	Pertinent PET/CT findings	Result	Conclusion
Bats et al. [42]	R	83	Complete cytoreduction was the only factor independently associated with survival	Compared with patients without mediastinal uptake, those with mediastinal uptake had significantly higher abdominal SUV_{max} (10.6 vs 6.3; $p=0.006$) and a significantly higher prevalence of stage IV disease (12/17, 70.6% vs 4/36, 11.1%; $p<0.001$)	Increased mediastinal 18F-FDG uptake was common in patients with advanced OC
Hynninen et al. [43]	P	49	Increased metabolic activity on end-of-treatment PET/CT was not associated with FIGO stage (III vs IV; $p=0.32$), residual tumor ($p=0.62$), or primary treatment ($p=0.09$)	Presence of metabolically active lesions (34%) on the end-of-treatment PET/CT did not predict earlier disease relapse in complete responders ($n=28$)	FDG PET/CT is not favored in complete responders after primary treatment
Martoni et al. [44]	P	42	AUC 0.884, mean ΔSUV_{max} after 3 courses was 64% ± 36.3%, and after 6 courses, 74% ± 39.3%	Significant difference in SUV_{max} at baseline (median 11) vs after 3 (median 3) and 6 courses (median < 2) and after 3 vs 6 courses of NACT	Normalization of SUV_{max} after 3 courses of NACT can predict prognosis after treatment
Ye et al. [45]	R	22	Median SUV_{max} was 7.25 (range 2.50–14.80)	On univariate analysis, stage, residual disease, platinum sensitivity, and MTV50 were significant predictors for both PFS and OS; the four metabolic parameters (MTV40, TLG40, TLG50, and TLG60) were significantly associated with OS	Metabolic volumetric parameters might be predicators for survival in ovarian cancer
Boers-Sonderen et al. [46]	P	20 (11 with ovarian cancer)	Median SUV of all lesions at baseline was 9.2 (range 3.4–27.6), after 2 weeks 6.8 (range 1.6–17.0), and after 6 weeks 6.4 (range 2.2–17.1)	Changes in TLG after 2 weeks predicted partial response after 10 weeks ($p=0.037$); a rise in SUV between the second and sixth week predicted progression ($p=0.034$) and was associated with worse PFS (HR 1.068, $p=0.013$)	Early response evaluation with PET/CT may predict subsequent radiologic partial response and progression

R retrospective, *SUV* standardized uptake value, *WBTLG* whole-body total lesion glycolysis, *HR* hazard ratio, *P* prospective, *MTV* metabolic tumor volume, *CI* confidence interval, *NACT* neo-adjuvant chemotherapy, *OS* overall survival, *AUC* area under the curve, SUV_{max} maximum standardized uptake value, *AC* adenocarcinoma, *TLG* total lesion glycolysis, *PFS* progression-free survival, *FIGO* International Federation of Gynecology and Obstetrics


A
B
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E
F

◂**Fig. 2** A 73-year-old woman with recurrent high-grade serous ovarian carcinoma, after neoadjuvant chemotherapy followed by surgery and additional chemotherapy. **a** Axial contrast-enhanced computed tomography (CT) and **b** axial positron emission tomography (PET)/CT images showed no evidence of FDG-avid recurrent or metastatic ovarian carcinoma. At follow-up after 3 months of systemic therapy, axial non-contrast-enhanced CT (**c**) and axial PET/CT images **d** showed interval progression with FDG-avid para-aortic adenopathy (arrow) and pericolonic nodule abutting the ascending colon (arrowhead). Coronal maximum intensity projection at baseline (**e**) and after 3 months of systemic therapy (**f**) showed interval progression. Bilateral ureteral stents were placed

role in surveillance, particularly in patients with increasing CA125 levels and negative CT and MRI findings.

Pitfalls

On cross-sectional imaging of early OC, it may be difficult to detect small implants which is a major limitation [76] (Fig. 3). False-negative results can occur in patients with low-grade tumors and in the early stages of OC [11, 77]. The clear cell or mucinous malignancies have been reported to have low-level FDG uptake [64, 78]. Hence, the sensitivity of FDG PET/CT for the detection of these neoplasms has been reported to be relatively low. Similarly, large cystic or necrotic tumors can yield false-negative results at PET/CT, due to the reduced cellularity and fewer viable cancer cells [11, 13]. Also, postoperative changes and granulation tissue may show FDG uptake and result in false-positive findings [11]. Also, the bowel uptake can be physiologic and may mask serosal involvement with tumor [11, 13]. In addition, false-positive findings can result from physiologic ovarian uptake, which is common during ovulation and the early luteal phase of the menstrual cycle in premenopausal women. Also postoperative abscesses and perforated viscera may demonstrate FDG uptake. Similarly, endometriomas, fibromas, and benign lesions such as corpus luteum cysts, dermoid cysts, serous cysts, and salpingitis may have increased metabolic activity [11, 79] (Fig. 4) [11, 77].

PET/MRI

PET/MRI is a hybrid imaging modality composed of PET and MRI, and can provide combined anatomical and metabolic imaging similar to PET and CT [80, 81]. The aim is to combine the high soft tissue contrast and functional information of MRI with the metabolic activity of whole-body PET. MRI is seen as more effective for local disease evaluation [82] and PET/CT as more effective for identifying distant metastasis and suspected recurrence in gynecologic cancers. There is, thus, an opportunity for "one-stop shopping" and better anatomic localization with integrated PET/MRI [76, 81, 83, 84].

Several recent publications have described initial experiences with PET/MRI in mixed populations of patients with various gynecologic malignancies (Table 5). These studies evaluated the role of PET/MRI in initial characterization and staging [85–87], evaluation of advanced disease [88], and detecting recurrence [89–91] of gynecologic malignancies (Figs. 5, 6, 7, 8, and 9).

In a retrospective assessment of 26 patients for evaluating adnexal lesions, PET/MRI had higher sensitivity (94% vs 74%), specificity (100% vs 80%), positive predictive value (100% vs 93%), and negative predictive value (83% vs 44%) compared with PET/CT [85]. In that study, PET/CT detected only 74% of malignant lesions (14/19), whereas PET/MRI detected 95% of malignant lesions (18/19). Another study used a three-point grading score and reported that PET/T2-weighted imaging (2.72 ± 0.54) localized the lesion in gynecologic malignancies significantly more convincingly than PET/CT (2.23 ± 0.50) or PET/T1-weighted imaging (2.29 ± 0.53; $p < 0.01$) [86]. Grueneisen et al. assessed the value of diffusion-weighted imaging in PET/MRI for diagnosis of primary and recurrent pelvic malignancies [87]. They reported that adding diffusion-weighting imaging to PET/MRI increased sensitivity (92.9% to 94.9%), NPV (75.0% to 80.0%), and diagnostic accuracy (91.8% to 92.6) [88].

The effectiveness of PET/MRI in detecting recurrent OC has also been evaluated. Grueneisen and group compared the diagnostic performance of PET/MRI with that of PET/CT for detecting recurrence of pelvic malignancies [90]. They found that, compared with PET/MRI, PET/CTs lesion-based sensitivity (82% vs 85%), specificity (91% vs 87%), positive predictive value (97% vs 96%), negative predictive value (58% vs 63%), and diagnostic accuracy (84% vs 86%) did not significantly differ ($p > 0.05$) in terms of detecting malignant lesions. Other studies have also reported equivalent diagnostic performance of PET/MRI compared to PET/CT [89, 91, 92, 94, 95, 97].

Challenges

Combining PET and MRI into a single acquisition is technically challenging. However, the development of new solid-state PET detectors, which function in the presence of magnetic fields, has made a single acquisition of PET and MRI possible [98].

One challenge is that MRI acquisitions are not based on X-rays and do not provide a direct reference for attenuation correction by the body [99]. To overcome this, Dixon-based technique (where one image is acquired with fat and water signals in phase and another image is acquired with fat and water signal out of phase) has been used as a reference for attenuation correction [100]. Segmenting the body from

Table 4 Studies evaluating positron emission tomography/computed tomography (PET/CT) for detection of recurrent ovarian cancer (ROC)

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Evangelista et al. [48]	R	125	Age and peritoneal recurrence on PET/CT were independent predictors of poor prognosis	CA125	PET/CT imaging has a sensitivity of 98.6% and a specificity of 77.8% for the assessment of recurrent disease and a sensitivity of 72.7% and a specificity of 88.9% for therapy evaluation	PET/CT is a useful imaging modality
Tawakol et al. [49]	P	111	PET/CT has a sensitivity of 96% and a specificity of 100% for detecting peritoneal metastases	CT	PET/CT outperformed CT ($p < 0.05$) in terms of sensitivity (96%), specificity (92%), NPV (90%), PPV (97%), and accuracy (95%)	PET/CT significantly outperformed CT
Hebel et al. [50]	R	48	FP 1, FN 1	–	Sensitivity 97%, specificity 90%, NPV 90%, PPV 97%	Negative PET/CT has a high NPV
Risum et al. [51]	P	60	PET/CT, FP 1 (endometriosis), FN 2	Ultrasound, CT	Ultrasound: sensitivity 66%, specificity 90%; CT: sensitivity 81%, specificity 90%; PET/CT: sensitivity 97%, specificity 90% for diagnosing ROC	Diagnostic value of PET/CT for detecting ROC was higher than that of ultrasound and CT
Gu et al. [52]	M	34	Diagnostic accuracy of interpreted CT images may have limited additional value on PET/CT in detecting ROC	CA125, PET, CT, MRI	PET/CT pooled sensitivity 0.91 (95% CI 0.88–0.94), pooled specificity 0.88 (95% CI 0.81–0.93), AUC 0.9555, $p = 0.109$	PET/CT might be a useful supplement to current surveillance
Ebina et al. [53]	R	44	Patients with TFI ≥ 6 months had a localized FDG uptake pattern vs those with a TFI < 6 months	–	For 58.4% of patients, PET/CT led to a change in management plan; 22.2% had miliary disseminated disease, which was not detected by PET	Useful for cytoreductive surgery patient selection
Sanli et al. [54]	R	47	Sensitivity, NPV, and diagnostic accuracy values of PET/CT were better than those of MRI for those with < 0.5-cm peritoneal implants and those with 0.5- to 1-cm peritoneal implants	MRI	For PET/CT, sensitivity was 97.5%, specificity 100%, PPV 100%, NPV 87.5%, and diagnostic accuracy 97.8%	PET/CT has greater accuracy than MRI in the detection of < 2-cm peritoneal implants
Peng et al. [55]	R	27	PET/CT changed the intended management in 14 (53.8%) of the patients	CA125	Detection rate of FDG PET/CT for recurrent ovarian cancer was 100% (15/15) in patients with > 35 U/mL CEA and 90.9% (10/11) in patients with progressive low-level CEA ($p = 0.423$)	PET/CT can detect ROC and second primary tumors with increases in CEA
Bhosale et al. [56]	R	66	31% of patients with no indication of cancer on contrast-enhanced CT had evidence of disease on PET/CT	CT	PET/CT has overall better sensitivity (95% vs 84%), specificity (100% vs 91%), and accuracy (95% vs 85%) than CT	PET/CT can detect ROC in patients with normal CA125 and has slightly better sensitivity than CT

Table 4 (continued)

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Mangili et al. [57]	R	32	All PET/CT findings were confirmed except 1 FP, 3 FN	CT	62.5% had CT images positive for ROC vs 90.6% on PET/CT; intermodality changes in management after PET/CT were indicated in 14/32 patients (44%)	PET/CT detects ROC better than CT
Menzel et al. [58]	R	90 PET studies	Within a CA125 range of 20–30 U/mL, PET detected tumor sites in 57% of patients; below 20 U/mL, PET rarely detected ROC	CA125	74% of PET studies indicated potential ROC with a median CA125 of 166.7 U/mL (range 13.3–4,060 U/mL)	PET may be considered in cases of suspected ROC
Pan et al. [59]	P	45	–	–	For PET/CT: sensitivity 100%, specificity 85%, accuracy 94%, PPV 92%, NPV 100%	Sensitive tool for early identification and ROC
Nasu et al. [60]	R	19	PET/CT had 4 FN	CA125, enhanced CT	For PET/CT: sensitivity 81.8%, specificity 100%, accuracy 100%, NPV 66.7%	Sensitive surveillance modalities
Hillner et al. [61]	P[b]	22,975 studies	83.7% PET/CT for staging, restaging, and recurrence	–	Physicians changed their intended management plan in 36.5% of cases (95% CI 35.9–37.2%) after PET	Change in intended management based on PET
Kim et al. [62]	R	55	Progression-free interval was 28.8 ± 12.7 months those who had PET and 30.6 ± 13.7 months in those who had a second laparotomy ($p = 0.29$)	–	For FDG PET, overall sensitivity 82%, specificity 88%, PPV 93%, NPV 70%, accuracy 84%	PET has a similar prognostic value to second look laparotomy
Rusu et al. [63]	R	42	PET/CT modified the treatment plan in 56.6% of patients and in 65.2% of patients when the CT was negative	CT	PET/CT provided a higher detection sensitivity than CT (92.2% vs 60.8%, $p < 0.001$)	Valuable diagnostic tool for suspected ROC
Takeuchi et al. [64]	R	48	TLG may be a predictor of survival after recurrence	CA125, CT	For PET/CT in the detection of low-grade serous carcinoma, sensitivity 94%, specificity 100%, accuracy 97%	PET/CT provides useful information during follow-up of low-grade serous carcinoma
Suppiah et al. [65]	M	10	Among 184 patients with peritoneal carcinomatosis who underwent PET/CT for staging, pooled sensitivity of 86.78% ($n = 184$)	CT, MRI, PET/MRI	PET/CT had a pooled sensitivity of 93.94% and specificity of 93.80% ($n = 426$) for detection of recurrence	High sensitivity and specificity
Vargas et al. [66]	R	55	Significantly shorter PFS in those with MTV above 7.52 mL ($p = 0.0191$) and/or TLG above 35.94 g ($p = 0.0069$); SUV_{max} was not significantly related to PFS ($p = 0.10$)	–	MTV ($p = 0.0025$) and TLG ($p = 0.0043$) were associated with optimal debulking; however, there was no significant association between SUV_{max} and debulking status ($p = 0.83$)	FDG PET metrics are associated with optimal secondary cytoreductive surgery and PFS

Table 4 (continued)

Study	Type	Patients	Pertinent PET/CT findings	Compared	Result	Conclusion
Sironi et al. [67]	P	31	Size threshold of 0.5 cm for detection of tumor by PET/CT was suggested	–	Overall lesion-based sensitivity 78%, specificity 75%, accuracy 77%, PPV 89%, NPV 57%	PET/CT had a high PPV
Sala et al. [68]	R	35	Size, number, and SUV_{max} of peritoneal deposits were significantly associated with poor survival for both readers ($p=0.01$ and $p<0.05$)	CT	Readers' AUCs in detection of recurrence were 0.85 and 0.78 for CT and 0.84 and 0.74 for PET/CT ($p=0.76$)	CT and PET/CT may have similar accuracy for ROC
Kim et al. [69]	R	56	Optimal cutoff value for SUV_{max} was 14, WBMTV 92 cm^3, and WBTLG 332 g	–	WBMTV and WBTLG were significant prognostic factors for PRS	Quantitative metabolic parameters at the time of the first relapse have significant predictive values for PRS
Simcock et al. [70]	P	56	PET/CT altered the known disease distribution in 64% of patients; overall, PET/CT showed less disease in 9% of patients and more disease in 52%	–	High impact on the management plan in 57% of patients, corresponding to 33 scans	PET/CT modifies the assessment of the distribution of ROC and alters management
Thrall et al. [71]	R	39	TN 4, TP 4, FN 2	–	Overall sensitivity 94.5% and specificity 100%; sensitivity 90% for localizing disease	Greatest utility in suspected recurrence
Fulham et al. [72]	P	34	New additional lesions below the diaphragm (85.7%), nodal lesions (30%), discrete peritoneal lesions (39%), and others	–	PET/CT identified new lesions in 68% of patients, additional lesions in 77%; 80% of patients had altered management after PET/CT results	PET/CT altered management, detected new lesions, and is superior in nodal, peritoneal, and subcapsular liver disease detection
Bristow et al. [73]	R	14	PET/CT failed to identify microscopic disease in 59.3% of pathologically positive nodes	–	For all target nodal basins, the sensitivity was 40.7%, specificity 94.0%, PPV 82.8%, NPV 69.3%, and accuracy 72.0% for ROC in dissected lymph nodes ($p<0.001$)	High PPV in identifying ROC in retroperitoneal lymph nodes
Antunovic et al. [74]	R	121	PET/CT has 3 FP, 17 FN	CA125, CT	PET/CT had an overall sensitivity 82%, specificity 87%, PPV 96%, NPV 55%, accuracy 83%, and was superior to CA123 and CT	FDG PET/CT was proven to be more efficient than serum CA125 assay and CT in detecting ROC after treatment

ROC recurrent ovarian cancer, *R* retrospective, *P* prospective, *NPV* negative predictive value, *PPV* positive predictive value, *FP* false positive, *FN* false negative, *M* meta-analysis, *MRI* magnetic resonance imaging, *TFI* treatment-free interval, *CEA* carcinoembryonic antigen, *CI* confidence interval, *TLG* total lesion glycolysis, *PFS* progression-free survival, *MTV* metabolic tumor volume, SUV_{max} maximum standardized uptake value, *AUC* area under the curve, *WBMTV* whole-body metabolic tumor volumes, *WBTLG* whole-body total lesion glycolysis, *PRS* post-relapse survival, *TN* true negative, *TP* true positive

[a]Prospective registry data

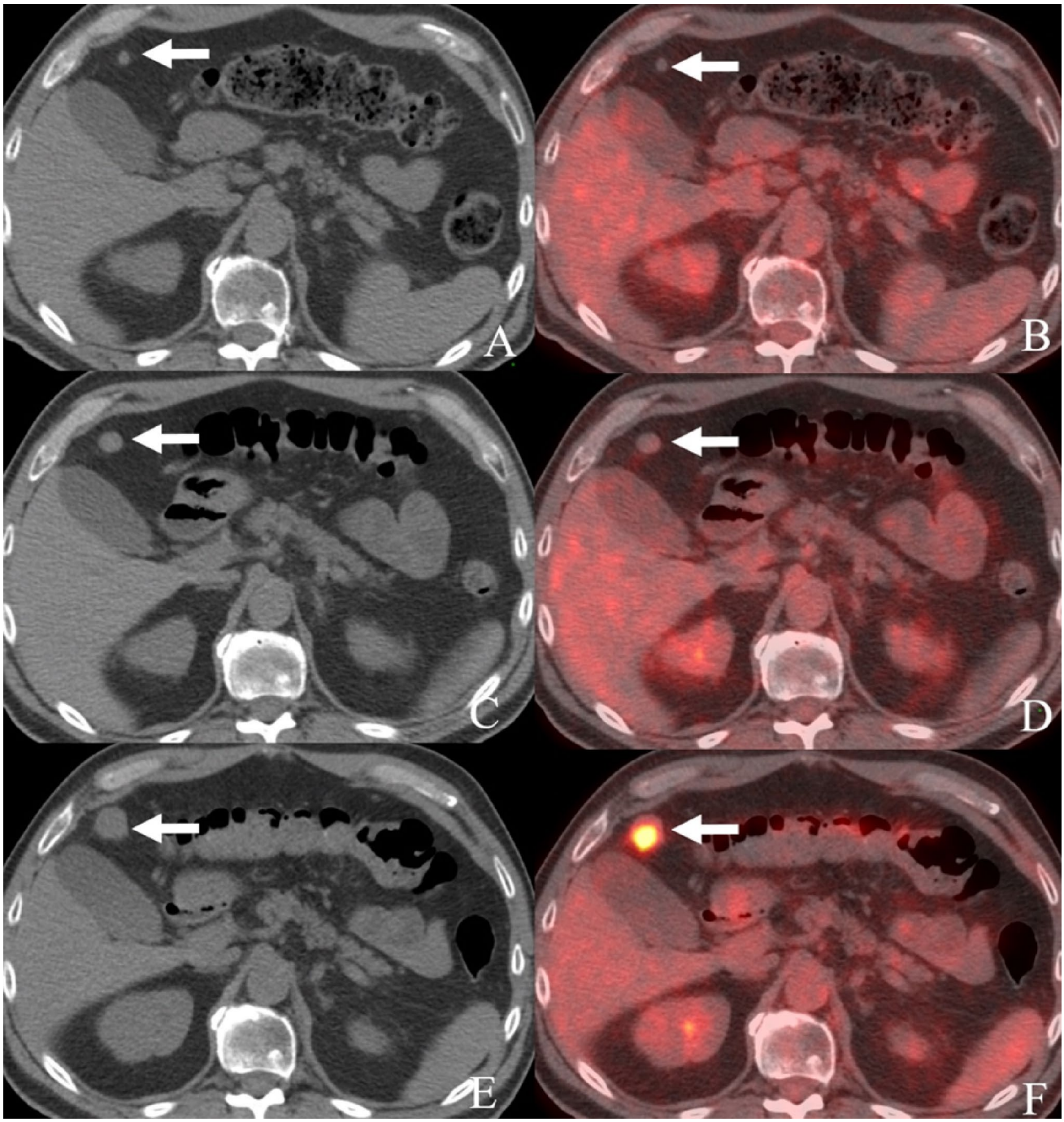

Fig. 3 Pitfalls of PET/CT. A 72-year-old female with metastatic esophageal carcinoma. **a** Axial non-contrast-enhanced CT and **b** Axial PET/CT images show a 0.5 cm right upper quadrant peritoneal nodule (arrow) with no FDG uptake due to small size. **c** Axial non-contrast-enhanced CT and **d** Axial PET/CT images after 4 months show interval increase in the 1.8 cm nodule (arrow) with no FDG uptake. **e** Axial non-contrast-enhanced CT and **f** Axial PET/CT images after 2 months show progressive increase in the size of the peritoneal nodule (arrow) with FDG uptake

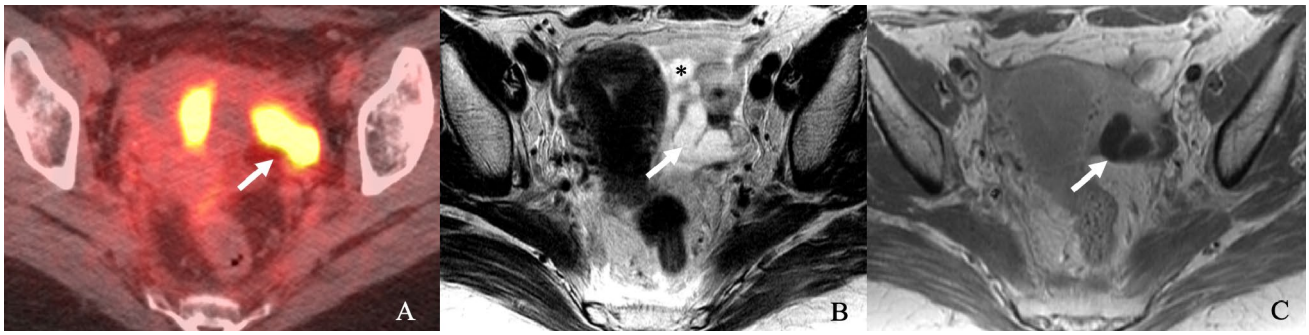

Fig. 4 False-positive PET/CT finding. A 65-year-old female with endometrial carcinoma. **a** Axial PET/CT images show hypermetabolic activity in left adnexa and uterine body (arrow). **b** Axial T2WI and **c** post-contrast T1WI show non-enhancing dilated tubular structure in the left adnexa suggestive of a hydrosalpinx (arrow) with some fluid (asterisk)

Dixon-based technique information allows an attenuation map to be generated [101].

Imaging of the lungs using MRI is also challenging. Ultrashort-echo and zero-echo time pulse could potentially be used to detect small nodules, but in general reduced sensitivity to small lung nodules remains a limitation of PET/MRI compared with PET/CT [102, 103]. Continuous respiratory and bowel motion occurs during PET/MRI acquisition, and this motion presents a particular challenge when acquiring images of the abdomen and upper pelvis [104].

Even though there is a benefit of lower radiation exposure reduction with PET/MR than PET/CT, the longer duration of imaging acquisition with PET/MR than to PET/CT and the lack of widespread availability of PET/MR in the radiology non-academic setting have abated the utilization of PET/MR in clinical practice. Finally, the National Comprehensive Cancer Network [105] and American College of Radiology appropriateness guidelines [106] do not have enough evidence to use PET-MR as standard of care imaging. However, since these guidelines do recommend use of PET and MRI individually in the management of OC, it is likely that this promising hybrid imaging technique would soon be included for this indication.

Future perspective

Newer MRI techniques such as dynamic contrast enhancement, diffusion-weighted imaging, intrinsic susceptibility weighting, and spectroscopy could increase the diagnostic ability of MRI to detect and characterize lesions [107–109]. In addition, the expanding field of radiomics in OC is also emerging as a promising tool [110, 111]. Numerous novel PET tracers have been introduced for the evaluation of tumors. Some other tracers, such as 18F-fluoromisonidazole [112], copper-labeled diacetyl-bis (N4-methylthiosemicarbazone) [113], 16a-18F-fluoro-17b-estradiol [114], and 18F-3′-fluoro-3′-deoxythymidine [115], have shown promising results in evaluating cancers. Novel MRI tracers, such as ferumoxytol [116] and hyperpolarized 13C [117], are under development as an alternative to FDG. Also, high-resolution delineation of the tumor in PET/MRI permits precise tumor delineation and can also be useful for optimal stereotactic radiosurgery [118].

Conclusion

PET/CT and PET/MRI may help in staging and assessment of recurrent disease in ovarian cancer. The metabolic parameters such as SUV, MTV, and TLG obtained from PET/CT and PET/MR have been shown to be useful surrogate markers for response to therapy, OS, and PFS. The development of novel targeted therapies and PET tracers will further expand the role of these imaging modalities. Nevertheless, more prospective studies with standardized protocols must be conducted before hybrid molecular imaging can be established as an acceptable mainstream imaging modality for OC and to outweigh the added cost and exposure to ionizing radiation.

Table 5 Studies evaluating positron emission tomography/magnetic resonance imaging (PET/MRI) for evaluation of gynecologic cancers, including ovarian cancer

Study	Type	Patients	Objective	Comparison	Result	Conclusion
Grueneisen et al. [90]	R	24 (13 ovarian cancer, 7 cervical cancer, 4 endometrial cancer)	Recurrence	PET/CT	For PET/MRI in lesion-based analysis, sensitivity 85%, specificity 87%, PPV 96%, NPV 63%, diagnostic accuracy 86% for detection of malignant lesions, lacking significant differences with PET/CT	Similarly high diagnostic performance to that of PET/CT
Virarkar et al. [92]	M	9 studies	Diagnostic performance	PET/CT	In patient-basis, PET/MRI had a pooled sensitivity and of 73.3% and specificity of 91.2%; in lesion-based analysis, PET/MRI had a pooled sensitivity of 84.7% and specificity of 89.3%	PET/MRI had slightly better diagnostic performance
Beiderwellen et al. [89]	P	19 (11 ovarian cancer, 8 cervical cancer)	Diagnostic value in recurrence	PET/CT	PET/CT and PET/MRI provided equivalent conspicuity (3.86 ± 0.35 for PET/CT, 3.91 ± 0.28 for PET/MRI; $p > 0.05$)	PET/MRI equivalently high diagnostic value
Grueneisen et al. [93]	P	34 (18 cervical cancer, 16 ovarian cancer)	Recurrence	MRI	PET/MRI offered correct and superior identification of all cancer recurrence in all 25 patients and correctly identified 88 of 89 (98.9%) malignant lesions	PET/MRI had a high diagnostic potential
Kirchner et al. [91]	P	43 (23 ovarian cancer, 12 cervical cancer, 3 endometrial cancer, 3 vulvar cancer, 1 vaginal cancer)	Recurrence	PET/CT, CT	In a lesion-based analysis, for PET/MRI, sensitivity 98%, specificity 83%, PPV 94%, NPV 94%, diagnostic accuracy 94%	PET/MRI equivalent diagnostic performance to that of PET/CT and superior diagnostic performance to that of CT
Grueneisen et al. [87]	P	48 (27 primary and 21 potentially recurrent)	Staging	DWI	PET/MRI with DWI had slightly higher values (sensitivity 94.9%, specificity 83.3%, PPV 95.9%, NPV 80.0%, accuracy 92.6%), but the difference was not significant ($p > 0.05$) vs non-DWI PET/MRI	DWI PET/MRI has no added diagnostic benefit

Table 5 (continued)

Study	Type	Patients	Objective	Comparison	Result	Conclusion
Zheng et al. [94]	M	7 articles	Recurrence	–	Patient-based analysis: pooled sensitivity 96%, specificity 95%, positive likelihood ratio 9.85, negative likelihood ratio 0.07, diagnostic odds ratio 201.41; lesion-based analysis: sensitivity 99%, specificity 94%, positive likelihood ratio 17.11, negative likelihood ratio 0.02, diagnostic odds ratio 1125.24	Excellent diagnostic performance
Virarkar et al. [95]	M	12 articles	Diagnostic performance	–	18F-FDG PET/MRI diagnosis of gynecologic malignancies, in patient-based analysis: pooled sensitivity 74.2%, specificity 89.8%, diagnostic odds ratio 26, area under the curve 0.834; in lesion-based analysis: sensitivity 87.5%, specificity 88.2%, diagnostic odds ratio 50, area under the curve 0.922	Promising diagnostic method for primary tumors, nodal staging, and recurrence
Nakajo et al. [86]	R	31	Diagnostic performance	PET/CT	Using a three-point grading score, PET/T2WI (2.72 ± 0.54) localized the lesion significantly more convincingly than PET/CT (2.23 ± 0.50) or PET/T1WI (2.29 ± 0.53; $p < 0.01$)	PET/T2WI images are superior for detection and localization
Fiaschetti et al. [85]	R	26 (12 ovarian cancer, 7 cervical cancer, 7 other)	Evaluating adnexal lesions	–	PET/MRI sensitivity 94%, specificity 100%, PPV 100%, NPV 83%	PET/MRI has higher sensitivity and specificity than other modalities vs MRI or PET/CT
Queiroz et al. [88]	P	23 with suspicious or proven advanced cancer (12 ovarian, 7 cervical, 4 other)	Staging and restaging	PET/CT	Primary tumor detection analysis: sensitivity 100%, specificity 66.7%, PPV 95.8%, NPV 100%, accuracy 97.2%; regional lymph node metastasis analysis: sensitivity 72.7%, specificity 91.7%, PPV 88.9%, NPV 78.6%, accuracy 82.6%	PET/MRI is superior to PET/CT for primary tumor delineation

Table 5 (continued)

Study	Type	Patients	Objective	Comparison	Result	Conclusion
Sawicki et al. [96]	R	71 (32 cervical cancer, 26 ovarian cancer, 13 other)	Recurrence	MRI	PET/MRI offered superior diagnostic accuracy (99.2% vs 79.3%, $p<0.001$) and diagnostic confidence in the categorization of malignant lesions (2.7 ± 0.5 vs 2.4 ± 0.7, $p<0.001$) vs MRI alone	PET/MRI has excellent diagnostic performance and outperforms MRI
Nie et al. [97]	M	7 articles	Diagnostic role and performance	-	18F-FDG PET/MRI for diagnostic performance: pooled sensitivity 95%, specificity 95%, positive likelihood ratio 7.51, negative likelihood ratio 0.12, summary diagnostic odds ratio 116.27; lesion-based assessment: pooled sensitivity 89%, specificity 87%, positive likelihood ratio 6.99, negative likelihood ratio 0.12, summary diagnostic odds ratio 55.82	PET/MRI is a very promising diagnostic modality

R retrospective, *PPV* positive predictive value, *NPV* negative predictive value, *CT* computed tomography, *M* meta-analysis, *P* prospective, *DWI*, diffusion-weighted imaging, *T2WI* T2-weighted imaging, *T1WI* T1-weighted imaging

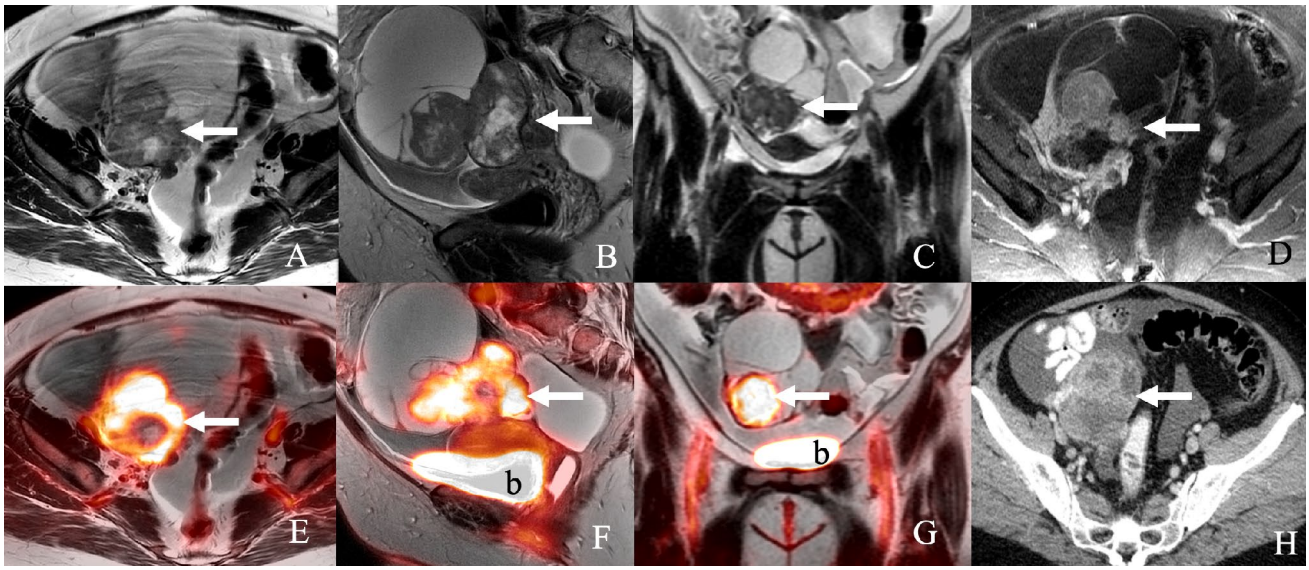

Fig. 5 A 55-year-old woman with high-grade Mullerian carcinoma. **a** Axial T2-weighted imaging (T2WI), **b** sagittal T2WI, **c** coronal fused and **d** axial post-contrast T1WI, T2WI magnetic resonance imaging (MRI) and **e** axial fused T2WI, **f** sagittal fused T2WI, and **g** coronal fused T2WI positron emission tomography/MRI showed an FDG-avid large complex right adnexal mass (arrow) with an enhancing soft tissue component within the mass and restricted diffusion. **h** An axial contrast-enhanced computed tomography image showed a complex right adnexal mass (arrow). b: urinary bladder

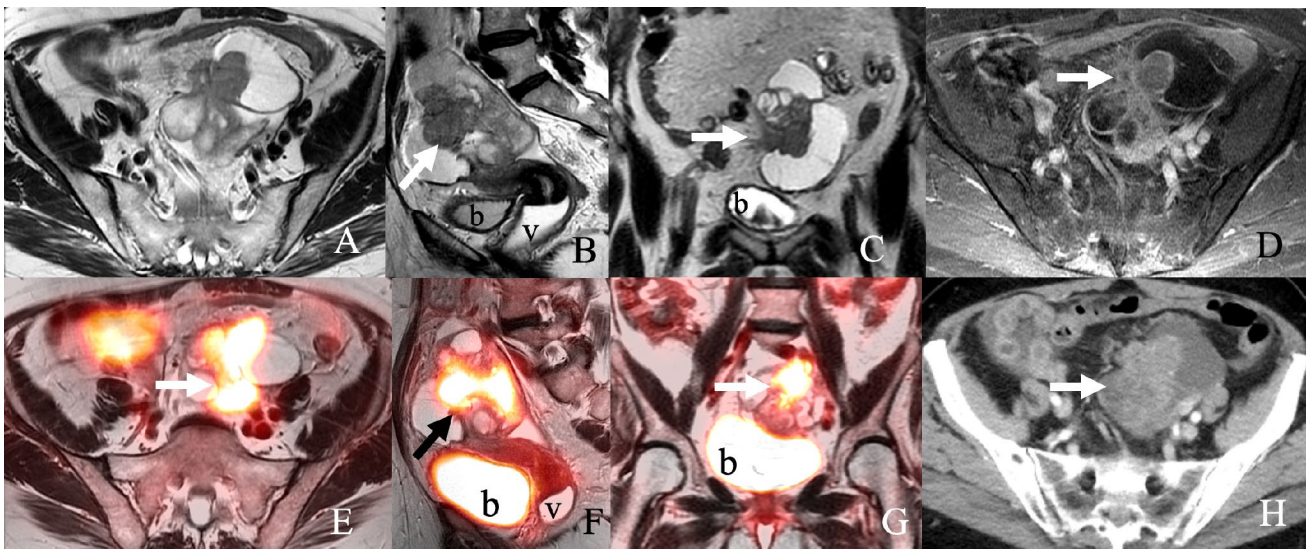

Fig. 6 A 71-year-old woman with high-grade serous carcinoma. **a** Axial T2-weighted imaging (T2WI), **b** sagittal T2WI, **c** coronal T2WI, **d** axial post-contrast T1WI magnetic resonance imaging (MRI), and **e** axial fused T2WI, **f** sagittal fused T2WI, and **g** coronal fused T2WI positron emission tomography/MRI showed an FDG-avid large complex left adnexal mass (arrow) with an enhancing soft tissue component within the mass and restricted diffusion. **h** An axial contrast-enhanced computed tomography image showed a complex left adnexal mass (arrow). b: urinary bladder, v: vagina

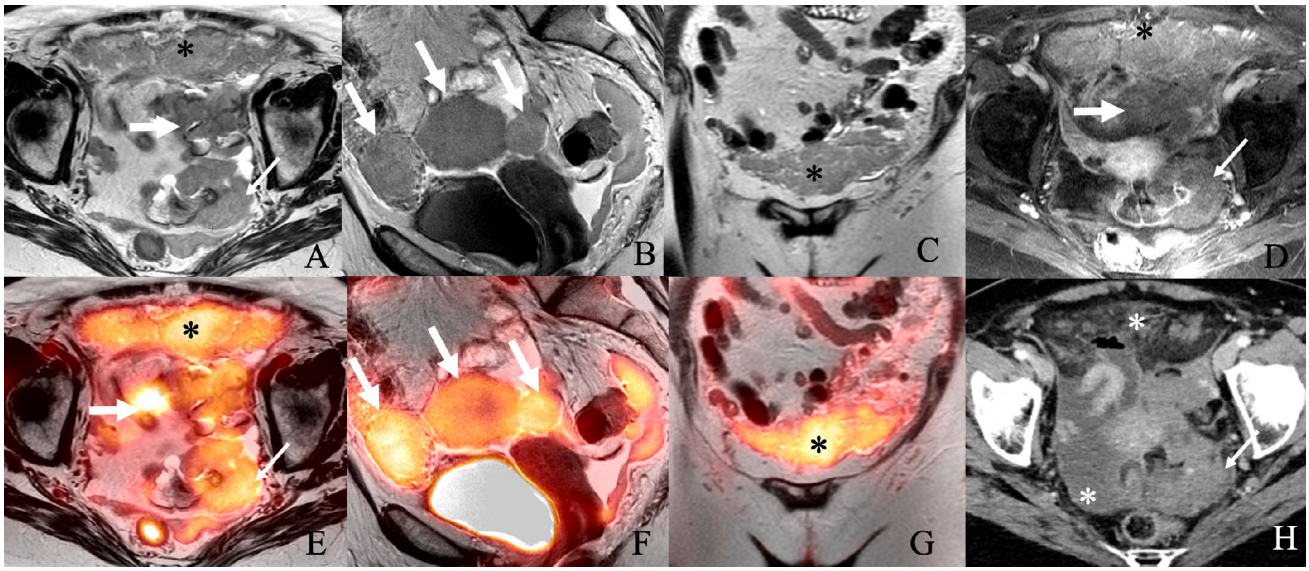

Fig. 7 A 72-year-old woman with high-grade serous carcinoma with peritoneal carcinomatosis. **a** Axial T2-weighted imaging (T2WI), **b** sagittal T2WI, **c** coronal fused T2WI, **d** axial post-contrast T1WI, magnetic resonance imaging (MRI), and **e** axial fused T2WI, **f** sagittal fused T2WI, and **g** coronal fused T2WI positron emission tomography/MRI showed an FDG-avid primary adnexal mass (thin arrow) with tumor implants (arrow) and extensive peritoneal disease (asterisk). **h** An axial contrast-enhanced computed tomography image from 1 month prior to the other images showed a complex left adnexal mass (arrow) with peritoneal disease (asterisk)

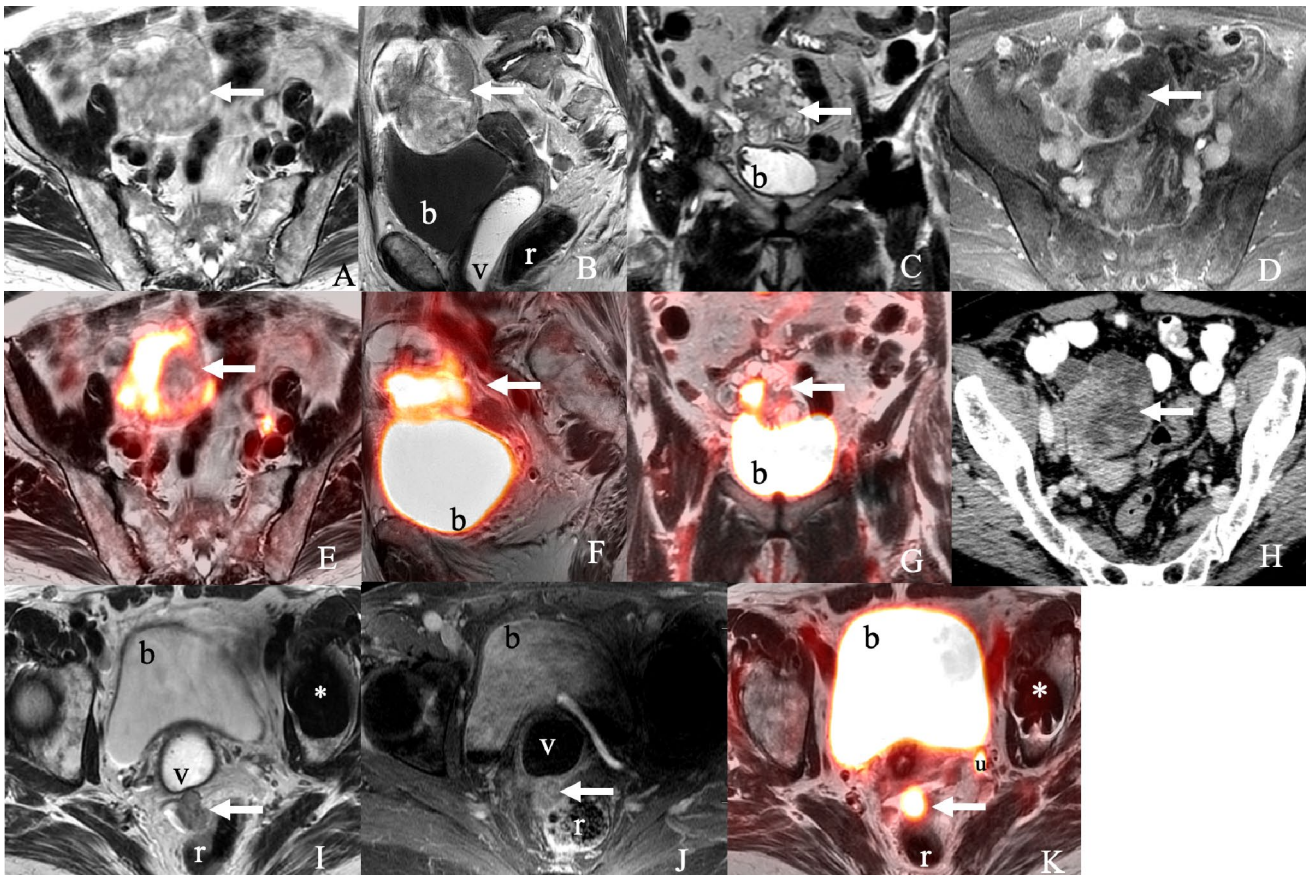

Fig. 8 A 68-year-old woman with high-grade serous carcinoma. **a** Axial T2-weighted imaging (T2WI), **b** sagittal T2WI, **c** coronal T2WI, **d** axial post-contrast T1WI, magnetic resonance imaging (MRI), and **e** axial fused T2WI, **f** sagittal fused T2WI, and **g** coronal fused T2WI positron emission tomography (PET)/MRI showed an FDG-avid mass in the right adnexa (arrow). **h** An axial contrast-enhanced computed tomography (CT) image showed a complex right adnexal mass (arrow). **i** Axial T2WI and **j** axial post-contrast T1WI MRI, and **k** axial fused T2WI PET/MRI. A left hip prosthesis was present (asterisk). b: urinary bladder, v: vagina, r: rectum, u: ureter

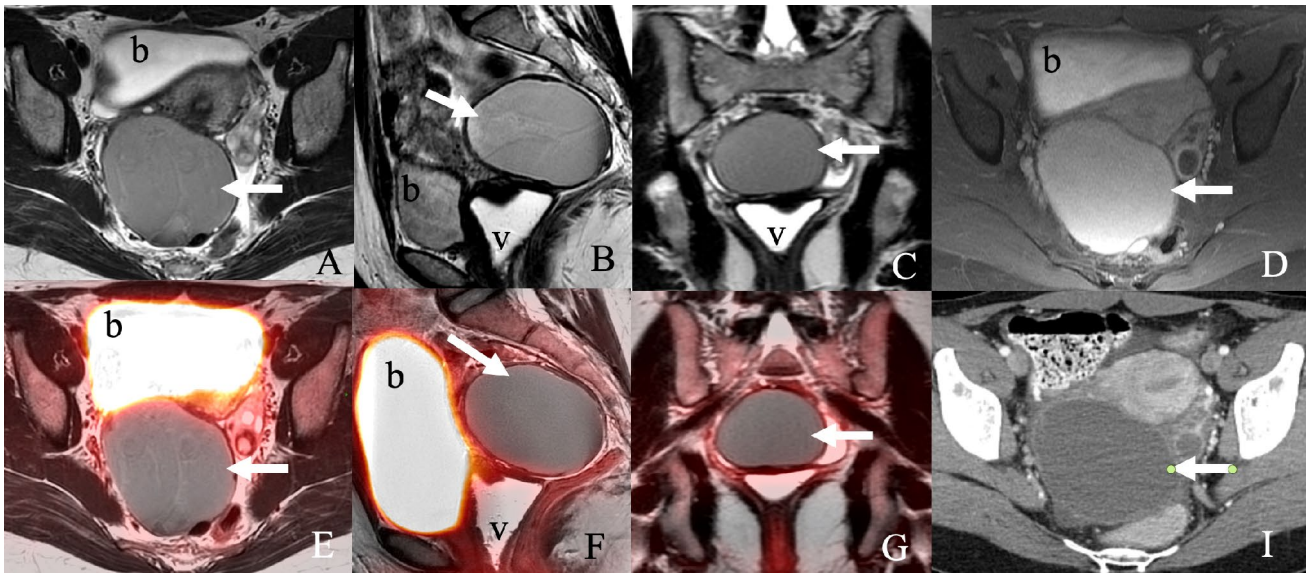

Fig. 9 A 29-year-old woman with endometrioma. **a** Axial T2-weighted imaging (T2WI), **b** sagittal T2WI, **c** coronal T2WI, **d** axial post-contrast T1WI magnetic resonance imaging (MRI), and **e** axial fused T2WI, **f** sagittal fused T2WI, and **g** coronal fused T2WI positron emission tomography/MRI showed a large right adnexal mass (arrow) with no enhancement and with mild restricted diffusion. **h** An axial contrast-enhanced computed tomography image showed a complex appearing right adnexal cystic mass (arrow). b: urinary bladder, v: vagina

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