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Review article

Systematic Review on the Accuracy of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography/Magnetic Resonance Imaging in the Management of Ovarian Cancer: Is Functional Information Really Needed?

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Abstract

Ovarian cancer (OC) often presents at an advanced stage with frequent relapses despite optimal treatment; thus, accurate staging and restaging are required for improving treatment outcomes and prognostication. Conventionally, staging of OC is performed using contrast-enhanced computed tomography (CT). Nevertheless, recent advances in the field of hybrid imaging have made positron emission tomography/CT (PET/CT) and PET/magnetic resonance imaging (PET/MRI) as emerging potential noninvasive imaging tools for improved management of OC. Several studies have championed the role of PET/CT for the detection of recurrence and prognostication of OC. We provide a systematic review and meta-analysis of the latest publications regarding the role of molecular imaging in the management of OC. We retrieved 57 original research articles with one article having overlap in both diagnosis and staging; 10 articles (734 patients) regarding the role of PET/CT in diagnosis of OC; 12 articles (604 patients) regarding staging of OC; 22 studies (1429 patients) for detection of recurrence; and 13 articles for prognostication and assessment of treatment response. We calculated pooled sensitivity and specificity of PET/CT performance in various aspects of imaging of OC. We also discussed the emerging role of PET/MRI in the management of OC. We aim to give the readers and objective overview on the role of molecular imaging in the management of OC.

Keywords: Cancer, fluorodeoxyglucose, molecular imaging, ovary

Introduction

Ovarian cancer (OC) is a gynecological malignancy with an insidious onset and often presents at a late stage. Once detected, accurate staging is required for optimal treatment such as primary cytoreduction or neoadjuvant chemotherapy followed by debulking surgery. Conventionally, staging of

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OC is performed using contrast-enhanced computed tomography (CECT).

Nevertheless, recent advances in the field of hybrid imaging as well as related publications have advocated positron emission tomography/computed tomography (PET/CT) as a potential tool for improved staging of this condition.[1,2] Furthermore, several studies have championed the role of PET/CT for the detection of recurrence and prognostication of OC.[3-6] In addition, studies have been conducted to evaluate the potential of PET/magnetic resonance imaging (PET/MRI) in the management of OCs.[7-9]

Although there is information available regarding the added benefits of hybrid functional imaging in the management of OC, there remain many questions about whether the risks outweigh the benefits and whether molecular imaging may enter as a mainstream imaging option. Therefore, we conducted a systematic review to assess the accuracy of PET/CT and PET/MRI in the management of OC for the purpose of diagnosis, staging, and detection of recurrence, as well as for the assessment of treatment response and disease prognostication.

Evidence Acquisition

The most recent search for this review was performed on December 8, 2016. We searched electronic databases of SCOPUS, MEDLINE (OvidSP), and EMBASE (OvidSP), using the keywords or search terms "ovarian cancer," "ovarian carcinoma," "PET/CT" 'PET/MRI," and 'PET/MR" and filtered it for full-text journal articles in English between the periods of January 2011 and December 2016.

Selection criteria

We selected studies that had defined cohorts with any accepted definition of OC with baseline or follow-up PET/CT or PET/MRI utilizing 18F-fluorodeoxyglucose (18F-FDG) that assessed the sensitivity, specificity, and accuracy of this imaging for the diagnosis, staging, and detection of recurrence as well assessment of treatment response. We also selected articles that highlighted the progression-free survival and overall survival for prognostication of OC patients based on PET/CT or PET/MR parameters.

All studies had to correlate the hybrid imaging findings with surgical, biopsy, cytology, or clinical findings based on the NICE Guidelines for Management of OC[10] or the American College of Obstetrics and Gynecology clinical guidelines.[11] Next, we excluded articles that were from case reports and proceedings, articles that were predominantly based on secondary metastasis to the ovaries, articles that did not involving human subjects, articles that used radiotracers other than 18F-FDG, and articles that concentrated on other gynecological malignancies and were not focused to OC.

Data collection and analysis

We screened all titles generated by electronic database searches. Two review authors independently assessed the abstracts of all potentially relevant studies. The identified full papers were assessed for eligibility and data were extracted to create two-by-two tables. Two independent assessors performed quality assessment using the QUADAS 2 tool. We grouped together studies that shared similar methodologies, for example, the use of contrast media and patient-based analysis to calculate pooled sensitivity and specificity. Studies in which the numbers of true negative, true positive, falsely positive, and falsely negative cases were not reported were excluded from pooled sensitivity and specificity calculation.

We extracted data regarding study design, whether it was prospective or retrospective or unknown. We also scrutinized patient selection, whether consecutive or not. We performed verification of bias, namely, no bias, limited, or considerable bias. No bias present was stated for articles that studied lesions on PET/CT and confirmed the diagnosis by histopathologic examination (HPE). Considerable bias was considered present for articles that did not use HPE to confirm the diagnosis or used only a small sample size. We also extracted data regarding the method used for interpretation of the test results, i.e. whether blinded or not.

Evidence Synthesis

Data extraction

Our initial search recovered 545 articles. After applying the exclusion criteria, we had 80 articles and added 12 more based on cross-reference from the bibliography of the recovered articles. A total of 92 articles were included in the final analysis [Figure 1]. From this figure, 57 were original scientific research articles and the remaining 35 were review articles and technical articles. There were a total of 10 research papers that investigated the role of PET/CT in diagnosis of OC, of which one article included comparison with PET/MRI. For the role of PET/CT in staging of OC, there were 12 articles plus one article which addressed both detection and staging of OC,[12] of which 3 articles included comparison with PET/MRI. Twenty-two papers addressed the topic of accuracy of PET/CT in detection of recurrence in OC patients; 13 articles referred to the role of PET/CT in assessment of treatment response and prognostication of OC.

Diagnosis of ovarian cancer

A total of 10 PET/CT studies which aimed to diagnose OC were reviewed [Table 1]. These studies included

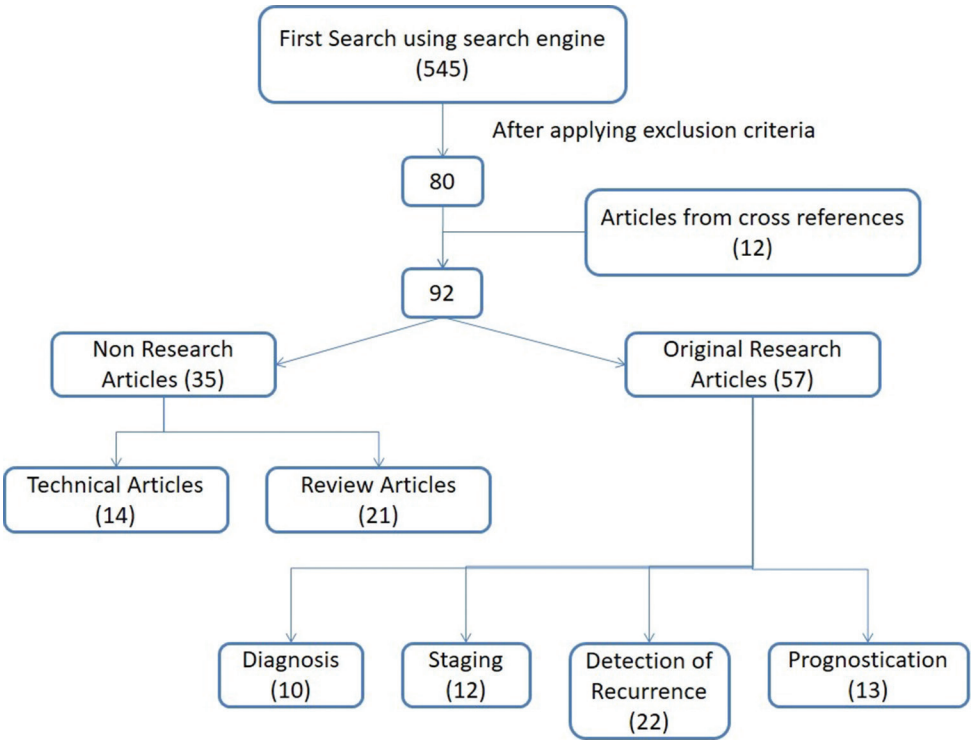

Figure 1: Flowchart of process for identifying relevant works

Table 1: Diagnosis of ovarian cancer using positron emission tomography/computed tomography

Author	Sample, *n* (B/M)	CT			PET/CT			Contrast media	Based analysis
		Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy		
Dauwen *et al*. (2013)	69 (13/56)	96.00	36.00	85.51	93.00	77.00	89.86	CECT, ce PET/CT	Patient
Kitajima *et al*. (2011)	108 (26/85)	-	-	-	82.40	76.90	81.80	ce PET/CT	Patient
Lee *et al*. (2014)	20 (7/13)	-	-	-	100.0	57.10	85.00	ce PET/CT	Patient
Lee *et al*. (2015)	72 (19/53)	-	-	-	98.10	78.90	91.70	ce PET/CT	Patient
Michielsen *et al*. (2014)	32 (4/28)	96.00	25.00	88.00	100.0	33.00	94.00	CECT, ce PET/CT	Patient
Tanizaki *et al*. (2014)	160 (79/81)	-	-	-	90.60	94.60	92.86	ld PET/CT	Patient
Alessi *et al*. (2016)	29 (6/23)	-	-	-	91.00	67.00	86.21	ld PET/CT	Patient

B: Benign; M: Malignant; CECT: Contrast-enhanced CT; ce PET/CT: Contrast-enhanced PET/CT; ld PET/CT: Low-dose PET/CT; PET: Positron emission tomography; CT: Computed tomography

734 cases. One of these studies had overlapping objective for both diagnosis and staging.[12] Five of these studies involved contrast-enhanced (ce) PET/CT imaging[1,12-15] whereas the rest utilized low-dose (ld) PET/CT for attenuation correction and anatomical localization. Three of these studies also incorporated MRI imaging in their study protocol. Analysis of studies that were lesion based was not included in the pooled analysis as the methodologies used were not standardized for direct comparison. Meta-analysis of these studies was not done as there was variable maximum standardized uptake value (SUV_{max}) cut-off points cited as well as variations in the methods incorporated to diagnose OC.

Of five studies utilizing ld PET/CT, two studies did not report sensitivity and specificity results but focused on comparison of SUV_{max} cut-off values and performance differences between modalities.[9,16] The range of sensitivity of ld PET/CT as reported in the remainder four studies was 80.6%–96.0% based on Tanizaki *et al*.[17] and Minamimoto *et al*.,[18] respectively. However, the range of specificity of ld PET/CT was reported to be 67.0%–94.6% based on Alessi *et al*.[19] and Tanizaki *et al*.,[17] respectively.

For PET/CT studies that utilized intravenous contrast media, the range of sensitivity based on 5 studies was 82.4%–100% based on Kitajima *et al*.[13] and Michielsen *et al*.,[12] respectively. Furthermore, for the assessment of specificity, the range for ce PET/CT was 33.0%–78.9% based on Michielsen *et al*.[12] and Lee *et al*.,[15] respectively.

In general, most studies considered raised maximum standardized uptake value levels that were above background uptake and were not attributed to physiological uptake, as pathological. Whereas, other

studies had variable SUV_{max} values cited as threshold for the detection of malignancy, for example, Kitajima *et al*. had cited a cut-off value of 2.55,[13] Lee *et al*. cited two cut-off values 3.2 and 3.9 for improved sensitivity,[14] and Tanizaki *et al*. had cited 2.9 as a cut-off value.[17] We did not consider these studies in the meta-analysis due to variations in the methodology for the detection of OC.

Three studies incorporated MRI analysis for the same cohort of patients to diagnose OC.[9,12,16] Tsuboyama *et al*. analyzed separately as well as with consensus MRI findings compared to PET/CT findings; however, it did not involve PET/MRI image fusion. They noted that by combining PET/CT with ce MRI, they had improved accuracy to correctly diagnose indeterminate lesions compared to MRI alone.[16]

Staging of ovarian cancer

A total of 13 PET/CT studies which aimed to stage OC were reviewed [Table 2]. These studies included 604 cases. Four of these studies were excluded as we were unable to create two-by-two tables[2,20-22] and one was excluded as it involved staging of mixed gynecological malignancies.[8] Thus, we included 8 studies and total of 380 patients that were focused on staging OC. Of these, two studies used ce PET/CT for analysis[12,23] and the rest of the studies used ld PET/CT for analysis.[24-29]

Ultimately, we only used three studies for our meta-analysis because some studies only analyzed lymph node involvement and we could not create two-by-two tables for the rest. Therefore, there were three studies[24,25,27] and 184 patients that analyzed peritoneal carcinomatosis for staging of OCs and achieved pooled sensitivity of 86.78%. We were not able to calculate pooled specificity as we did not have information on the number of benign cases in one of the studies.[25]

The majority of studies used lesion-based PET/CT staging to correlate with HPE findings. We note that extra-abdominal spread could be missed or underdiagnosed on conventional imaging (ci) because the gold standard to diagnose metastatic disease is based on laparotomy findings alone, which does not explore extra-abdominal regions.

Detection of recurrence of ovarian cancer

A total of 22 PET/CT studies which studied the accuracy of the detection of recurrence of OC were reviewed [Table 3]. These studies included 1429 cases. Two of these studies were excluded as we were unable to create two-by-two tables[4,30] and one was excluded as it involved detection for recurrence of mixed gynecological malignancies.[31] Thus, we included 19 studies and total of 1067 patients that were focused on accuracy of detection of recurrence of OC. Of these, ten studies used ce PET/CT for analysis[5,31-39] and nine studies had used ld PET/CT for analysis.[3,6,40-46]

Ultimately, we only used thirteen studies, involving 661 patients for our meta-analysis because we could not create two–by-two tables for the rest of the studies. Therefore, for the detection of recurrence of OC using ld PET/CT, there were five studies[3,6,41-44] involving 235 patients that were analyzed. We noted that the pooled sensitivity and specificity were 89.84% and 89.58%, respectively. Furthermore, there were eight publications[5,7,33-36,38,39] that studied the accuracy for the detection of recurrence of OC using ce PET/CT involving 426 patients and achieved pooled sensitivity and specificity of 93.94% and 93.80%, respectively.

Overall, most studies advocated the use of PET/CT for detection of recurrence as it gave higher accuracy than serial CA-125 tumor marker levels monitoring

Table 2: Staging of ovarian cancer using positron emission tomography/computed tomography

Author	Sample, *n* (NM/M)	CT			PET/CT			Contrast media	Based analysis
		Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy		
Kim *et al*. (2013)	46 (20/26)	88.50	65.00	78.30	96.20	90.00	93.50	CECT, ld PET/CT	Patient
Lopez *et al*. (2016)	59 (4/55)	80.00	98.00	-	83.63	93.00	-	CECT, ld PET/CT	Patient
Signorelli *et al*. (2013)	68 (12/56)	-	-	-	83.30	98.20	95.60	ld PET/CT	Patient
Rubini *et al*. (2014)	79 (39/40)	-	-	-	85.00	92.31	88.61	ld PET/CT	Patient
Hynninen *et al*. (2013)	463	41.00	92.00	57.00	51.00	89.00	64.00	ce PET/CT	Lesion
Michielsen *et al*. (2014)	475 (267/208)	-	-	-	91.00	91.00	91.00	ce PET/CT	Scan
Schmidt *et al*. (2015)	135	96.00	92.00	-	95.00	96.00	-	CECT, ld PET/CT	Site
De Iaco *et al*. (2011)	346 (38/308)	-	-	-	78.90	68.40	-	ld PET/CT	Lesion

NM: No metastasis; M: Metastasis; CECT: Contrast-enhanced CT; ce PET/CT: Contrast-enhanced PET/CT; ld PET/CT: Low-dose PET/CT; PET: Positron emission tomography; CT: Computed tomography

Table 3: Detection of recurrence of ovarian cancer using positron emission tomography/computed tomography

	Author	Sample, *n* (NR/R)	CT			PET/CT			Contrast media	Based analysis
			Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy		
1	Abdelhafez *et al*. (2016)	54 (28/26)	73.00	57.00	65.00	92.00	93.00	93.00	CECT, ce PET/CT	Scan
2	Antunovic *et al*. (2012)	121 (24/97)	NA	NA	NA	82.00	87.00	83.00	ld PET/CT	Patient
3	Chen *et al*. (2014)	155 (34/121)	NA	NA	NA	98.30	91.20	96.80	ld PET/CT	Scan
4	Dragosavac *et al*. (2013)	45 (3/42)	NA	NA	NA	100.0	100.0	100.0	ce PET/CT	Patient
5	Ghosh *et al*. (2013)	16 (1/15)	NA	NA	NA	100.0	100.0	NA	ld PET/CT	Patient
6	Gouhar *et al*. (2013)	73	NA	NA	NA	90.00	98.00	97.00	ce PET/CT	Lesion
		39 (4/35)	NA	NA	NA	97.00	75.00	95.00	ce PET/CT	Patient
7	Grueneisen *et al*. (2015)	24 (3/21)	NA	NA	NA	95.50	100.0	NA	ce PET/CT	Patient
		NA	NA	NA	NA	82.00	91.00	84.00	ce PET/CT	Lesion
8	Kitajima *et al*. (2012)	120 (74/46)	NA	NA	NA	86.90	95.90	92.50	ce PET/CT	Patient
		NA	NA	NA	NA	78.30	95.00	88.30	ld PET/CT	Patient
9	Kitajima *et al*. (2014)	30 (7/23)	NA	NA	NA	82.60	100.0	86.70	ce PET/CT	Patient
		NA	NA	NA	NA	78.30	85.70	80.00	ld PET/CT	Patient
10	Nasu *et al*. (2011)	30 (8/22)	95.50	100.0	NA	81.80	100.0	NA	CECT, ce PET/CT	Lesion
11	Panagiotidis *et al*. (2012)	73 (20/53)	NA	NA	NA	92.40	85.00	91.00	ce PET/CT	patent
12	Sanli *et al*. (2012)	47 (8/39)	NA	NA	NA	97.50	100.0	97.80	ce PET/CT	Patient
13	Sari *et al*. (2012)	34 (9/25)	NA	NA	NA	96.10	100.0	97.00	ld PET/CT	Patient
14	Takeuchi *et al*. (2014)	144 (9/39)	89.00	95.00	93.00	94.00	100.0	97.00	CECT, ld PET/CT	Scan
15	Pan *et al*. (2011)	37 (13/24)	NA	NA	NA	100.0	85.00	94.00	ld PET/CT	Patient
16	Peng *et al*. (2011)	27 (1/26)	NA	NA	NA	96.15	100.0	96.30	ld PET/CT	Patient
17	Fularz *et al*. (2015)	68	NA	NA	NA	90.90	80.00	85.30	ld PET/CT	Patient
18	Evangelista *et al*. (2015)	78	NA	NA	NA	98.60	77.80	96.10	ld PET/CT	Patient
19	Hebel *et al*. (2014)	48 (10/38)	NA	NA	NA	97.00	90.00	95.83	ce PET/CT	Patient

NR: No recurrence; R: Recurrence; CECT: Contrast-enhanced CT; ce PET/CT: Contrast-enhanced PET/CT; ld PET/CT: Low-dose PET/CT; PET: Positron emission tomography; CT: Computed tomography; NA: Not applicable

and ci as well as had good negative predictive value.[42] PET/CT is able to give an accuracy of 80% compared to CA-125 (64%) and ci (62%) in the detection of recurrence of high-grade OCs.[3] It is also able to give improved accuracy (87%) compared to CA-125 (60%) and ci (70%) for detection of recurrence in low-grade OCs.[3] Furthermore, recurrence of OC has been detected in 63% of patients scanned with PET/CT who interestingly had CA-125 levels within normal range.[44] In addition, symptomatic patients followed up due to suspected OC recurrence despite normal CA-125 and normal ci and thought to have false positive PET/CT scans have been confirmed to have recurrence 2 years later.[41] This suggests that PET/CT can detect recurrence of OC at an early stage. PET/CT also changed the intended management in 53.8% of patients by detecting recurrence in 90.9% of a subgroup of patients that had only low-level increases in CA-125 levels.[6]

Kitajima *et al*.[35] advocated the use of ce PET/CT compared to ld PET/CT as it gave higher confidence level for the detection of recurrence. They stated that the sensitivity, specificity, and accuracy of ce PET/CT versus ld PET/CT were 86.9%, 95.9%, and 92.5% versus 78.3%, 95.0%, and 88.3%, respectively. Subsequently, in 2014, Kitajima *et al*.[36] recommended the utility of fusion PET/MRI as it gave comparable results and enabled reduction in radiation exposure. They stated that the accuracy of ce MRI and ce PET/CT had similar accuracy of 86.7%, whereas ld PET/CT and PET/MRI had accuracies of 80.7% and 93.3%, respectively.

Furthermore, another study also expounded upon the advantages of PET/MRI versus PET/CT as it gave comparable results for sensitivity and specificity, i.e. 85% and 87% versus 82% and 91%, respectively.[7] They advocated FAST MRI sequence and fusion with PET imaging for the detection of recurrence as it enabled markedly reduced radiation exposure for the patients. In addition, PET imaging has been noted to have greater accuracy in detecting small-to-medium-sized peritoneal implants measuring <2 cm as compared to conventional MRI alone.[38]

Moreover, molecular imaging has enabled improved localization of abdominopelvic as well as subdiaphragmatic lymph nodes,[33] peritoneal implants,[5] hence decreasing the rate for second look surgery.[34] Negative PET/CT scan findings also have negative predictive value of 90% for detection of recurrence; patients with negative scans were associated with progression-free survival in approximately 2-year follow-up.[39]

Assessment of treatment response and prognostication

PET/CT metabolic parameters frequently used in the assessment of treatment response and prognostication include SUV_{max}, metabolic tumor volume (MTV), and total lesion glycolysis (TLG). MTV indicates the volume of metabolically active tumor and is stated using the unit cm^3; thus, whole-body MTV indicates MTV of the primary tumor including metastatic deposits. It is usually calculated using semi-automated or automated computer programs. Whereas, TGV is a composite of metabolic activity and volume within the tumor mass and, therefore, has the unit of SUV_{mL}.[47] In addition, whole-body TLG (wbTLG) indicates the metabolic tumor burden of the primary lesion including metastatic deposits.

There were 13 original articles that addressed utility of PET/CT in prognostication of OC. Some articles discussed mediastinal uptake as an indicator for poor prognosis,[48] tumor histology such as serous carcinoma versus endometrioid type as having a higher risk of recurrence,[49] and the role of mid-cycle PET/CT imaging as a prognostic factor for the assessment of early metabolic response to neoadjuvant chemotherapy.[50] One study also utilized PET/CT to assess treatment response toward novel therapeutics such as temsirolimus, using metabolic parameters such as SUV_{max} and TLG to predict subsequent radiological response or disease progression.[51]

However, only nine articles actually assessed certain metabolic parameters such as SUV_{max}, MTV, and TLG and gave the hazard ratio and 95% confidence interval values for prediction of risk factors of OC recurrence.[49,52-59] Six studies stated that SUV_{max} was not a significant prognostic predictor for OC recurrence [Table 4], whereas only one study stated that it could play a role in predicting disease recurrence.[57] Several studies advocated MTV as a useful predictor of recurrence,[53,56] however, there is a consensus by all studies that identified TLG as a significant predictive factor for prognostication of OC.[49,53-56] Thus, evidence of high wbTLG is accepted as a statistically significant indicator for poor prognosis and increased risk of recurrence of OC.

Discussion

OC is a deadly malignancy affecting many women worldwide and is often detected at an advanced stage, as it often presents with non-specific symptoms like bloatedness and progressive abdominal distension. Once symptomatic, diagnosis is usually made by correlating ultrasound findings and CA-125 tumor marker levels. Subsequently, confirmation of diagnosis is made by peritoneal tapping, laparoscopic biopsy or exploratory laparotomy, and primary debulking surgery. In advanced cases, preoperative staging is often performed using conventional imaging such as CECT scan. Furthermore, the role of molecular imaging, such as PET/CT and PET/MRI, is slowly gaining popularity as it can give both anatomical and functional information for accurate staging and detection of recurrence. Nevertheless, due to concerns for increased ionizing radiation exposure, increased cost involved, and nonstandardized methods for reporting imaging findings, molecular imaging has yet to establish its role in the mainstream management of OC.

PET/CT involves injecting intravenous radioactive isotopes such as 18F-FDG followed by approximately 60 min uptake time and, subsequently, performing either ld CT scan or CECT scan. CECT scan allows for diagnostic staging to be performed simultaneously during a single examination. However, the former, i.e., ld CT scan is performed for attenuation correction and anatomical localization alone. Following the CT component scanning, the patient then undergoes PET examination in the same gantry with several bed positions to cover the required body parts in a particular examination. Attenuation correction of the PET images from PET/MRI can be performed with a segmentation-based attenuation correction maps which can be generated using vendor-provided image registration and fusion software.

Table 4: Assessment of treatment response and prognostication

Author (year)	Survival (months), median (range)	Sample size	SUV_{max}			MTV			TLG		
			HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Chung *et al.* (2012)	11 (3-43)	55	NA	NA	NA	5.571	1.279-24.272	NA	2.967	1.065-8.265	NA
Kim *et al.* (2015)	NA	56	NA	NA	0.083	NA	NA	0.004	NA	NA	0.004
Lee *et al.* (2014)	NA	175	NA	NA	NA	NA	NA	NA	NA	NA	0.008
Liao *et al.* (2013)	NA	47	1.077	0.923-1.256	0.345	1.124	0.954-1.326	0.163	1.043	1.01-1.078	0.011
Mayoral *et al.* (2015)	12.5 (10.7-20.6)	26	NA	NA	0.083	NA	NA	0.008	NA	NA	0.013
Nakamura *et al.* (2012)	14.9 (1-38)	51	NA	NA	0.049	NA	NA	NA	NA	NA	NA
Risum *et al.* (2011)	30.2 (1.1-58.3)	201	NA	NA	0.86	NA	NA	NA	NA	NA	NA
Shim *et al.* (2015)	NA	343	1.015	0.964-1.068	0.58	NA	NA	NA	NA	NA	NA
Vallius *et al.* (2016)	NA	26	1.02	0.98-1.06	0.32	NA	NA	NA	NA	NA	NA

MTV: Metabolic tumor volume; TLG: Total lesion glycolysis; HR: Hazard ratio; 95% CI: 95% confidence interval; NA: Not applicable; SUV_{max}: Maximum standardized uptake value

PET/MRI is gaining popularity as an emerging functional imaging tool which promises added advantage in oncologic imaging. Apart from the excellent soft-tissue resolution provided by MRI, the advantages of PET/MRI include the option for multiparametric studies to be performed simultaneously as a complementary examination as well as reduced exposure to potentially cancer-inducing ionizing radiation.[60] One meta-analysis of 57 studies compared the performance of PET/CT and PET/MRI in various types of malignancies, including head and neck cancers, lung cancers, and gynecological cancers among others.[60] It was noted that although PET/CT was superior for the detection of small lung nodules, the diagnostic performance of simultaneous PET/MRI was similar or even better to that of PET/CT in most cancers.[60]

Nevertheless, there are several technological challenges, such as development of PET detectors that can withstand the high magnetic field generated by MRI scanners, correct for the PET/MRI interactions, and use MRI images to produce attenuation maps.[60] As a matter of fact, there are currently two types of PET/MRI equipment which are available according to their mode of acquisition, i.e., sequential type and simultaneous type. The former involves consecutive PET and MRI acquisition followed by fusion and the latter involves simultaneous acquisition, thus providing better image co-registration at a reduced scan time.[60]

Bagade *et al*.[61] in their narrative review advocated the use of combined PET/CT and MRI systems, allowing for simultaneous imaging because tandems systems which perform sequential imaging lead to potential co-registration errors and prolonged imaging time. They also pointed out that the challenges of simultaneous imaging are to create robust photomultiplier tubes in PET systems that can withstand the high magnetic fields of MRI scanner. Despite these challenges, PET/MRI has its advantages as it can help resolve pathological lymph nodes in the para-iliac regions, which could be mistaken for a functional ovary on PET/CT as well as limit the radiation dose received by patients.[61]

Due to its improved soft-tissue contrast, PET/MRI may be more useful compared to PET/CT in detecting military disseminated metastases for evaluation of suspected OC recurrence.[61] Fuccio *et al*.,[62] in their review in 2011, concluded that PET/CT gives high false negative results which predisposes it to miss low-grade tumors and early adenocarcinomas. Therefore, they recommended it to be used in conjunction with transvaginal ultrasound or MRI for characterization of adnexal masses and detection of OC. However, they concluded that PET/CT is a powerful method to stage OC with a major advantage of detecting extra-abdominal metastases.

Nonetheless, Kitajima *et al*.,[63] in their narrative review in 2011, advised to exercise caution regarding the pitfalls of interpreting PET/CT scans, especially caused by physiological FDG uptake in premenopausal women, due to increased FDG uptake in ovaries during ovulation and early luteal phase of the menstrual cycle. They also declared that the resolution of PET/CT is limited to lesions larger than 1 cm and that lesions smaller than 5 mm frequently lead to false positive results. Therefore, they postulated that PET/MRI would give added benefits in oncologic imaging due to its improved soft-tissue resolution. Furthermore, sophisticated sequences such as diffusion-weighted imaging, functional MRI, and MR spectroscopy can all be incorporated with molecular imaging, giving added important information but with less radiation exposure. This can be especially important in patients who require follow-up imaging.

Yuan *et al*.[64] in their meta-analysis of 18 studies which included 882 patient concluded that PET/CT is more accurate than CT and MRI alone in the detection of lymph node metastasis for staging of OC. However, they admitted to the limitations of the study such as bias caused by the fact that the reference standard of imaging findings was sometimes based on follow-up imaging and not histopathological examination, as it is impossible to investigate all detected lesions by invasive procedures. They added that the accuracy of the results is also dependent on surgical efforts and extent as well as the degree of cytoreduction.

Our meta-analysis noted that the pooled sensitivity and specificity of ld PET/CT compared to ce PET/CT to detect recurrence of OC to be 89.84% and 89.58% versus 93.94% and 93.80%, respectively. This is comparable to previous meta-analysis by Limei *et al*.[65] that noted that the pooled sensitivity, specificity, positive and negative likelihood ratios, and the area under the curve of PET/CT scan for detection of OC recurrence were 91.0%, 89.7%, 6.140, 0.123, and 0.9497, respectively.

Conversely, Hildebrandt *et al*.[66] addressed the issue of methodological challenges in the diagnostic imaging arena, especially so in detection of recurrence. As biopsies are not obtainable from all lesions, this leads to variable sensitivity and specificity of PET/CT, which is based on histopathological results from only operable lesions. They emphasized the need for prognostic randomized controlled trials in the diagnostic field to justify the added benefit of imaging to the currently available effective treatment, which can make an impact on disease-free survival or overall survival.

Conclusion

PET/CT and PET/MRI have a lot to offer in terms of management of OC, in particular for accurate staging and detection of recurrence. Its role for the assessment of treatment response will evolve with development of novel targeted therapies. Nevertheless, the added accuracy of these modalities needs to be justified by improved survival of OC patients, so as to outweigh the added cost and exposure to ionizing radiation caused by utilizing these methods. Thus, many more prospective studies with standardized methodologies need to be conducted before hybrid molecular imaging can be established as an acceptable mainstream imaging for OC.

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Conflicts of interest

There are no conflicts of interest.

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