Original
Nuclear Medicine Review 2022, 25, 2: 78–84
DOI: 10.5603/NMR.a2022.0018
Copyright © 2022 Via Medica
ISSN 1506–9680, e-ISSN 1644–4345

VIA MEDICA

[^{18}F]FDG PET/CT and CA-125 in the evaluation of ovarian cancer relapse or persistence: is there any correlation?

Francesco Dondi, Domenico Albano, Francesco Bertagna, Raffaele Giubbini
Nuclear Medicine, Spedali Civili Brescia, Brescia, Italy

[Received 13 I 2022; Accepted 27 IV 2022]

Abstract

Background: Ovarian cancer relapse can be diagnosed by serum tumor markers measurements and ^{18}F-fluorodoxyglucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) findings. The aim of our study was to analyze the potential relationship between cancer antigen 125 (CA-125) and PET/CT results in patients affected by ovarian cancer.

Material and methods: Ninety-two [^{18}F]FDG PET/CT scans in sixty-one patients with diagnosis of ovarian cancer were analyzed and compared to CA-125 values. PET/CT results were compared to other imaging modalities, histology or follow-up data in order to define its diagnostic accuracy. PET/CT studies were analyzed qualitatively and semiquantitatively by measuring the maximum and mean standardized uptake value body weight max (SUVbw max, SUVbw mean), maximum SUV lean body mass (SUVlbm), maximum SUV body surface area (SUVbsa), metabolic tumor volume (MTV) and total lesion glycolysis (TLG) of hypermetabolic lesions. All measurements were compared with CA-125 values.

Results: Twenty PET/CT studies were true negative, sixty-three true positive, five false positive and four false negative with sensitivity of 94%, specificity of 80%, negative predictive value of 83%, positive predictive value of 93% and accuracy of 90%. CA-125 levels were significantly correlated with PET/CT results and all PET/CT semiquantitative parameters. CA-125 cutoff values of 17 UI/mL is the best compromise between sensitivity and specificity in discriminating between positive and negative PET/CT result.

Conclusions: [^{18}F]FDG PET/CT has good accuracy in evaluating patients with relapse or persistance of ovarian cancer. CA-125 levels were significantly correlated with metabolic PET/CT parameters.

KEY words: PET/CT; ovarian cancer; tumor markers; CA-125

Nucl Med Rev 2022; 25, 2: 78–84

Introduction

Ovarian cancer is the leading cause of death among all gynecological cancers in developed countries. Because of its silent nature, most of the patients are diagnosed at advanced stages, defined as the spread of the tumor outside the pelvis [1, 2]. The staging system used worldwide for ovarian cancer is the International Federation for Gynecology and Obstetrics (FIGO) staging classification [3]. Staging of the disease is usually performed by multiple imaging modalities such as ultrasonography (US), particularly useful for the assessment of ovarian masses, computed tomography (CT), and magnetic resonance (MR). ^{18}F-fluodeoxyglucose positron emission tomography/computed tomography ([^{18}F]FDG PET/CT) is not usually performed for staging purposes, but its utility for the assessment of retroperitoneal lymph nodes is proved [4].

Cancer antigen 125 (CA-125) is a high-molecular-weight glycoprotein expressed on the surface of epithelial cells and is also a tumor marker that can play an important role in staging and restaging of ovarian cancer [1, 5]. Standard treatment of the disease includes aggressive cytoreductive surgery followed by platinum-/taxane-based chemotherapy [6].

Recurrence of this tumor is extremely frequent and in particular, 75% to 80% of all patients and 90% to 95% of patients with advanced disease (FIGO stage III/IV) will relapse within 2 years after primary treatment [7]. According to this, early identification of tumor recurrence is crucial to defining subsequent therapeutic approach.

Cancer antigen 125 (CA-125) is a sensitive and reliable tumor marker to investigate possible relapse or persistence of ovarian

Correspondence to: Omer Francesco Dondi, Nuclear Medicine, Spedali Civili di Brescia, P.le Spedali Civili, 1; 25123, Brescia, Italy
phone: +380303995461; e-mail: f.dondi@outlook.com

This article is available in open access under Creative Common Attribution-Non-Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) license, allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.

cancer: in particular in literature, it is reported an accuracy of 79% to 95%, and its values increase from 3 to 6 months before the clinical presentation of recurrence [8–9]. A progressive low-level increase of this marker is strongly predictive of disease relapse among patients who are in complete clinical remission [10].

Conventional imaging (CI), such as CT and MR, is also used in the evaluation of recurrence or persistence of disease with high variability in terms of sensitivity and specificity [1]. Furthermore, [^{18}F]FDG PET/CT is frequently performed in the work-up of possible recurrence, given its ability to identify relapse of the disease in both asymptomatic and symptomatic patients [11].

The purpose of our study was to assess the accuracy of [^{18}F]FDG PET/CT in detecting tumor relapse or persistence in patients previously treated for ovarian cancer. Furthermore, a possible a possible correlation between PET/CT parameters and CA-125 values was also investigated.

Material and methods

A total of 92 [^{18}F]FDG PET/CT scans were retrospectively included in the study. The scans came from 61 patients with a previous diagnosis of ovarian cancer and were performed in our center from July 2007 to October 2019. Patients with a history of multiple tumors expressing CA-125 (*i.e.* breast) were excluded from the study. All PET/CT scans were performed at least 1 month after the end of chemotherapy and 3 months after the end of surgery or radiotherapy.

A dose of 3–3.5 MBq/kg of [^{18}F]FDG was administered intravenously to the patient 60 minutes before image acquisition. Patients were instructed to void before acquisition and no contrast agents were administrated; written consent was also obtained before studies. PET/CT scans were performed from the skull base to the midthigh on a Discovery ST or Discovery 690 PET/CT tomograph (General Electric Company, GE, Milwaukee, Wisconsin) with standard parameters (CT: 80 mA, 120 kV; PET: 2.5–4 min per bed position, PET step of 15 cm). Reconstruction of images was performed in a 256×256 matrix and 60 cm field of view.

All PET/CT scans were visually and semiquantitatively analyzed by two experienced nuclear medicine physicians by consensus. In this setting, readers were aware of the clinical history of the patient but not about CA-125 levels. Focal tracer uptakes diverging from physiological distribution of radiotracer and background were regarded as suggestive of disease recurrence or persistence. For semiquantitative analysis the measure of the maximum and mean standardized uptake value bodyweight max (SUVbw max, SUVbw mean), maximum SUV lean body mass (SUVlbm), maximum SUV body surface area (SUVbsa), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) of hypermetabolic lesions were performed. In this setting, MTV was extracted from [^{18}F]FDG PET images corrected for attenuation, with an SUV-based automated contouring program (Advantage Workstation 4.6, GE HealthCare). This operation was performed with an isocontour threshold method based on 41% of the SUVmax, as previously recommended by the European Association of Nuclear Medicine, because of its high interobserver reproducibility [12]. Furthermore, TLG was calculated by summing the product of MTV of each lesion for its SUVmean.

Cancer antigen 125 (CA-125) values were collected in a range of times within 2 months from the PET/CT scan. In particular, CA-125 was considered positive when higher or equal to 35 UI/mL, according to the reference values of our institution. In order to evaluate PET/CT diagnostic accuracy, the reference standard was a combination of clinical and imaging follow-up data collected for at least 12 months. When available, also histopathologic information was taken into account.

Statistical analysis

Statistical analyses were carried out using MedCalc Software version 17.1 for Windows (Ostend, Belgium). Categorical variable were presented with the calculation of simple and relative frequencies while the numeric variables were described with mean, standard deviation, minimum and maximum values. Furthermore, using final diagnosis as a reference, sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy (AC) were calculated based on Bayes's law, with 95% confidence intervals (CIs).

To assess the possible correlation between qualitative PET/CT results in tumor markers positivity or negativity, age (considering a threshold of 75 years), and stage (I/II *vs.* III/IV FIGO stage), Chi-Square test was performed. Furthermore, the Kruskall-Wallis test was performed to evaluate a possible correlation between PET/CT results and tumor markers considered as absolute values and with a cutoff of 35 UI/mL (positivity or negativity) and PET/CT semiquantitative parameters (SUVmax, SUVmean, SUVbsa, SUVlbm, MTV and TLG). P-value was considered statistically significant if < 0.05.

In order to identify the best CA-125 values able to discriminate between positive and negative PET/CT, receiver operating characteristic (ROC) curve analysis was then performed. Area Under Curve (AUC), SE, and SP were then obtained from this analysis.

Results

Mean age of patients was 64 (range 45–85) years; 2 of them had stage I disease according to FIGO staging system, 4 had stage II disease, 36 had stage III while stage IV was present in 19 patients. All patients had a PET/CT scan after surgical removal of the primary tumor. Of these patients, 2 didn't perform any therapy after surgery, 56 had chemotherapy after surgery, 1 performed radiotherapy after surgery while 2 patients performed a mix of radio- and chemotherapy after surgery.

Seventeen patients performed more than a single [^{18}F]FDG PET/CT scan, resulting in 32 scans carried out for re-staging or follow-up purposes. In particular, 10 patients performed 2 scans, 3 patients performed 3 scans, one performed 4 scans, 2 performed 5 scans and only one patient performed 6 PET/CT scans. Furthermore, of the 32 scans performed after a prior one, 8 were carried out to evaluate relapse of disease after a negative [^{18}F]FDG PET/CT exam, 3 were performed as a part of the follow-up of the patients, while 21 scans were performed for the evaluation of disease during or after treatment (in particular in one case the patients had radiotherapy before the scan while 20 patients had chemotherapy before PET/CT evaluation). The mean imaging follow-up time of patients with CT or MR scans was 22.7 months.

Serous carcinoma was the most frequent histotype with 53 cases; endometrioid carcinoma was present in 3 patients, carcinosarcoma in 2 while one patient had a mixed carcinoma, one an undifferentiated, and one a clear cell carcinoma respectively

Table 1. The main features of our 61 patients

	n (%)
Age [years] (mean, range)	64 (45–85)
FIGO stage	
I	2 (3%)
II	4 (7%)
III	36 (59%)
IV	19 (31%)
Therapy	
Surgery	2 (3%)
Surgery + chemotherapy	56 (92%)
Surgery + radiotherapy	1 (2%)
Surgery + chemotherapy + radiotherapy	2 (3%)
Histology	
Carcinosarcoma	2 (3%)
Clear cell	1 (2%)
Endometrioid	3 (5%)
Mixed	1 (2%)
Serous	53 (86%)
Undifferentiated	1 (2%)

FIGO — International Federation for Gynecology and Obstetrics

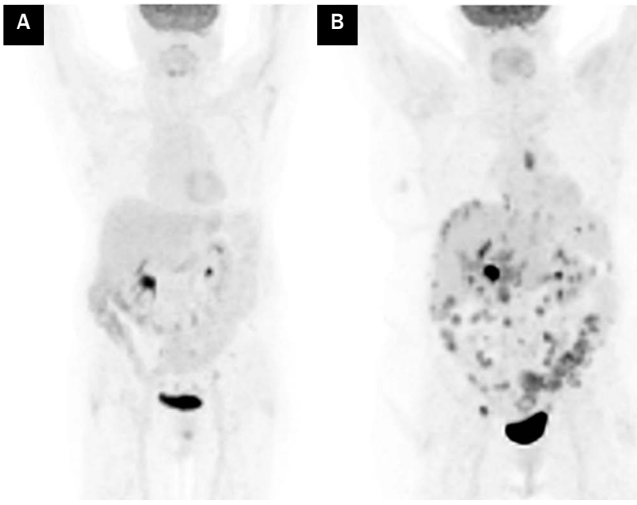

Figure 1. (**A**) Maximum intensity projection (MIP) of a negative [^{18}F]FDG PET/CT scan performed in a patient with negative CA-125; (**B**) MIP of a positive [^{18}F]FDG PET/CT scan performed in a patient with negative CA-125 showing peritoneal, thoracic, and abdominal localization of the disease

(Tab. 1). Cancer antigen 125 (CA-125) values were available in conjunction with PET/CT for all studies: 42 of them were under the normal limit while 50 were above.

Of the 92 PET/CT scans performed, 68 (74%) demonstrated the presence of recurrence of the disease while 24 (26%) were negative (Fig. 1). In the group of positive PET/CT, 43 (63%) demonstrated peritoneal localization of disease, 13 (19%) had a local relapse, 30 (44%) had abdominal nodal metastasis, 15 (22%) had thoracic nodal metastasis, 9 (13%) had hepatic metastasis, 3 (4%) had lung metastasis and 3 (4%) had spleen metastasis. One (2%) patient also had adrenal localization of the disease.

Among 68 positive PET/CT scans, 63 were confirmed as true positive while on subsequent follow-up 5 were classified as false positive. Histopathological diagnosis was possible for 41 (65%) of these studies. In one case we found a diffuse uptake in the left iliac wing that on a subsequent MR scan was classified as not pathological. Three false-positive scans were characterized by peritoneal focal uptakes interpreted as localization of disease that were not confirmed on subsequent radiological follow-up. Interestingly, in one patient we found a focal peritoneal uptake suggestive of localization of ovarian cancer but when removed this was diagnosed as a neuroendocrine tumor (Fig. 2).

Among 24 negative scans, 20 were confirmed as true negative while 4 resulted as false negative on subsequent follow-up (imaging follow-up with CT or MR scans for at least 12 months, in particular with a mean follow-up of 26.3 months): 2 of them had peritoneal or nodal metastasis of disease with dimension under 5 mm while in 2 cases PET/CT wasn't able to recognize lung localization for the same reason. Sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and accuracy (AC) of [^{18}F]FDG-PET/CT were 94% (85–98%), 80% (61–93%), 93% (85–96%), 83% (67–93%) and 90% (82–95%), respectively. Positive and negative likelihood ratios were 4.70 and 0.07, respectively.

Of the total of 92 PET/CT scans, 80 were performed by patients with a diagnosis of serous ovarian carcinoma while 12 patients were present with other histotypes. In the first group of patients, there were 4 false-negative scans, 5 false positives, 18 true negatives and 53 true positives; CA-125 was above the limit of 35 UI/mL in 42 cases while under this limit in 38. In the group of patients without serous carcinoma, 2 scans turned out to be true negative while 10 were true positive; CA-125 was positive in 8 cases and negative in 4.

A significant correlation was found between PET/CT results and CA-125 findings dichotomized as positive and negative ($p < 0.01$). No significant correlation was found between PET/CT results and stage or age (Tab. 2); the same happened when evaluating CA-125 results and stage or age.

A significant correlation between PET/CT results and CA-125 absolute values was found ($p < 0.01$) and as well as comparing CA-125 positivity or negativity and PET semiquantitative parameters ($p < 0.01$). A significant association was also found between CA-125 absolute values and semiquantitative PET parameters ($p < 0.01$) (Tab. 3).

In order to evaluate the possible influence of histotype on the correlation between PET/CT and CA-125, we decided to perform the aforementioned statistics by dividing the group of patients with serous carcinoma from other ones. In the group of the 80 patients with serous carcinoma, the significant correlation between PET/CT and CA-125 exposed before was confirmed. Otherwise, in the group of the 12 patients without serous carcinoma, the significant correlation wasn't confirmed.

Applying ROC curves analysis to all the 92 PET/CT scans, a value of 17 UI/mL for CA-125 (AUC 0.732, SE 84%, SP 62%) was extracted (Fig. 3). Furthermore, when comparing serum marker values using the aforementioned cutoff with PET/CT results, a significant association was observed ($p < 0.01$) (Tab. 4).

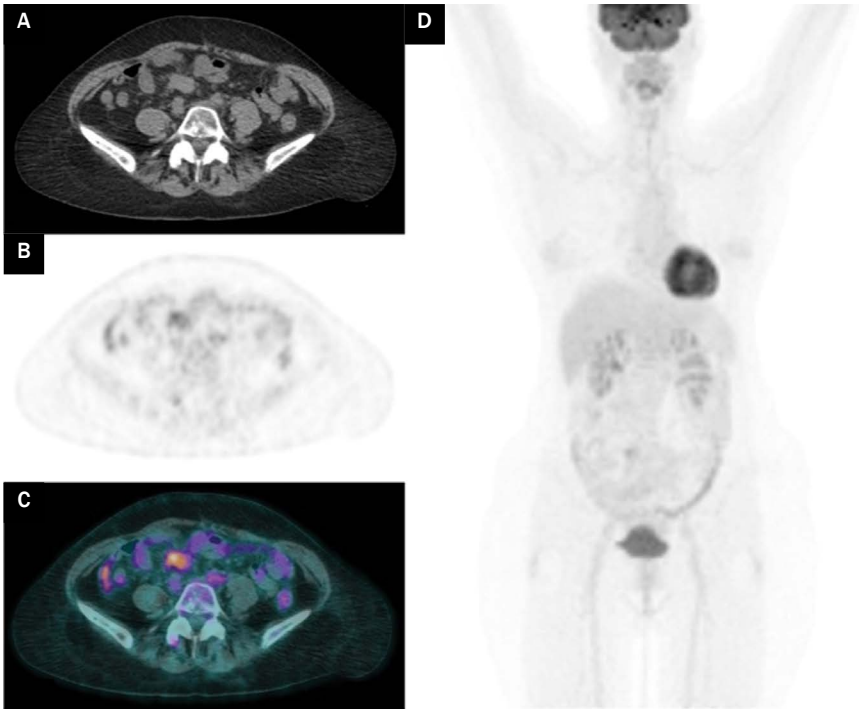

Figure 2. (**A**) Axial CT; (**B**) axial PET; (**C**) axial fused PET/CT; (**D**) and maximum intensity projection (MIP) images of an [^{18}F]FDG PET/CT scan demonstrating a focal peritoneal uptake in a patient with negative CA-125; subsequent removal of the lesion demonstrated the presence of a neuroendocrine tumor

Table 2. Correlation between PET/CT results and the main clinical features

	PET/CT		p-value
	Positive (%) n. 68	Negative (%) n. 24	
Age [years]			0.237
< 75	53 (78%)	22 (92%)	
≥ 75	15 (22%)	2 (8%)	
FIGO stage			0.357
I	1 (1%)	1 (4%)	
II	4 (6%)	0 (0%)	
III	37 (54%)	17 (71%)	
IV	26 (39%)	6 (25%)	
Therapy			
Surgery	1 (1%)	1 (4%)	
Surgery + chemotherapy	65 (97%)	22 (92%)	
Surgery + radiotherapy	1 (1%)	0 (0%)	
Surgery + chemotherapy + radiotherapy	1 (1%)	1 (4%)	
CA-125			0.002
Positive	44 (65%)	6 (25%)	
Negative	24 (35%)	18 (75%)	
CA-125 as continuos values	68 (100%)	24 (100%)	< 0.001

FIGO — International Federation for Gynecology and Obstetrics

Discussion

Relapse of ovarian cancer is extremely frequent affecting approximately 75% to 80% of all patients; 90% to 95% of patients with advanced disease (FIGO stage III/IV) will relapse within 2 years after primary treatment [7]. Furthermore, the role of [^{18}F]FDG PET/CT for the evaluation of relapse or persistence of disease and for the follow-up of patients has been underlined [11]. In a previous meta-analysis, Limei et al. [13] pointed out the fact that PET/CT may be the most accurate test for diagnosis of suspected recurrent ovarian cancer with high sensitivity and specificity and also a useful tool to evaluate the deextent of disease. In this context, the greatest value of [^{18}F]FDG PET/CT in ovarian cancer is represented by the high accuracy in detecting residual disease after primary treatment and in identifying recurrent disease in both symptomatic and asymptomatic patients [11]. PET/CT has also a role in optimizing the management plan in patients with recurrent ovarian cancer as was established previously (Ebina et al. [14] and Soussan et al. [15]).

Likewise, CA-125 is a sensitive and reliable tumor marker to investigate possible relapse of disease, with a reported accuracy of 79% to 95%, and its values increase from 3 to 6 months before the clinical presentation of recurrence [8–9]; it is also the simplest tool to trigger imaging and is a better approach than regular routine imaging for the diagnosis of recurrent ovarian cancer, as mentioned by the guidelines [2].

Table 3. Correlation between mean semiquantitative parameters and CA-125 values

	SUV-max	p-value	SUV-mean	p-value	SUVlbm	p-value	SUVbsa	p-value	MTV	p-value	TLG	p-value
CA-125 absolute values	9.52	< 0.001	5.09	< 0.001	6.67	< 0.001	2.49	< 0.001	21.94	< 0.001	184.71	< 0.001
CA-125		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001
positive	9.66		5.09		6.69		2.53		23.01		194.45	
negative	3.61		3.91		2.83		1.02		8.20		67.92	

MTV — metabolic tumor volume; TLG — total lesion glycolysis

Table 4. Receiver operating characteristic (ROC) curves analysis for CA-125

	Value	AUC	Standard error	95% CI	Significance level	Sensitivity	Specificity
CA-125	17	0.732	0.055	0.629–0.819	0.0001	83.8	62.5

AUC — area under curve; CI — confidence interval

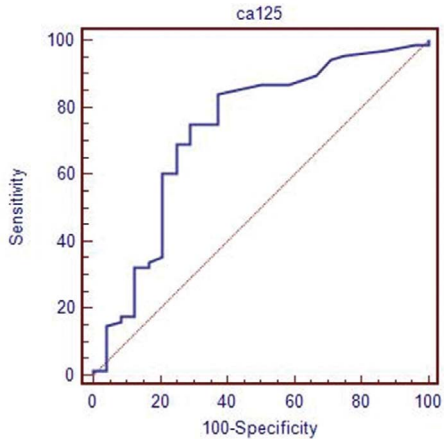

Figure 3. Receiver operating characteristic (ROC) curve was obtained when searching for the best tumor marker value for CA-125 to discriminate between positive PET/CT or negative one: a value of 17 UI/mL was obtained (AUC 0.732, SE 84%, SP 63%)

A meta-analysis by Gu et al. [5] reported that [^{18}F]FDG PET/CT could be a useful tool for current surveillance techniques, in particular for those patients with increasing CA-125 levels and negative CT or MR imaging. In this context, rising CA-125 levels in patients who were radically treated for ovarian cancer but show no evidence of relapse is the most frequent indication for PET/CT and high overall sensitivity (97%) has been obtained using PET/CT in asymptomatic patients with high serum CA-125 levels and non-conclusive results at CT [16–18]. A correlation between PET/CT and CA-125 could be therefore very useful since it can provide metabolic information allowing for differentiation between tumor recurrence and post-therapy scarring/fibrosis [1].

Our analysis confirmed the diagnostic value of [^{18}F]FDG PET/CT for the restaging of ovarian cancer after primary therapy. In particular, most of the exams resulted true positives and just a small amount of scans turned out to be false positives: in one case we found a diffuse uptake in the left iliac wing that on a subsequent MR scan was classified as not pathological, 3 were characterized by peritoneal focal uptakes interpreted as localization of disease that weren't confirmed and in 1 scan we found a focal peritoneal uptake suggestive of localization that was then diagnosed as a neuroendocrine tumor. Most of negative scans were confirmed as true negative and in the small amount of false negative, PET/CT was not able to identify pulmonary, peritoneal, or nodal lesions under its resolution power (5 mm).

The ranges of SE, SP, PPV, NPV and AC reported in literature for [^{18}F]FDG PET/CT in the restaging of ovarian cancer from some meta-analysis are 88% to 98%, 71% to 100%, 85% to 100%, 67% to 100% and 71% to 100% [5, 19]. Our results confirmed these evidences.

We find a significant correlation between PET scan positivity or negativity and CA-125 one. In the past Menzel et al. pointed out the correlation between CA-125 and PET/CT by demonstrating that serum marker levels were higher in patients whit positive PET/CT compared with patients with negative one and this finding was confirmed by other studies [1, 17].

Most of our patients had a diagnosis of serous carcinoma (87%) and this fact is really important to underline because it's known that this is the ovarian carcinoma histotype that expresses CA-125 the most; in other histotypes such as mucinous, endometrioid, and clear cell, the prognostic value of CA-125 is less known according to European guidelines [2]. In detail, 80% of serous ovarian cancer can express CA-125, while fewer than 30% of mucinous-, clear-cell-, and endometrioid cancer are positive for this surface antigen [20]. In this context, when applying statistical analysis between the two different groups of serous *vs.* non-serious carcinomas we reported a significant correlation between PET/CT and CA-125 just in the first group, underlying this different expression of tumor marker between different histotypes.

A significant correlation was also found between CA-125 absolute values and all PET semiquantitative parameters, CA-125 absolute values and PET/CT scan positivity or negativity, and PET semiquantitative parameters with CA-125 positivity or negativity. In the past, Kim et al. [21] pointed out a correlation between MTV and TLG with serum CA-125 levels at relapse in a patient with recurrence of ovarian epithelial cancer but they did not find any correlation between SUVmax and CA-125. These findings agree only in parts with ours, where also SUVmax is strongly correlated with CA-125 serum levels.

In the past, Kim et al. [6] reported a significant correlation of changes in [^{18}F]FDG PET/CT SUVmax, with recurrence in advanced epithelial ovarian cancer. Moreover, other papers noticed that the doubling time of CA-125 strongly correlates with recurrence and outcomes of ovarian cancer [22–23]. Evangelista et al. [24], observed that overall survival (OS) is significantly higher in patients with negative CA-125 values at the time of PET/CT, with negative PET/CT scan, and with no evidence of peritoneum recurrence and distant metastases. Moreover, Kim et al. [21] pointed out a significant correlation between MTV, TLG, and SUVmax with post-relapse survival. By underlying the significant correlation of PET/CT parameters and CA-125, we think that our study can confirm these findings.

A discriminating value of 17 UI/mL for CA-125 (AUC 0.732, SE 84%, SP 63%) for PET/CT positivity or negativity was underlined when applying ROC curve analysis. This value is very similar to the one found by Palomar et al. [16] in the past (18 UI/mL) when evaluating the role of [^{18}F]FDG PET/CT in 175 patients treated for ovarian cancer and with raised CA-125 levels. Similar results were also obtained by Fularz et al. [25] (17.6 UI/mL) in a study with 68 patients with suspicion of ovarian cancer relapse. Furthermore, when comparing serum marker values using the aforementioned cutoff with PET/CT results, a statistically significant association was observed.

Our work is not without limitations. First of all, its retrospective nature with heterogeneous clinical features of the population. Moreover, all 92 [^{18}F]FDG PET/CT came from a relatively low sample of patients. Lastly, a definitive histopathological diagnosis was not available for all PET/CT scans.

Conclusions

In conclusion, [^{18}F]FDG PET/CT is an accurate diagnostic tool to evaluate possible relapse or persistence of ovarian cancer after primary therapy. A strong correlation between PET qualitative and semiquantitative parameters and CA-125 values was underlined.

Conflict of interest

All the authors declare that they have no conflict of interest.

References

1. Marzola MC, Chondrogiannis S, Rubello D. Fludeoxyglucose F 18 PET/CT Assessment of Ovarian Cancer. PET Clin. 2018; 13(2): 179–202, doi: 10.1016/j.cpet.2017.11.005, indexed in Pubmed: 29482749.
2. Colombo N, Sessa C, Bois Adu, et al. ESMO–ESGO Ovarian Cancer Consensus Conference Working Group. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease. Int J Gynecol Cancer. 2019 [Epub ahead of print], doi: 10.1136/ijgc-2019-000308, indexed in Pubmed: 31048403.
3. Forstner R. Radiological staging of ovarian cancer: imaging findings and contribution of CT and MRI. Eur Radiol. 2007; 17(12): 3223–3235, doi: 10.1007/s00330-007-0736-5, indexed in Pubmed: 17701180.
4. Signorelli M, Guerra L, Pirovano C, et al. Detection of nodal metastases by 18F-FDG PET/CT in apparent early stage ovarian cancer: a prospective study. Gynecol Oncol. 2013; 131(2): 395–399, doi: 10.1016/j.ygyno.2013.08.022, indexed in Pubmed: 23988414.
5. Gu P, Pan LL, Wu SQ, et al. CA 125, PET alone, PET-CT, CT and MRI in diagnosing recurrent ovarian carcinoma: a systematic review and meta-analysis. Eur J Radiol. 2009; 71(1): 164–174, doi: 10.1016/j.ejrad.2008.02.019, indexed in Pubmed: 18378417.
6. Kim TH, Kim J, Kang YK, et al. Identification of Metabolic Biomarkers Using Serial F-FDG PET/CT for Prediction of Recurrence in Advanced Epithelial Ovarian Cancer. Transl Oncol. 2017; 10(3): 297–303, doi: 10.1016/j.tranon.2017.02.001, indexed in Pubmed: 28314183.
7. Antunovic L, Cimitan M, Borsatti E, et al. Revisiting the clinical value of 18F-FDG PET/CT in detection of recurrent epithelial ovarian carcinomas: correlation with histology, serum CA-125 assay, and conventional radiological modalities. Clin Nucl Med. 2012; 37(8): e184–e188, doi: 10.1097/RLU.0b013e31825b2583, indexed in Pubmed: 22785525.
8. Goonewardene TI, Hall MR, Rustin GJS. Management of asymptomatic patients on follow-up for ovarian cancer with rising CA-125 concentrations. Lancet Oncol. 2007; 8(9): 813–821, doi: 10.1016/S1470-2045(07)70273-5, indexed in Pubmed: 17765190.
9. Rustin GJ, Nelstrop AE, McClean P, et al. Defining response of ovarian carcinoma to initial chemotherapy according to serum CA 125. J Clin Oncol. 1996; 14(5): 1545–1551, doi: 10.1200/JCO.1996.14.5.1545, indexed in Pubmed: 8622070.
10. Santillan A, Garg R, Zahurak ML, et al. Risk of epithelial ovarian cancer recurrence in patients with rising serum CA-125 levels within the normal range. J Clin Oncol. 2005; 23(36): 9338–9343, doi: 10.1200/JCO.2005.02.2582, indexed in Pubmed: 16361633.
11. Ghosh J, Thulkar S, Kumar R, et al. Role of FDG PET-CT in asymptomatic epithelial ovarian cancer with rising serum CA-125: a pilot study. Natl Med J India. 2013; 26(6): 327–331, indexed in Pubmed: 25073988.
12. Boellaard R, Delgado-Bolton R, Oyen WJG, et al. European Association of Nuclear Medicine (EANM). FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging. 2015; 42(2): 328–354, doi: 10.1007/s00259-014-2961-x, indexed in Pubmed: 25452219.
13. Limei Z, Yong C, Yan Xu, et al. Accuracy of positron emission tomography/computed tomography in the diagnosis and restaging for recurrent ovarian cancer: a meta-analysis. Int J Gynecol Cancer. 2013; 23(4): 598–607, doi: 10.1097/IGC.0b013e31828a183c, indexed in Pubmed: 23502451.
14. Ebina Y, Watari H, Kaneuchi M, et al. Impact of FDG PET in optimizing patient selection for cytoreductive surgery in recurrent ovarian cancer. Eur J Nucl Med Mol Imaging. 2014; 41(3): 446–451, doi: 10.1007/s00259-013-2610-9, indexed in Pubmed: 24221243.
15. Soussan M, Wartski M, Cherel P, et al. Impact of FDG PET-CT imaging on the decision making in the biologic suspicion of ovarian carcinoma recurrence. Gynecol Oncol. 2008; 108(1): 160–165, doi: 10.1016/j.ygyno.2007.07.082, indexed in Pubmed: 17961640.
16. Palomar A, Nanni C, Castellucci P, et al. Value of FDG PET/CT in patients with treated ovarian cancer and raised CA125 serum levels. Mol Imaging Biol. 2012; 14(1): 123–129, doi: 10.1007/s11307-010-0468-9, indexed in Pubmed: 21240639.
17. Menzel C, Döbert N, Hamscho N, et al. The influence of CA 125 and CEA levels on the results of (18)F-deoxyglucose positron emission tomography in suspected recurrence of epithelial ovarian cancer. Strahlenther Onkol. 2004; 180(8): 497–501, doi: 10.1007/s00066-004-1208-3, indexed in Pubmed: 15292970.
18. Thrall MM, DeLoia JA, Gallion H, et al. Clinical use of combined positron emission tomography and computed tomography (FDG-PET/CT) in recurrent ovarian cancer. Gynecol Oncol. 2007; 105(1): 17–22, doi: 10.1016/j.ygyno.2006.10.060, indexed in Pubmed: 17208284.
19. Suppiah S, Chang WL, Hassan HA, et al. 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? World J Nucl

Med. 2017; 16(3): 176–185, doi: 10.4103/wjnm.WJNM_31_17, indexed in Pubmed: 28670174.

20. Mainguené C, Aillet G, Kremer M, et al. Immunohistochemical study of ovarian tumors using the OC 125 monoclonal antibody as a basis for potential in vivo and in vitro applications. J Nucl Med Allied Sci. 1986; 30(1): 19–22, indexed in Pubmed: 3528419.
21. Kim CY, Jeong SY, Chong GOh, et al. Quantitative metabolic parameters measured on F-18 FDG PET/CT predict survival after relapse in patients with relapsed epithelial ovarian cancer. Gynecol Oncol. 2015; 136(3): 498–504, doi: 10.1016/j.ygyno.2014.12.032, indexed in Pubmed: 25557270.
22. Han LY, Karavasilis V, Hagen Tv, et al. Doubling time of serum CA125 is an independent prognostic factor for survival in patients with ovarian cancer relapsing after first-line chemotherapy. Eur J Cancer. 2010; 46(8): 1359–1364, doi: 10.1016/j.ejca.2010.02.012, indexed in Pubmed: 20303743.
23. Varughese E, Kondalsamy-Chennakesavan S, Obermair A. The value of serum CA125 for the development of virtual follow-up strategies for patients with epithelial ovarian cancer: a retrospective study. J Ovarian Res. 2012; 5: 11, doi: 10.1186/1757-2215-5-11, indexed in Pubmed: 22436532.
24. Evangelista L, Palma MD, Gregianin M, et al. Diagnostic and prognostic evaluation of fluorodeoxyglucose positron emission tomography/computed tomography and its correlation with serum cancer antigen-125 (CA125) in a large cohort of ovarian cancer patients. J Turk Ger Gynecol Assoc. 2015; 16(3): 137–144, doi: 10.5152/jtgga.2015.15251, indexed in Pubmed: 26401105.
25. Fularz M, Adamiak P, Czepczyński R, et al. Utility of PET/CT in the diagnosis of recurrent ovarian cancer depending on CA 125 serum level. Nuklearmedizin. 2015; 54(4): 158–162, doi: 10.3413/Nukmed-0709-14-11, indexed in Pubmed: 26076719.