Diagnostic accuracy of PET/CT scan in evaluation of clinically suspected recurrent ovarian cancer

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ABSTRACT

Background: Accurate evaluation of ovarian carcinoma is utmost important for effective management. PET/CT is reported to be effective in evaluation of suspected recurrence of ovarian carcinoma. This study aims to assess the accuracy of PET/CT in evaluation of recurrent ovarian cancer among clinically suspected cases with rising tumor marker or suspicious clinic-radiological findings.

Patients and methods: This prospective cross-sectional study was conducted at Radiology department of Jinnah Postgraduate Medical Centre Karachi from 22nd April 2019 to 21st April 2020. Patients having age of 40 to 60 years and referred for PET scan with suspected recurrence of ovarian carcinoma were consecutively enrolled. Patients were suspected due to relevant history, clinical findings and initial imaging investigations with elevated CA-125 level. Results of 18FDG PET/CT scan was correlated with the raised tumor findings. The PET/CT scan showing abnormally elevated FDG take-up and higher SUV values than the background activity considered recurrence. Diagnostic accuracy of PET/CT was calculated taking raised tumor level as reference category.

Results: Of 65 patients, median age was 50 (43-56) years. The findings showed positive cases in 57 (87.7%) while negative in 8 (12.3%) patients, whereas the findings of tumor marker showed raised tumor marker in 61 (93.8%) patients. Diagnostic accuracy of PET/CT showed sensitivity, specificity, positive predicted value, negative predated value, and overall diagnostic accuracy as 93.44%, 100%, 100%, 50%, and 93.85% respectively.

Conclusion: A higher accuracy of PET/CT was observed in the diagnosis of recurrent ovarian cancer among clinically suspected cases, thus helping in devising an appropriate management plan by the treating physician.

Keywords
Diagnostic accuracy, PET/CT, Recurrent ovarian cancer

INTRODUCTION

In females, ovarian carcinoma is responsible for approximately 3% cases of cancer.[1] Various studies have reported a delay in the presentation of ovarian cancer due to which most cases presented at advanced phase of the disease and adjuvant chemotherapy and reductive surgery are the earlier treatment measures.[1,2] It is also reported in several studies that on average 25% to 35% of the cases at the initial-stage and 70% of the cases with the advanced disease showed recurrence in 2 years, despite of preferable response after treatment measures.[2,3] The ovarian cancer response for treatment is assessed through sequential assessment of CA-125.[4,5] Still, the disease cannot be excluded only by normal levels of CA-125, and elevated CA-125 levels cannot distinguish localized from diffused tumor reappearance.[4,5] Therefore, a major role has been played by imaging in order to evaluate recurrence of ovarian cancer.[5-7] Ultrasonography, computed tomography, and magnetic resonance imaging are conducted for suspecting ovarian cancer recurrence either by increased CA-125 or clinical symptoms. The sensitivity of post contrast CT is limited in diagnosis of minimal serosal and peritoneal implants. Furthermore, its ability for distinguishing post-operative fibrosis is doubtful from the recurrence of tumor even though it is utilized on a wide spectrum.[6,7] PET/CT plays important role in evaluating the recurrence of ovarian cancer.[8,9] It is reported in a review paper that diagnostic accuracy of 18F-FDG PET/CT in ovarian cancer ranges from 64-96%.[10] However, literature is still deficient regarding the role of PET/CT in detecting ovarian cancer recurrence. This study was designed to assess the accuracy of PET/CT to diagnose the recurrence of ovarian cancer between clinically suspected cases with high tumor markers or suspected radiological studies.

PATIENTS AND METHODS

A prospective analytical study was carried out at the Radiology Department of Jinnah Post Graduate Medical Centre (JPMC), Karachi from 22nd April 2019 to 21st April 2020 after obtaining ethical approval.

Consecutive patients having age of 40 to 60 years referred with suspicion of recurrence of ovarian cancer to Radiology Department for PET/CT scan by primary oncologist were enrolled. All women already treated for ovarian cancer referred to Radiology Department for PET/CT scan with sign and symptoms of ascites, pain/deteriorating general conditions or continuously rising CA-125 level to a value greater than 35 U/ml within last six months were termed as 'clinically suspected recurrent ovarian cancer'. Abnormally elevated FDG take-up and higher SUV values than the background on PET/CT was labeled as confirmed recurrent ovarian cancer. PET scan was avoided in patients with recent post-operative condition and abnormal blood glucose level. Moreover, patients were asked to fast for at least 6 hours. Before the procedure, intravenous injection radionuclide was administered to each patient of 10 to 15 mCi, according to weight of patient. The patients were requested for lying supine in quiet room for approximately 45-60 minutes post injection. For the purpose of attenuation correction, a low-dose unenhanced routine CT scan was conducted at beginning of examination. Afterwards, PET study was performed via Toshiba and ABT biomarker generator. In addition, enhanced diagnostic CT scanning was used based on 60 to 100 ml non-ionic intravenous contrast. The CT components were estimated at "150 kV", slice thickness "3.5 mm", pitch "0.9", and "200-220" mAs. For the correction of attenuation with volume information from CT, corrected reconstructed PET images with contrast was incorporated. In an automated workstation to ensure a suitable environment for the images to have CT, PET and fused PET-CT images, the images are recorded with special software. The images were shown on the trans axial in coronal and sagittal form. Two radiologists and one nuclear physician reviewed the PET/CT scans. The reporting radiologists were aware of the history of patients and level of serum CA-125. The PET/CT scan showing abnormally elevated FDG take-up and higher SUV values than the background activity considered recurrence, whereas the presence of any observed abnormality on CT, but the absence of FDG uptake on PET was considered negative. A standardized uptake value was measured using semi-quantitative analysis to differentiate benign from malignant uptake. Different locations such as abdominal or pelvic lymphadenopathy, peritoneal lesions, distant metastasis, and local recurrence in pelvis and in vaginal stump were assessed anatomically on CT scan and FDG uptake on PET image to suggest disease recurrence.

Table 1. Distribution of metastasis in positive patients (*n*=57)

Metastasis sites	No.	%
Local recurrence	15	26.3
Pelvic lymphadenopathy	12	21.1
Para-aortic lymph nodes	16	28.1
Distant lymphadenopathy	2	3.5
Peritoneal implants	15	23.1
Distant metastasis	4	7.0
Distant metastasis (n=4)		
Liver	1	25
Spleen	0	0
Bone	0	0
Lung	0	0
Pleura	4	100

SPSS version 22 was used for the purpose of statistical analysis. Median and interquartile range were computed for age, duration of treatment, and CA-125 level. Frequency and percentages were calculated for treatment modality, pathology subtype, PET/CT finding, and raised tumor level.

RESULTS
Total of 65 patients were evaluated. Median age was 50 (43-56) years. Total 41 (63%) presented ≤50 years of age. The median duration of initial treatment was 19 (15-22) months whereas the median CA-125 level was found to be 103 (67-889) U/mL. Most of the patients (*n*=61, 94.1%) had surgery and adjuvant chemotherapy and radiotherapy while chemotherapy alone was used in 4 (6.2%) patients. The epithelial tumor was reported in 61 (93.8%) and non-epithelial tumor in 4 (6.2%) patients. The findings of PET/CT scan in evaluation of recurrence ovarian cancer showed positive cases in 57 (87.7%) while negative in 8 (12.3%) patients whereas the findings of tumor marker showed raised tumor marker in 61 (93.8%) and normal tumor marker in 04 (6.2%) patients. The distribution of disease in positive cases showed that local recurrence, pelvic lymphadenopathy and peritoneal implants were observed in 12 (21.1%) and 15 (23.1%) patients respectively. The para-aortic lymph node was observed in 16 (28.1%) while distant metastasis in 4 (7%) patients (Table 1, Figures 1-3). Diagnostic accuracy of PET/CT scan in evaluation of recurrent ovarian cancer among clinically suspected cases showed sensitivity, specificity, positive predicted value, negative predicted value, and overall diagnostic accuracy was found to be 93.44%, 100%, 100%, 50%, 93.85% respectively.

DISCUSSION
The findings of this study have reported a higher accuracy of PET/CT scan in evaluation of ovarian cancer recurrence. This is similar to other several international studies that also shows the PET/CT
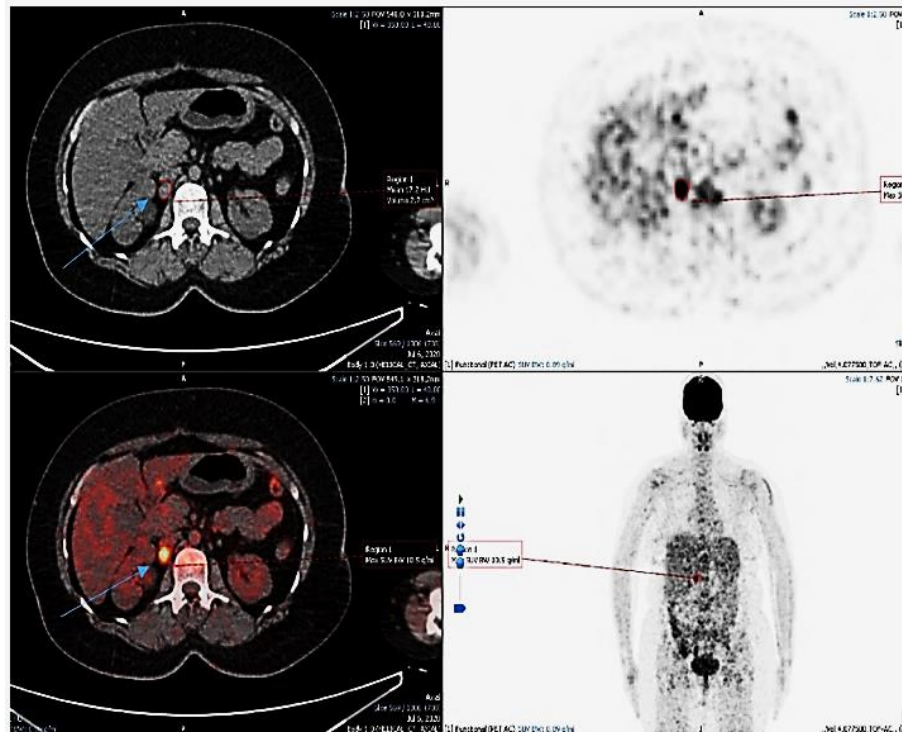
Figure 1. A 30 years old known ovarian carcinoma patient, PET/CT showing hypermetabolic right paracaval lymph node (blue arrow) which is the cause of raised CA-125 levels. It is not well appreciated on CT scan and can easily be missed
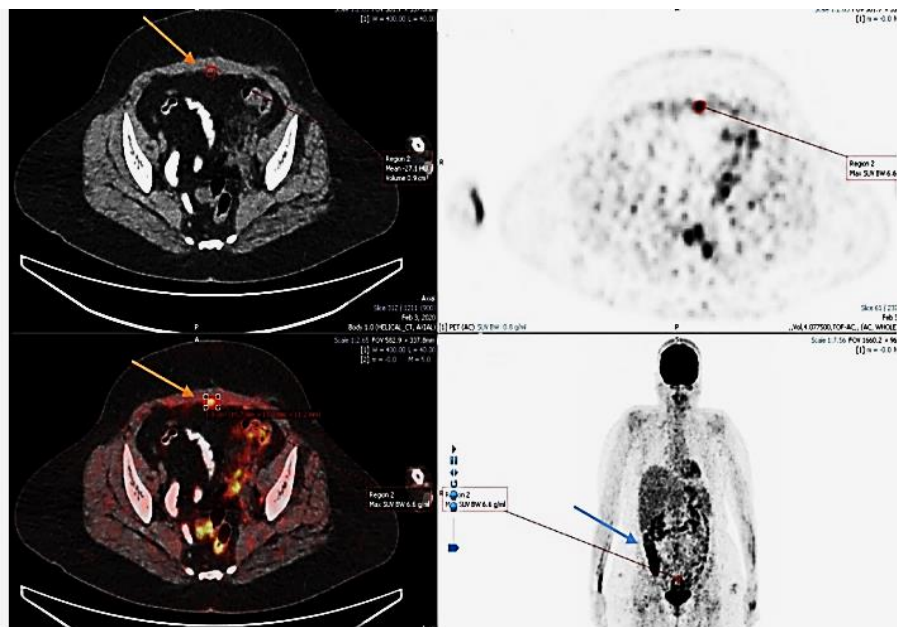

Figure 2. A 50 years old known ovarian CA patient with raised CA-125 levels, PET/CT shows lower abdominal wall nodule representing scar deposit (orange arrow), while blue arrow shows normal bowel uptake.
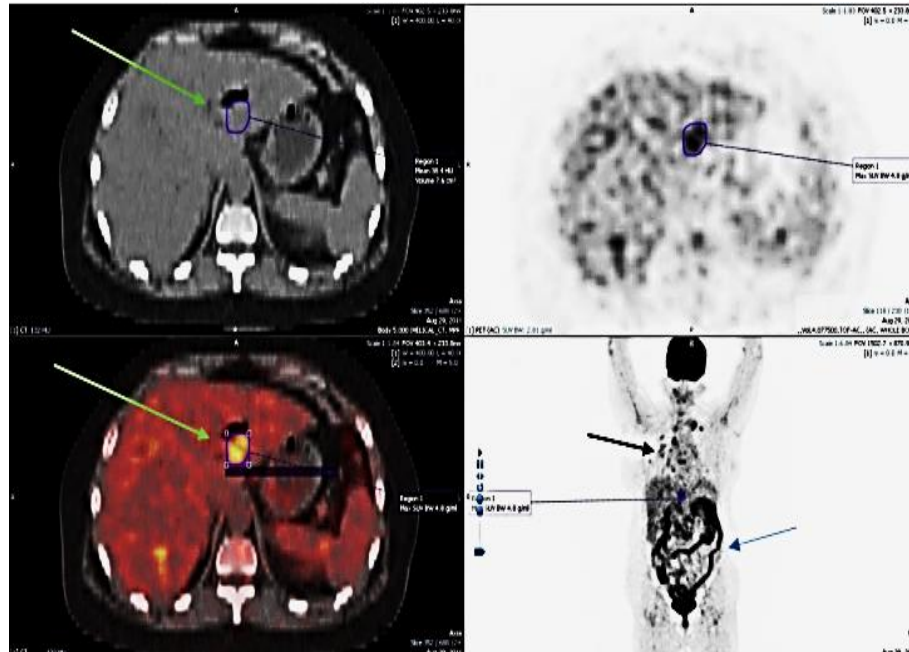
Figure 3. A 40 years old known CA ovary patient presents with raised CA-125 level, showing metabolically active areas in liver (green arrows) with higher SUV value than background on PET/CT scan, these are not well appreciated on CT. Black arrow showing metabolically inactive pulmonary nodules. Normal bowel uptake shown by blue arrow.

higher efficacy in detection of ovarian cancer.[10-16] In a study, the sensitivity of CT was reported as 85-100%.[9] The spatial resolution of PET for detecting lesions of less than 1 cm was approximately 5-10 mm.[17] Gu and coworkers described that specificity was found higher (92%) for CA-125 levels, whereas sensitivity was found higher for PET/CT (90%).[18] Authors also showed that diagnostic capability was comparable for CT and MRI based on estimated specificity 84% and 78%, and estimated sensitivity 79% and 75% respectively.[18] The effect of 18 FDG PET/CT was measured in a study in order to treat 90 cases with ovarian cancer recurrence and measured the data provided by 18-FDG PET/CT examination. The findings showed that treatment plan was modified in almost 60% of cases. PET / CT has been shown to be active against CT alone in the identification of nodal metastases, peritoneal nodules, as well as in the detection of high risk of disease progression over 12 months.[9] The role of FDG PET has been assessed by Torizuka and colleagues in order to detect the ovarian cancer recurrence among 25 cases.[19] The study reported that sensitivity and accuracy of 80% and 84% was reported through FDG PET as compared to lower sensitivity and accuracy for CT imaging. The study further indicated that PET/CT can easily detect the recurrence because of its metabolic activity. Several studies have shown the competency of FDG PET to identify apparent tumor tissue following treatment, which traditional imagery such as CT may

neglect.[20-22] Simcock and coauthors reported a massive change, in the course of treatment in approximately 58% of patients after PET / CT scans.[23] In present study, the current study finding showed that in positive cases the distribution of metastasis showed higher local recurrence, pelvic lymphadenopathy and peritoneal implants were observed. PET / CT was apparently seen to have a high PPV (100%). This finding implies an in-depth confirmation of its reliability in order to detect patients with macroscopic disease as well as to perform the adequate management plan. On the contrary, a low negative PPV was obtained in this study and is supported with previous studies.[19,24] This finding implies to restricted ability of PET/CT in order to detect smaller or microscopic lesions. Overall, the diagnostic accuracy is found quite similar in current as well as previous studies.[22,25,26] Therefore, the effectiveness of combined PET with contrast enhanced CT is more helpful in patients monitoring with suspicious recurrence of ovarian cancer as well as raised/normal tumor markers than PET alone. The limitation of this study was that there was no clinical confirmation of all irregular 18FDG sites. Nevertheless, the validation of all sites would not have been ethically accepted solely for the purpose of validating the results of the PET / CT scan. PET/CT was supported by high false positive rates of contrast enhanced CT as the first imaging method in those patients. It is therefore suggested to validate the initial discovery of tumor

metastases or recurrence on survival and quality of life through prospective clinical trials by possibly integrating the new target therapies. PET/CT is certainly a valuable tool for determining the recurrence of ovarian carcinoma. It can identify and locate recurrence with high precision so that it can affect and adjust the treatment plan and reduce the need for surgery to look at it.

CONCLUSION

PET/CT has higher accuracy in evaluation of recurrence of ovarian cancer in our cohort. It could be projected that PET/CT may contribute to adequate assessment of disease recurrence in the precise location of suspected FDG uptake enabling the disease to be restaged as well as improving the treatment plan for such patients accordingly.

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