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Original Research

CAN ^{18}F-FDG PET/CT be the preferred investigation in Suspected Recurrent Ovarian Carcinoma cases with Raised CA-125 levels? – A correlative study with Contrast Enhanced Computed Tomography (CECT)

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***ABSTRACT*:**

Introduction: Imaging has a well-established role in the evaluation of recurrent ovarian cancer.^{18}F-FDG PET/CT is an effective whole-body imaging technique that detects metabolic changes preceding structural findings. The aim of this retrospective study was to determine whether ^{18}F-FDG PET/CT can replace contrast enhanced computed tomography (CECT) as an initial imaging modality for recurrence detection in ovarian carcinoma patients with raised CA-125 levels. **Material and Methods:** The present study was carried among 52 women with suspected recurrence i.e. raised CA-125 levels and/or CECT scan findings, referred for ^{18}F-FDG PET/CT were studied. 44 patients underwent both ^{18}F-FDG PET/CT & CECT studies (Group A-I, A-II and B) and 8 patients underwent ^{18}F-FDG PET/CT only (Group C). Data analysis was done using Wilcoxon Match Pairs Signed Rank test. **Results:** In 44 patients where both ^{18}F-FDG PET/CT & CECT were done, ^{18}F-FDG PET/CT & CECT detected lesions in 42/44 (95.5%) and 26/44 (59%) patients respectively. Comparison of 42 positive ^{18}F-FDG PET/CT studies with CECT showed that ^{18}F-FDG PET/CT modified disease distribution in 34 patients i.e. more extensive disease in 18 (Group A-II) and detected disease in 16 CECT negative patients (Group B), ($p < 0.001$). Recurrence was detected in all 8 patients who underwent ^{18}F-FDG PET/CT only (Group C). No statistical significant difference was found between the mean (p 0.378) & median (p 0.760) values of CA-125 in all the 4 groups. **Conclusion:** ^{18}F-FDG PET/CT should be preferred initial imaging modality in suspected recurrent ovarian cases as it depicts larger disease burden when compared to CECT and can modify the treatment plan in cases with solitary lesions on CECT.

Keywords: Ovarian carcinoma; Recurrence**;** ^{18}F-Fluorodeoxyglucose (FDG); Positron Emission Tomography/Computed Tomography (PET/CT)

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INTRODUCTION

Ovarian cancer is one of the most leading cause of cancer death among women.[1] It is a genetically heterogeneous disease with a poor prognosis. Even though it is sensitive to platinum-based chemotherapy, the 5-year survival rate is only 30% for patients with advanced disease (stage III and higher)[2] and this poor survival rate is associated with frequent persistence or recurrence of disease.[3]

Recurrence may occur in 50-80% of these patients in spite of effective treatment and complete response.[1] There is also burgeoning evidence that combining

anatomical and functional imaging through ^{18}F-fluorodeoxyglucose (FDG) Positron Emission Tomography/Computed Tomography (PET/CT) may be helpful for evaluating patients with suspected ovarian cancer recurrence but negative or indeterminate contrast enhanced Computed Tomography (CECT) findings.[4]

Early detection of recurrence is clinically important and can improve the prognosis and survival of patients with cancer.[5] Imaging has a well-established role in the evaluation of recurrent ovarian cancer.[4] Contrast enhanced Computed tomography (CECT), considered the primary method of investigation because of its low cost and widespread availability, provides high-resolution anatomic details but may underestimate the actual tumor burden by overlooking small tumor clusters in areas of distorted anatomy after treatment.[5] Thus, CECT provides a "roadmap" of the disease distribution and facilitates surgical planning and assessment of the feasibility of optimal secondary cytoreduction.[4] ^{18}F-FDG PET is an effective whole-body imaging technique that detects metabolic changes preceding structural findings. However, the specificity of PET is impaired by false-positive or equivocal results attributable to the lack of precise anatomic landmarks and to sites of increased ^{18}F-FDG uptake of non-malignant etiology.[5] The aim of this retrospective study was to determine whether ^{18}F-FDG PET/CT can replace CECT as initial imaging modality for recurrence detection in ovarian carcinoma patients with raised CA-125 levels.

MATERIAL AND METHODS

The present study was carried among 52 women who had under-went treatment at Amrita Institute of medical sciences, Cochin, Kerala, India. Patient aged 35-74 years who reported to the department with suspected recurrence i.e. raised CA-125 levels and/or CECT scan findings, referred for ^{18}F-FDG PET/CT were studied. 8 patients underwent only ^{18}F-FDG PET/CT and 44 patients both ^{18}F-FDG PET/CT & CECT studies.

Examinations were performed on PET/CT system after at least 6 hours of fasting and documentation of blood glucose <150 mg/dL, 300–370MBq ^{18}F-FDG was injected intravenously and followed by a 45 +/− 15-minute uptake period. A contrast enhanced CT scan (100–120 kV, approximately 250-300 mA) was acquired, followed by PET emission images from brain to mid thigh. Oral contrast material was administered 45 minutes before imaging to patients. Intravenous contrast was given to patients without any contraindications.

^{18}F-FDG PET/CT images were interpreted by trained nuclear medicine physician and radiologist. Data analysis was done using Wilcoxon Match Pairs Signed Rank test.

RESULTS:

In 44 patients where both ^{18}F-FDG PET/CT & CECT were done, ^{18}F-FDG PET/CT & CECT detected lesions in 42/44 (95.5%) and 26/44 (59%) patients respectively.

42 ^{18}F-FDG PET/CT positive patients were divided in 3 groups A-I, A-II, and B as follows:

Group A-I (n = 8) both ^{18}F-FDG PET/CT, CECT were positive and both detected same number of lesions (9). (Fig 1)

Group A-Il (n-18) both ^{18}F-FDG PET/CT,CECT were positive but ^{18}F-FDG PET/CT detected more number of lesions (102 versus 26).(Fig 2)

Group B (n = 16) positive PET/CT with negative CECT, ^{18}F-FDG PET/CT detected 79 lesions. (Fig 3)

Recurrence was detected in all 8 patients who underwent ^{18}F-FDG PET/CT only (Group C).

Thus, comparison of 42 positive ^{18}F-FDG PET/CT studies with CECT showed that ^{18}F-FDG PET/CT modified disease distribution in 34 patients i.e. more extensive in 18 (Group A-II) and detected disease in 16 CECT negative patients (Group B), ($p < 0.001$). In 26 patients (Group A-I & A-II), where both ^{18}F-FDG PET/CT and CECT were positive, ^{18}F-FDG PET/CT detected more number of lesions (111 versus 35, $p<0.001$). Distribution of all lesions is shown in Table 1.

20/26 patients had solitary lesion on CECT. ^{18}F-FDG PET/CT found more than 1 lesion in 13 of these 20 patients. Thus, ^{18}F-FDG PET/CT modified treatment plan in 13/52(25%) patients by obviating planned surgical intervention. Only 2/50(4%) patients with positive ^{18}F-FDG PET/CT had above diaphragm disease (CI-95%). No statistical significant difference was found between the mean (p 0.378) & median (p 0.760) values of CA-125 in all the 4 groups. Distribution of CA-125 in all 4 groups is shown in Fig 4.

Table 1: Different Group

	Lymph nodes		Soft tissue deposits		Liver		Others		Total	
	PETCT	CECT	PETCT	CECT	PETCT	CECT	PETCT	CECT	PETCT	CECT
Group A-I	0	0	4	4	5	5	0	0	9	9
Group A-II	40	7	43	11	15	8	4	0	102	26
Group B	35	0	29	0	10	0	5	0	79	0
Group C	10	NA*	17	NA	0	NA	3	NA	30	NA

*NA – not applicable

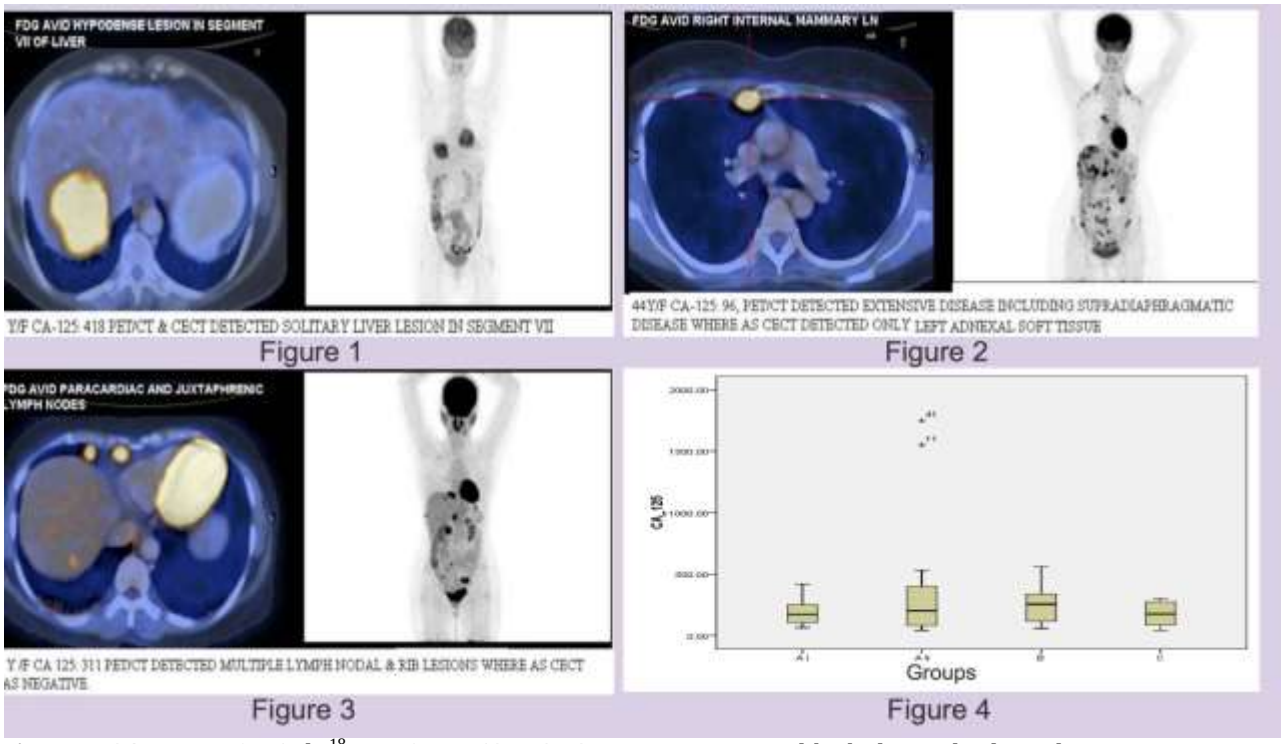

Figure1: CA-125: 418 U/ml; ^{18}F-FDG PET/CT, CECT were positive and both detected solitary lesion in segment VII.

Figure 2: CA-125: 96 U/ml; ^{18}F-FDG PET/CT detected extensive disease including supra- diaphragmatic disease whereas CECT detected only left adnexal soft tissue.

Figure 3: CA-125: 311 U/ml; ^{18}F-FDGPET/CT detected multiple lymph nodes and rib lesions whereas CECT as negative.

DISCUSSION

Many studies have established the superiority of using ^{18}F-FDG PET/CT over conventional imaging in suspected cases of recurrent ovarian carcinoma. Chung HH et al.[6] evaluated the accuracy of integrated positron emission tomography (PET) and computed tomography (CT) for depiction of suspected recurrent ovarian carcinoma after treatment, with use of clinical or histological findings as the reference standard. 45 of the 77 (58.4%) patients had documented recurrence during surgical exploration or clinical follow-up, while 32 patients (41.6%) had no evidence of recurrent tumour. Of the 45 patients with recurrent disease, 27 patients (60%) were confirmed to have recurrence by surgical biopsy. A correlation was found between ^{18}F-FDG PET/CT and histological or clinical analyses. Thus, integrated ^{18}F-FDG PET/CT is a sensitive post-therapy surveillance modality for the detection of recurrent ovarian cancer; it aids decisions on treatment plans and may ultimately have a favourable impact on prognosis.

Sala E et al.[3] compared accuracy and inter-observer variability in the detection and localization of recurrent ovarian cancer with contrast enhanced computed tomography (CECT) and positron emission tomography (PET)/CT and found that preliminary data suggest that CECT and PET/CT may have similar accuracy in detection of recurrent ovarian cancer. Tumor size, number, and SUV_{max} may have potential as prognostic biomarkers for patients with recurrent ovarian cancer.

Grigsby PW et al.[7] reported sensitivity and PPV of ^{18}F-FDG PET/CT for detection of recurrent disease at least 1 cm in size are 83.3% and 93.8%, respectively.

SironiS et al.[8] prospectively determine the diagnostic accuracy of ^{18}F-FDG PET/CT in the detection of recurrence in patients with treated uterine cancers. Tumour recurrence was found at histopathological analysis or follow-up examinations after ^{18}F-FDG PET/CT in 14 (56%) of the 25 patients. Patient-based sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ^{18}F-FDG PET/CT for detection of tumour recurrence were 92.9%, 100.0%, 100.0%, 91.7% and 96.0%, respectively. Lesion site-based sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ^{18}F-FDG PET/CT were 94.7%, 99.5%, 94.7%, 99.5% and 99.0%, respectively. Thus,this preliminary study showed that ^{18}F-FDG PET/CT may be an accurate method for the evaluation of recurrence in patients who have been treated for uterine cancers and are undergoing follow-up.

Vargas HA et al.[4] evaluated the associations between quantitative ^{18}F-FDG PET uptake metrics, optimal debulking (OD) and progression-free survival (PFS) in patients with recurrent ovarian cancer undergoing secondary cytoreductive surgery and concluded that ^{18}F-FDG PET metrics that reflect metabolic tumour burden are associated with optimal secondary cytoreductive surgery and progression-free survival in patients with recurrent ovarian cancer.

Nakamoto Y et al.[9] concluded that ^{18}F-FDG PET(/CT) has a major role in the evaluation of recurrent ovarian cancer when there is an increase in serum CA-125 and inconclusive or negative conventional (CT/MRI) imaging findings.

Therefore, positron emission tomography with 2-deoxy-2-[fluorine-18]-fluoro-D-glucose integrated with computed tomography (^{18F}-FDG PET/CT) has emerged as a powerful imaging tool for the detection of various cancers. The combined acquisition of PET and CT has synergistic advantages over PET or CT alone and minimizes their individual limitations. It is a valuable tool for staging and restaging of some tumors and has an important role in the detection of recurrence in asymptomatic patients with rising tumor marker levels and patients with negative or equivocal findings on conventional imaging techniques. It also allows for monitoring response to therapy and permitting timely modification of therapeutic regimens.[10]

^{18}F-FDG PET/CT provides fused images that demonstrate the complementary roles of functional and anatomic assessments in the diagnosis of cancer recurrence through the precise localization of suspected ^{18}F-FDG foci and their characterization as malignant or benign. In addition to the accurate diagnosis and definition of the whole extent of recurrent cancer, ^{18}F-FDG PET/CT has an impact on patient management because it can assist in defining potential candidates for surgery for cure, planning the appropriate surgical or radiotherapy approach, and referring patients with unresectable disease to other therapeutic options.[5]

CONCLUSION

^{18}F-FDG PET/CT should be preferred initial imaging modality in suspected recurrent ovarian cases as it depicts larger disease burden when compared to CECT and can modify the treatment plan in cases with solitary lesions on CECT.

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