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ORIGINAL ARTICLE

Role of PET–CT Scan in Gynaeconcology

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About the Author

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Abstract

The purpose of this study This study was undertaken to evaluate the role of positron emission tomography–CT (PET–CT) in diagnosis and management of gynecological malignancies in primary and recurrent settings and also to investigate its role in inappropriately treated patients, for pretreatment evaluation (staging) to help in proper therapeutic management.

Method This is a retrospective study of 56 patients of gynecological malignancy registered in Gujarat Cancer Research Institute from June 2011 to December 2013.

Results Out of 56 cases where PET was done, the results were as follows: carcinoma cervix—23, carcinoma ovary—20, carcinoma endometrium—9, carcinoma vulva—1, carcinoma vagina—2, and GTN—1. PET scan was negative in 37 % of patients where CT scan was suspicious, which changed the therapeutic modality and prevented further unnecessary interventions. In cases where clinical suspicion of recurrence was high based on rising tumor marker and CT scan was negative, subsequent PET–CT was able to pick up malignancy in 75 % cases. Eleven patients (25 %) with suspected recurrence with inconclusive CT scan and negative PET–CT scan were kept on follow-up, thus reducing further morbidity and cost.

Conclusion Addition of PET-CT, a noninvasive method to the oncologist's imaging armamentarium may ultimately improve both outcomes and costs by altering management strategies in primary and recurrent settings. The potential use of PET–CT appears promising in several decision-making steps in the management of patients with gynecological malignancy. It defines the extent of metastatic disease which enables the clinician to decide regarding salvageable surgical intervention or palliative measures.

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Keywords PET–CT scan · CT scan · SUV-max

Introduction

Computed tomography scan (CT scan) and magnetic resonance imaging (MRI) are anatomical high-resolution imaging techniques that are commonly used to guide the management of patients with gynecological cancer (Ca). Despite their widespread use, concerns still remain regarding the use of these conventional imaging techniques that may result in false negatives due to their inability to resolve small volumes (diameter <1 cm) of disease and false positives due to their inability to distinguish between viable tumor masses and masses consisting of necrotic or scar tissue. In the last two decades, the invention of PET, a noninvasive method, which can establish the metabolic or functional parameters of tissue, may aid in these distinctions. Instead of using anatomical deviations to identify areas of abnormality, PET uses radioactive tracer 18-Flurodeoxyglucose (FDG), a glucose analog which is preferentially taken up by and retained within malignant cells. The peak standardized uptake values (SUVs) were measured for each lesion with FDG accumulation. As PET alone lacks in its ability to give precise anatomical information, combined PET–CT integrating morphological data of CT scan and functional data of PET have gained wide clinical acceptance. Thus, compared with structural imaging techniques, FDG-PET has the potential to be a more accurate technique for diagnosis, staging, and aiding treatment decisions in oncology [1–4].

Material and Method

A retrospective analysis was conducted in 56 cases to study the role of PET–CT in the management of different gynecological malignancies in the patients who have registered for treatment in Department of Gynecological Oncology at Gujarat Cancer Research Institute (GCRI) from June 2011 to December 2013. Of these patients, clinical information, hematological and radiological investigations, PET–CT studies, and histopathological reports were considered.

Inclusion criteria The decision for PET–CT was made when there were suspicious or inconclusive lesions on CT, in the absence of clinical findings with normal serum tumor markers. Also it was done when there were persistently raised serum tumor markers in the presence of negative clinical findings and normal CT. PET–CT was used for pretreatment evaluation, diagnosing recurrence, and for monitoring therapeutic response.

Imaging techniques PET–CT was performed with BGO plus, Full ring PET–CT (GE Discovery 600) using radio isotope 18-FDG under 60-min uptake period. Extent of study is from vertex to upper mid of thigh. The SUV values are mentioned in gm/ml. Imaging started 60 min after intravenous bolus injection of (18F) FDG.

Image analysis CT scan and PET images were evaluated separately, and fused images in consensus by the same nuclear physician and radiologist. The peak SUVs were measured for each lesion with FDG accumulation. The SUV-max is a unique and noninvasive marker for studying the biochemical and metastatic changes in cancer tissues. SUV-max value has been reported to be correlated with tumor proliferation, tumor grade, and expression of glucose transporters, all of which are biomarkers for various types of malignant tumors. If SUV was over 3 gm/ml, it was determined as positive [5].

Analysis

The accuracies of the imaging studies were confirmed by histology (obtained during the second-look laparotomy or guided biopsies), by clinical (if any), or by radiological outcomes after subsequent management.

Results

Figure 1 and Table 1 show overall distribution of cases, and maximum cases where PET–CT scan was used were Ca Cervix—23 and Ca Ovary—20. Figure 2 indicates that PET–CT scan was used maximally for recurrence cases, thus indicating its role in recurrent cases—helping in proper therapeutic management.

Table 2 shows distribution of cases of Ca cervix. Five cases of pretreatment evaluation had normal paraaortic node on PET–CT, thus restricting radiation to pelvis avoiding unnecessary radiation toxicity. PET–CT was done in 14 cases of recurrence, out of which 4 (29 %) were kept

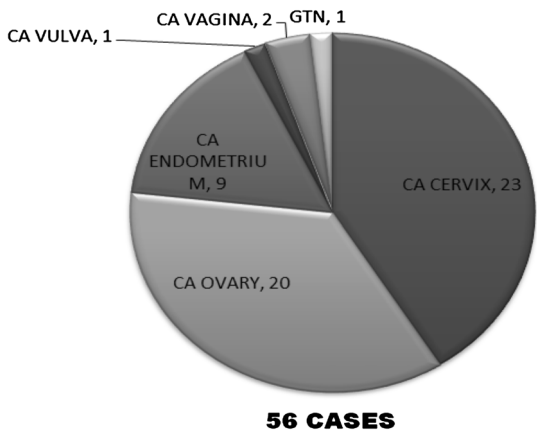


Fig. 1 Total cases

Table 1 Total cases

	Ovary	Cervix	Endometrium	Vulva	Vagina	GTN	Total
Staging (pretreatment)	2	5	1	–	–	–	8
Recurrence	18	14	7	1	2	1	43
Response	–	4	1	–	–	–	5
	20	23	9	1	2	1	56

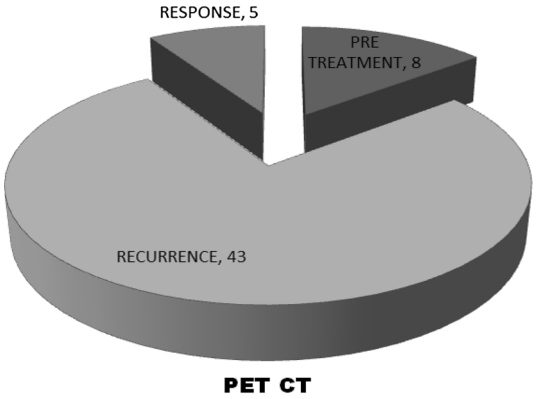


Fig. 2 Indications

on observation, avoiding further interventions and morbidity. In all the remaining cases where CT was suspicious, PET–CT confirmed recurrence, guiding further management decisions.

In this study, in the case of Ca ovary young patient treated outside suboptimally operated and unstaged, CT scan showed residual lesion, but PET–CT was normal; patient was given chemotherapy avoiding re-exploration which could have interfered with her fertility. Five cases (72 %) of recurrence had gradually elevating tumor marker but normal imaging, so PET–CT was done which showed recurrences, thus indicating early starting of chemotherapy (Table 3). In three patients (28 %), PET–CT was normal when CT showed recurrence, thus reducing morbidity of further treatment.

Table 4 shows two cases of Ca Endometrium (29 %). The patients were kept on follow-up as PET–CT was normal. In one case of ca vulva with the recurrence on CT scan, PET–CT was normal. Out of two cases of Ca vagina, one case was of vaginal melanoma which had undergone excisional biopsy, where CT was normal, but PET showed iliac lymphadenopathy. Thus, the patient went for chemotherapy. In a case of GTN undergoing chemotherapy, there was rise in beta HCG levels, but CT scan was normal, and subsequent PET–CT showed lung metastasis.

Table 5 shows overall result—PET scan was negative in 37 % of patients where CT scan was suspicious, which changed the therapeutic modality and prevented further unnecessary interventions in these patients. In cases where clinical suspicion of recurrence was high based on rising tumor marker and CT scan was negative, subsequent PET–CT was able to pick up malignancy in 75 % cases.

Discussion

Our institute being a tertiary referral cancer center, it is not unusual to have suboptimally operated, unstaged patients referred to us for further management. These patients pose a therapeutic dilemma. Despite continuing advances in surgical and nonsurgical therapeutic strategies, cancer recurrences and distant metastasis after initial treatment are often a major problem for women with gynecological cancer. PET Scan has been useful in differentiating benign from malignant tumor and in evaluating metastases and tumor recurrence.

Cervical cancer

The primary value for PET–CT in cervical cancer is to diagnose extrapelvic disease in initial staging and in detection of recurrence. In our study, five cases who were inappropriately treated outside were referred to our hospital with CT scan suspicious of para-aortic node enlargement, but their PET–CT scans were negative. Thus, PET–CT helped in proper pretreatment evaluation of disease spread to decide radiation field, reducing radiation toxicity. Grigsby et al. [6] and Kerr et al. [7] found that FDG-PET is a sensitive method for detecting regional and distant metastases in patients with cervical carcinoma and has the potential to replace conventional imaging studies and allow for more appropriate treatment-planning strategies. In a retrospective analysis of 41 patients by Wong et al. [8], ^{18}F-FDG-PET showed 100 % accuracy in detecting disease for initial staging. FDG-PET had a sensitivity of 82 % and specificity of 97 % (accuracy 92 %) for the evaluation of local recurrence. In another study of 101 patients with carcinoma of the cervix, Grisby et al. [6] observed that FDG-PET detects the involved lymph nodes more often than CT, and the findings of PET are superior predictors of survival than those of CT in patients with carcinoma of the cervix.

Another role of PET–CT in cervical cancer that is being evaluated is its value in monitoring the patients post

Table 2 Carcinoma cervix

Sr No.	Primary Site	CT Scan	PET/CT	Further Management
1	Pre treatment (5)	+ve (4)	+ve (2)	5 – RT (PELVIS)
			ve (2) 50%	
		-ve (1)	ve (1)	
2	Recurrence(14) Pelvic-6, extrapelvic 8	+ve (14)	+ve (10)	4 – Follow up, 6- CT, 2 - Surg, 1 –RT, 1 -Palliative
			-ve (4) 29%	
3.	Response (4)	+ve (3)	+ve (1)	1 – Follow up, 3 - RT
			-ve (2) 67%	
		-ve (1)	+ve (1)	

Table 3 Carcinoma ovary

Sr No.	Primary Site	CT Scan	PET/CT	Further Management
1	Pre treatment (2)	+ve(2)	-ve (2)	1-Surgery, 1- chemo
2	Recurrence (18)	+ve (11) Pelvic (5), extrapelvic(6)	+ve (8)	6- chemo, 1- surg, 1- palliative
			-ve (3) 28%	2- follow up , 1- surgery
			+ve (5) 72% Extrapelvic	
		-ve (7)		3-Chemo,1-surg, 1-palliative
			-ve (2)	2 – Follow up.

treatment. In this study, while assessing response to therapy—when CT was positive, PET was negative in 67 % of patients, guiding further treatment. According to Grigsby et al. [9], PET is valuable to evaluate the response to treatment and for the surveillance of patients after initial therapy. Schwartz et al. [10], in their prospective study on 92 patients after chemoradiation, showed that the 3-year progression-free survival rates, according to the metabolic response, were 78 % for a complete response, 33 % for partial response, and 0 % for progressive disease.

The major advantage of 18F-FDG-PET in cervical cancer is the diagnosis of relapse. In this study, PET–CT was negative when CT scan showed recurrence (pelvic 3, extrapelvic 1) in 29 % cases which avoided further unnecessary treatment, associated morbidity, and also cost. Grigsby et al. [11] found that PET is sensitive method for detecting regional and distant metastasis in 73 % patients. Yen et al. [12] compared PET findings with histopathology on follow-up: in 58 patients with biopsy-proven, 52 patients were with CT or MRI-proven relapse and 40 patients with complete remission, and found that 18F-FDG-PET provided an important value addition over conventional imaging in 73.8 % of patients, mainly in detecting distant metastases.

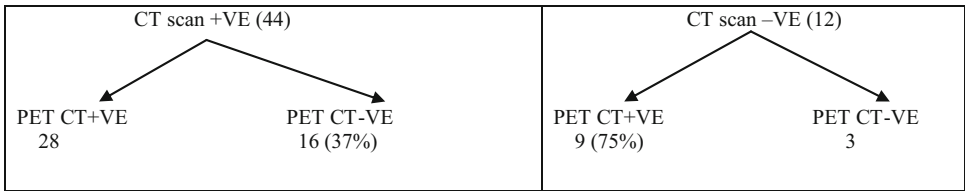
Carcinoma Ovary

PET–CT helped in avoiding repeat surgery in patients of ca ovary who were inappropriately treated outside (2 cases), where CT was suspicious. PET is of great benefit as a diagnostic tool in ovarian carcinoma when there is an increase in serum Ca 125 and CT/MRI or when conventional imaging are inconclusive or negative. FDG PET/CT has a reported sensitivity of 80–100 % for the detection of recurrent ovarian cancer [13]. Zimny et al. [14] reported that PET has a sensitivity of 96 % for localizing recurrent disease in patients with rising CA-125 levels. PET evidence of recurrent ovarian cancer preceded CT findings by

Table 4 Carcinoma endometrium

Sr no.	Primary Site	CT Scan	PET/CT	Further Management
1	Pre treatment (1)	−ve (1)	−ve (1)	Chemotherapy
2	Recurrence (7)	+ve (7)	+ve (5)	2—Follow up, 1—RT, 2—CT, 2—Palliative
			−ve (2) (29 %)	
3	Response (1)	+ve (1)	+ve (1)	Palliative

Table 5 Overall result



6 months, allowing for earlier reintroduction of therapy. In our study, in the case of clinical e/o recurrence with rising tumor marker, PET–CT could pick up recurrence (extrapelvic) in 72 % who had normal CT scan, thus allowing them to receive early treatment. Nanni et al. [15], demonstrated that fused PET/CT is capable of detecting recurrent ovarian carcinoma with high sensitivity and specificity and recommended its usage for patients' follow-up in the presence of high-risk disease relapse, equivocal findings at conventional radiological imaging, and increased serum Ca 125 levels.

Carcinoma Endometrium

In 29 % of cases, PET–CT was normal when CT scan was suspicious for recurrence, which allowed changing treatment modality. According to Chung et al. [16], PET/CT in detection of recurrent endometrial ca has an accuracy of 92.3 %, and allowed changing treatment modality in 22.6 % patients.

In our study, a case of operated ca vulva, on follow-up, showed CT scan of recurrence in lung but PET–CT was normal, allowing changing further modality. Also a case of vaginal melanoma on excisional biopsy had no nodal involvement on CT scan, but PET–CT showed nodal involvement. Data for PET–CT in ca vulva and vagina are sparse, but they help in staging of the disease and detecting nodal metastasis. Cohn et al. [17] carried out a prospective study, evaluating the role of FDG-PET in staging disease with respect to groin nodal metastasis. The study found a sensitivity of 80 %, specificity of 90 %, PPV of 80 %, and NPV of 90 % for detection of nodal metastases on a patient-specific analysis. It appears from here that PET is of value and more effective than conventional imaging with respect to detecting nodal as well as distant metastases for vulva carcinoma.

There was one case of gestational trophoblastic tumor, high risk with vaginal, lung, and brain metastases, who underwent six cycles of chemotherapy EMACO with cranial RT. Beta HCG was reducing initially, but demonstrated sudden rise on treatment. All imaging modalities were normal, but PET–CT scan showed metabolic active foci in lung, and then the patient responded to second-line chemotherapy.

Despite the relatively high sensitivity of FDG-PET, there are several disadvantages. False negatives can occur with lesions smaller than 1.0 cm and with certain tumor types that demonstrate low metabolic activity. Relatively low specificity with false-positive results can be seen due to the increased FDG uptake in normal organs, severe inflammatory disorders such as tuberculosis, and granulomatous disease.

Conclusion

PET–CT provides high management impact and superior prognostic stratification compared with conventional techniques in the restaging of a range of gynecological malignancies. It offers high diagnostic accuracies both in the evaluation of suspected tumor recurrence and persistent disease in selected cases. The whole-body FDG-PET scan

is a sensitive post-therapy surveillance modality for detection of recurrent gynecological cancer and aids in deciding treatment plans and eventually, may have favorable impact on prognosis and survival. It is not only a useful tool for early detection of subtle recurrences, but also allows to individualize optimal treatment plan by selecting patients for curative intent with localized recurrence and avoiding administration of unnecessary treatment to patients with incurable disease. Based on the literature reviews available to date, the potential use of PET–CT appears promising in several decision-making steps in the management of patients with gynecological malignancies.

PET–CT, a noninvasive method, defines the extent of metastatic disease which enables the clinician to decide regarding salvageable surgical intervention or palliative measures. In our study, PET–CT allowed changing management modality in 37 % patients. Thus, addition of PET–CT to the oncologist's imaging armamentarium may ultimately improve both outcomes and costs by enabling alterations in management strategies in primary and recurrent settings.

Compliance with ethical requirements and Conflict of interest The authors declare that they have no ethical conflicts. Dr. Ashwini Pawar, Dr. Digvijay Patil, Dr. Shilpa Patel, Dr. Meeta Mankad, and Dr. Pariseema declare that they have no conflict of interest.

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