Original Article

Evaluation of Positron Emission Tomography and Contrast-Enhanced Computed Tomography Scan in Nodal Staging of Early Operable Uterine Cancers

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Abstract

Introduction: In early operable stages of cervical an endometrial malignancies, surgical staging of lymph nodes is advocated as contrast-enhanced computed tomography (CECT) has limited sensitivity and accuracy. Although fluorine-18 (F-18) fluorodeoxyglucose (FDG)/positron emission tomography (PET)-CT has potential to identify subcentimeter-sized nodal metastases, higher prevalence of pelvic inflammatory disease in developing countries could result in lower accuracy. The present study was undertaken to assess the incremental value of PET scan over CECT for nodal staging before radical surgery. **Methods:** Forty-four patients with the International Federation of Gynecology and Obstetrics (FIGO) Stage IA2–IIb carcinoma cervix and 28 patients of FIGO Stage I–II carcinoma endometrium underwent F-18 FDG-PET-CECT scan. A SUV_{max} value >2.5 g/ml based on body weight was considered as positive. An enhancing node with >1 cm size in the shortest dimension, with loss of fatty hilum was considered positive on CT images. The histological findings were considered the gold standard against which the two modalities were compared. **Results:** All 1226 pelvic nodes were dissected, of which 65 were found to be metastatic (i.e., 5.3%). Of the 72 patients, 15 (20.83%) had pelvic nodal metastases. The overall accuracy of PET and CECT for assessment of pelvic nodal metastases was comparable (i.e., 86% vs. 85%). **Conclusion:** PET and CECT scans have similar accuracy in pelvic nodal staging of operable uterine malignancies. Granulomatous inflammation may not be a major cause of false-positive results. The sensitivity and negative predictive values are not high enough to obviate need of surgical nodal staging.

Keywords: *Carcinoma cervix, contrast-enhanced computed tomography, endometrial carcinoma, fluorodeoxyglucose/positron emission tomography-computed tomography scan*

Introduction

Cervical and endometrial cancers are the most common gynecological malignancies worldwide followed by ovarian cancer. Cervical cancer is the most common gynecological cancer in India in women accounting for 22.86% of all cancer cases in women. Although lymph nodal involvement is an independent prognostic factor, it is not incorporated in the International Federation of Gynecology and Obstetrics (FIGO) staging system.[1-3] Conventionally used computed tomography (CT) has limited sensitivity and accuracy for nodal metastases in early operable stage of these malignancies due to which surgical staging of lymph nodes is usually advocated. Fluorine-18 (F-18) fluorodeoxyglucose (FDG) positron emission tomography-CT (PET-CT) has potential to identify subcentimeter (subcm)-sized nodal metastases. However, higher prevalence of pelvic inflammatory disease in developing countries could result in false-positive results limiting its specificity and accuracy. In view of paucity of literature, the present study was undertaken to assess the incremental value of PET scan, if any, over the conventionally used contrast-enhanced CT (CECT) scan of abdomen and pelvis for nodal staging before radical hysterectomy and retroperitoneal lymphadenectomy (RH-RPLND).[4]

Methods

This prospective study comprised 72 consecutive patients of early uterine carcinoma. It comprised 44 patients with FIGO Stage IA2–IIb carcinoma cervix and 28 patients of FIGO Stage I–II carcinoma endometrium. The mean age of the studied

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population was 54.3 ± 10.61 years (a ge ranging from 36 to 81 years). Informed written consent was obtained from each patient. The patients underwent a preoperative F-18 FDG PET scan and CECT before RH-RPLND.

PET-CECT imaging was performed on GE discovery STE PET-CT scanner (GE Healthcare, Waukesha, Wisconsin, US) within 45–60 min of F-18 FDG injection (5 MBq/kg body weight). The scan was performed from base of skull to mid-thigh. CT scan acquisition parameters included DFOV: 70 cm, kV: 120, and mA: 80–200 (auto mA). The slice thickness was 3.75-mm interval with 3.75-mm pitch. Filtered back projection was used for reconstruction with matrix: 512 × 512, and CTAC algorithm for attenuation correction PET scans was acquired at 2 min/bed position in 3D mode with iterative reconstruction, using matrix: 128 × 128, subset: 21, iteration: 2, Z-filter: std, attenuation correction: CTAC, and scatter and random correction based on stored correction matrix.

A SUV_{max} value >2.5 g/ml based on body weight was considered as positive for the present study. An enhancing node with >1 cm size in the shortest dimension with loss of fatty hilum was considered positive on CT images. The histological findings were considered the gold standard against which the sensitivity, specificity, positive, and negative predictive value, and accuracy of the two modalities was compared using the Chi-square test.

Results

The studied population comprised 44 patients with FIGO Stage IA2–IIb carcinoma cervix and 28 patients of FIGO Stage I–II carcinoma endometrium.

All 1226 pelvic nodes were dissected, of which 65 were found to be metastatic (i.e., 5.3%). Of the 72 patients, 15 (20.83%) had pelvic nodal metastases.

All 117 para-aortic nodes were dissected, of which 7 were found to be metastatic (i.e., 6%). Of the 72 patients, 4 (i.e., 5.5%) had para-aortic nodal metastases.

Pelvic nodal assessment

PET scan was found to have a higher sensitivity in detecting pelvic nodal metastases when compared to the conventionally used CECT (i.e., 73% vs. 67%). It correctly identified metastases in subcm-sized nodes in one case [Tables 1 and 2 and Figures 1 and 2].

False-positive nodes were seen in six cases on PET scan and CECT scan. These were due to enlarged reactive nodes. None of the false-positive nodes revealed granulomatous inflammation [Figure 3].

False-negative nodes were seen in four cases on PET scan and five cases on CECT scan. These were due to microscopic metastases in subcm-sized nodes. This resulted in better negative predictive value of PET over CECT scan (i.e., 93% vs. 91%).

In one case, synchronous ascending colon carcinoma was detected on both the imaging modalities [Figure 4].

The overall accuracy of PET and CECT for assessment of pelvic nodal metastases was 86% versus 85%, respectively. This difference was comparable and not found to be statistically significant ($P > 0.05$).

Para-aortic nodal assessment

Among the 72 cases studied, 4 cases showed para-aortic nodal metastases (i.e., 5.55%). PET-CECT correctly identified para-aortic nodal metastases in two cases, resulting in the sensitivity of 50% [Table 3]. The other two cases which were missed by both the modalities were due to microscopic metastases in subcm-sized nodes. PET was false positive in three cases. Histopathological report was suggestive of reactive lymphadenitis in these cases. None of these nodes showed granulomatous inflammation. Overall, CT had better accuracy than PET scan (i.e., 99% vs. 93%).

Discussion

Majority of the cases of carcinoma cervix and endometrium present in locally advanced or metastatic stage. With

Table 1: Pelvic nodes

	Carcinoma cervix		Carcinoma endometrium		Combined	
	PET	CT	PET	CT	PET	CT
True positive	6	6	5	4	11	10
True negative	33	34	18	17	51	51
False positive	2	1	4	5	6	6
False negative	3	3	1	2	4	5
Total	44	44	28	28	72	72

PET: Positron emission tomography, CT: Computed tomography

Table 2: Pelvic nodes Analysis

	Cervix		Endometrium		Combined	
	PET	CECT	PET	CECT	PET	CECT
Sensitivity (%)	67	67	83	67	73	67
Specificity (%)	94	97	82	77	89	89
PPV (%)	67	86	56	44	65	62
NPV (%)	92	92	95	90	93	91
Accuracy (%)	89	91	82	75	86	85

PET: Positron emission tomography, CT: Computed tomography, CECT: Contrast-enhanced CT, NPV: Negative predictive value, PPV: Positive predictive value

Table 3: Para-aortic nodes

	Carcinoma cervix		Carcinoma endometrium		Total	
	PET	CT	PET	CT	PET	CT
True positive	0	0	2	2	2	2
True negative	42	42	23	25	65	67
False positive	0	0	3	1	3	1
False negative	2	2	0	0	2	2
Total	44	44	28	28	72	72

PET: Positron emission tomography, CT: Computed tomography

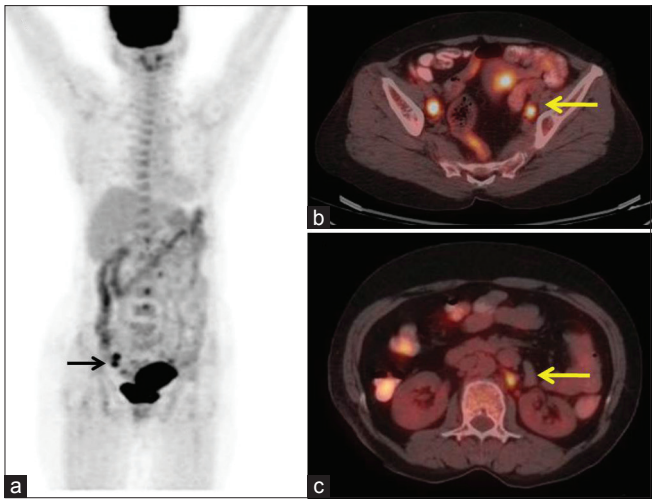

Figure 1: True positive: Fluorine-18 fluorodeoxyglucose positron emission tomography maximum intensity projection (a) and axial-fused positron emission tomography-computed tomography (b and c) images showing enlarged metastatic right external iliac and left para-aortic nodes (arrows). Histopathological report was suggestive of metastasis

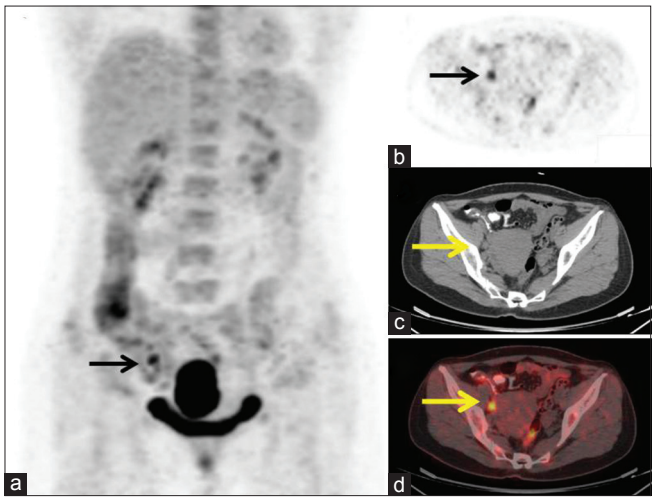

Figure 3: False positive: Fluorine-18 fluorodeoxyglucose positron emission tomography maximum intensity projection (a), axial positron emission tomography (b), and axial-fused positron emission tomography-computed tomography (d) images show hypermetabolism in the right iliac fossa (arrows) which correspond to the enlarged left external iliac node on axial computed tomography image (c). Histopathological report was suggestive of reactive lymphadenitis

cervical cancer screening program, the cases diagnosed in early stage is on a rise.[5]

The FIGO clinical staging is most commonly used for staging of these malignancies. Although nodal staging is the most important independent prognostic factor, especially for early-stage disease, it is not a part of FIGO clinical staging. The survival of patients with positive pelvic nodes has been reported to be half that of patients with negative pelvic nodes.[3,6]

CT and MRI scans are the most commonly used imaging modalities for nodal staging and use size criteria of >1 cm for assessment of nodal metastases. Hence, these imaging

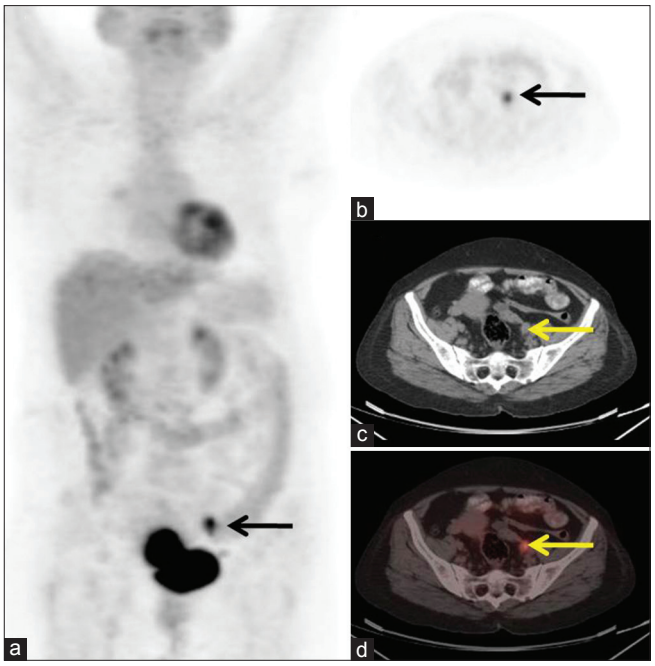

Figure 2: Incremental value of positron emission tomography over computed tomography. Fluorine-18 fluorodeoxyglucose positron emission tomography maximum intensity projection (a), axial positron emission tomography (b), and axial-fused positron emission tomography-computed tomography (d) images show hypermetabolism in the left iliac fossa (arrows) which correspond to subcentimeter-sized left external iliac node on axial computed tomography image (c). Histopathological report was suggestive of metastasis

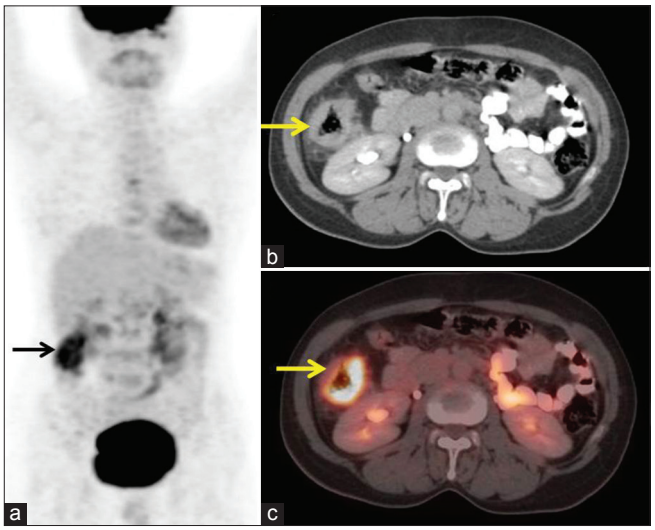

Figure 4: Synchronous carcinoma ascending colon. Fluorine-18 fluorodeoxyglucose positron emission tomography maximum intensity projection (a), axial computed tomography (b), and axial-fused positron emission tomography-computed tomography (c) images show hypermetabolism in the ascending colon thickening (arrows). Biopsy was suggestive of adenocarcinoma

techniques have a limitation in assessing metastases in subcm-sized nodes. Furthermore, reactive nonmetastatic nodes can have a size >1 cm. These limitations have resulted in lower sensitivity and accuracy of conventional imaging in nodal staging of uterine malignancies. Therefore, surgical staging of lymph nodes is considered

as the gold standard to determine lymphatic involvement in cervical cancer and high-risk endometrial cancer. The histopathological study of the lymphadenectomy specimen enables adjuvant treatment planning with chemotherapy and/or radiotherapy. Surgical nodal dissection, however, is associated with immediate and delayed complications.[7-9] Hence, there is a need for an imaging modality to accurately diagnose retroperitoneal lymph nodal metastases so that need for surgical nodal staging can be avoided or obviated.

F-18 FDG PET scan being a functional imaging modality is independent of size criteria. Ability to detect metastases in subcm-sized nodes can improve sensitivity. However, F-18 FDG is not a cancer-specific radiopharmaceutical. Reactive lymphadenitis and granulomatous inflammation are common causes of false-positive FDG/PET-CT in oncology. With the higher prevalence of pelvic inflammatory disease in developing countries, there is a theoretical possibility of higher false-positive results lowering the overall accuracy.

Meta-analysis by Selman *et al*. has proved superiority of PET scan over CT and MRI scan for nodal staging of locally advanced carcinoma cervix.[10] However, there is a paucity of literature on its role in early uterine malignancies.[11-15] Hence, the present study was undertaken to assess the role of PET scan in nodal staging of early uterine malignancies.

In the present study, pelvic nodal metastases were noted in 21% cases. The sensitivity, specificity, PPV, NPV, and accuracy of PET scan were 73%, 89%, 65%, 93%, and 86%, respectively. The sensitivity, specificity, PPV, NPV, and accuracy of CT scan was 67%, 89%, 62%, 91%, and 89%, respectively. The results for both these modalities were comparable. The sensitivity and negative predictive values are not high enough to obviate the need of surgical nodal staging. Similar results were obtained in a meta-analysis by Bansal *et al*.[4]

PET scan correctly identified metastases in subcm-sized node in one case. On the other hand, microscopic metastases resulted in false-negative nodes in four cases on PET scan and five cases on CECT scan. This resulted in lower overall sensitivity for both these modalities (73% vs. 67%).

False-positive nodes were seen in six cases on PET scan. These were due to enlarged reactive nodes. However, interestingly, none of the false-positive nodes revealed any inflammatory pathology. This study highlights the fact that granulomatous inflammation may not be a major cause of false-positive results as initially thought.

Unsuspected synchronous primary malignancies are detected in a small percentage of cases but with a positive influence on the management of considerable part of such patients.[16] In the present study, synchronous ascending colon carcinoma was diagnosed in one case, and right hemicolectomy was performed for the same.

The overall accuracy of PET and CECT scan for pelvic nodal metastases was comparable (i.e., 86% vs. 85%). The accuracy noted in the present study was comparable to the already published literature.[11]

Conclusion

PET and CECT scans have similar accuracy in pelvic nodal staging of operable uterine malignancies. Granulomatous inflammation may not be a major cause of false-positive results as initially thought. However, the sensitivity and negative predictive values are not high enough to obviate the need of surgical nodal staging.

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Conflicts of interest

There are no conflicts of interest.

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