Original Article

Comparative Study of Positron Emission Tomography/Computed Tomography and Computed Tomography in the Evaluation of Post-treatment Carcinoma Cervix Patients

Saurabh Pantola, Sanjay Kala[1], Chayanika Kala[2], Santhosh Sampath[3], Mukesh Shukla[4]

Department of Radiodiagnosis, Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Departments of [1]Surgery and [2]Pathology, Ganesh Shankar Vidyarthi Memorial Medical College, Kanpur, Uttar Pradesh, [3]Department of Nuclear Imaging and Molecular Medicine, Institute of Nuclear Imaging and Molecular Medicine, Tamil Nadu Government Multi Super Specialty Hospital, Chennai, Tamil Nadu, [4]Department of Community and Family Medicine, All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, India

Abstract

Purpose of Study: To evaluate and compare imaging findings using computed tomography (CT) alone and positron emission tomography/CT (PET/CT) fusion imaging in posttreatment carcinoma cervix patients for recurrence. **Subjects and Methods:** From June 2014 to May 2016, 50 posttreatment carcinoma cervix patients were referred to our institution for PET/CT imaging. In all 50 of these patients referred for evaluation, a reliable reference standard was available. The reference standard was established by histopathological examination of accessible locoregional and nodal/distant metastatic involvement or follow-up of patients. CT and PET/CT were performed and analyzed for locoregional, pelvic nodal, and distant metastasis involvement in posttreatment carcinoma cervix cases. **Results:** In the evaluation of locoregional involvement, CT alone was found to have a sensitivity of 75% and specificity of 90% while PET/CT was found to have a sensitivity of 95% and specificity of 100%. Furthermore, in evaluation of pelvic nodal involvement, CT alone was found to have a sensitivity of 72% and specificity of 92.6% while PET/CT was found to have a sensitivity of 95.5% and specificity of 92.9%. In context to distant metastasis involvement (including para-aortic nodes), CT alone was found to have a sensitivity of 91.7% and specificity of 96.2% while PET/CT was found to have a sensitivity of 95.8% and specificity of 100%. PET/CT fusion in comparison to CT alone is better in sensitivity and specificity in the detection of locoregional involvement, pelvic node invasion, and distant metastasis in posttreatment carcinoma cervix cases.

Keywords: *Carcinoma, cervical cancer, positron emission tomography/computed tomography*

Introduction

Cervical cancer is one of the common gynecologic malignancies in India. The incidence of cervical cancer varies geographically within the country, with age-adjusted incidence of 22.3/100,000 females in Chennai, making up to ~18.5% of all cancers among females in India.[1] Risk factors for carcinoma cervix include earlier age at initiation of sexual activity, multiple sexual partners, multiparity, cigarette smoking, immunosuppression, low socioeconomic-cultural status, and infection with human papillomaviruses 16 and 18.[2]

The incidence of locoregional spread is higher in carcinoma cervix compared to other gynecological malignancies due to increased prevalence of capsular break in carcinoma cervix. There are three lymphatic pathways of drainage for the cervix through which tumor can spread. The lateral route is along the external iliac vessels, the hypogastric route is along the internal iliac vessels, and the presacral route is along the uterosacral ligament. All three routes eventually drain into the common iliac lymph nodes, possibly leading to the involvement of the para-aortic nodes, which represents distant metastatic disease.

The American Cancer Society reports that the death rate from cervical cancer has significantly reduced attributed to a significant increase in detection of early-stage, small cancers due to the development of the Papanicolaou smear.[3] However, only minor improvement has been achieved in the survival rate for invasive cervical cancer. Even after treatment, disease will recur in approximately one-third of patients treated for locally advanced cancer, and most of these recurrences will be within the first 2 years after initial therapy.[4,5] In the posttherapy scenario, the timely detection

How to cite this article: Pantola S, Kala S, Kala C, Sampath S, Shukla M. Comparative study of positron emission tomography/computed tomography and computed tomography in the evaluation of post-treatment carcinoma cervix patients. Indian J Nucl Med 2018;33:194-201.

Address for correspondence:
Dr. Saurabh Pantola, 96-HA Vihar, Panigaon, Indiranagar, Lucknow - 226 016, Uttar Pradesh, India.
E-mail: saurabhpantola@gmail.com

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.IJNM_13_18

Quick Response Code:

of recurrence is helpful for guiding management which may be potentially curative in a subgroup and may lead to increased survival in others.[6]

Several modalities are being used in the follow-up of posttreatment carcinoma cervix patients. Though increasing serum squamous cell carcinoma antigen SCC-Ag can precede the clinical diagnosis of relapse in 46%–92% of cases, with a median lead time ranging from 2 to 8 months, still the marker falls short of a widely available and acceptable tumor marker in the present scenario.[7]

Fluorodeoxyglucose–positron emission tomography/computed tomography (FDG–PET/CT) fusion imaging can play a crucial role in all aspects of carcinoma cervix patients workup which include initial diagnosis, staging, restaging (evaluation of the patient for recurrent or residual disease), and assessing the response to chemotherapy/radiotherapy. Therefore, when available, patients should undergo a PET/CT examination. Because 18F-FDG PET results have been shown to be prognostic of patient survival, the National Cancer Comprehensive Network guidelines state that a single PET/CT examination can be performed 3–6 months after chemoradiation. Patients with new, residual, or no disease on posttreatment imaging demonstrate 5-year survival rates of 0%, 46%, and 92%, respectively.[8]

The usefulness of PET/CT in patients with cervical cancer includes determining local tumor extension (along with inputs about metabolic activity of tumor and possible endometrial/parametrical/vaginal involvement), assessing pelvic nodal involvement and detection of distant metastasis. PET/CT is also useful to evaluate extrapelvic disease before much intensive pelvic exenteration, radiation therapy planning (for determining lymph nodes status in locoregional and extrapelvic site), identification of residual/recurrent disease (especially in the setting of neoadjuvant therapy), and prognosis (with an inverse response–survival relationship).

There are limited data on the role of integrated PET/CT in the detection of recurrence in cancer cervix. Only a limited number of studies have evaluated the efficacy of 18F-FDG PET/CT for recurrent carcinoma cervix, especially in the Indian population which this study seeks to expand upon. The study aimed to evaluate and compare imaging findings using CT alone and PET/CT fusion imaging in posttreatment carcinoma cervix patients for recurrence. CT as well PET/CT findings were evaluated and compared in locoregional and distant metastasis with histopathology/follow-up.

Subjects and Methods

The study was conducted prospectively, however, some of the of the data were gathered retrospective for few patients. The study was conducted over a period of 2 years. The sample size for the study was 50 cases. All patients who met the eligibility criteria (posttreatment follow-up cases of carcinoma cervix and patients with known carcinoma cervix being referred for staging of recurrent disease after the course of chemotherapy/radiotherapy) and underwent PET/CT imaging during the study period were enrolled in the study. Patients with carcinoma cervix being referred for primary staging and those with coexistent malignancies in other organ system were excluded from the study. During the study duration of 2 years, 50 patients referred to our institution for PET/CT imaging with suspected recurrence/follow-up after posttreatment were included in the study. In all included patients referred for restaging/follow-up, a reliable reference standard was available. The reference standard was established by histopathological examination of accessible metastatic sites in both locoregional and distant areas or by follow-up of patients. Data were collected as and when cases were performed after choosing patients who were eligible for study. Patient's random blood glucose levels, serum creatinine, and blood urea were analyzed before the study, and the study was performed only when random blood glucose levels were <160 mg/dl and serum creatinine and blood urea levels were within normal limits. Before the data collection begins, written informed consent was taken from patients for participation in the study. Then, after having detailed relevant clinical history and examination, complete set of data were made for each patient in preformed formats. Observation and follow-up of cases was done.

Image acquisition

CT and PET/CT imaging were performed using the 64-slice PET/CT scanner (GE Discovery VCT, Wisconsin, USA). This system combines a 64-slice detector CT scanner with a PET scanner. While resting on a reclining chair, the patients received a 10 mCi of 18F-FDG intravenously (up to a maximum of 20 mCi) and were asked to drink 900 mL of oral contrast. All possible physical activities were restricted to prevent physiological uptake in muscles. The imaging sequence began 45 min after tracer injection. Patients were positioned on the imaging table with their arms up by the side of the head. After determining the imaging field (Vertex to mid thighs) with an initial scout scan, CT acquisition with intravenous contrast material (Iohexol at concentration of 1 ml/kg body weight, iodine concentration 350 mg/ml) was performed using the following low dose parameters: 120 kVp, 300 mAs, 0.5 s tube rotation, 3.75 mm slice collimation, pitch and speed of 0.984:1, 39.37 mm/rot. The CT scan was followed by the PET scan. PET images were acquired in 3D mode. Patients were instructed to breathe shallowly during the PET and CT portions of the study to minimize misregistration between PET and CT images.

Image reconstruction

CT images were reconstructed using conventional filtered back projection, at 3.4-mm axial intervals to match the slice separation of the PET data. PET images were reconstructed by using iterative algorithms (ordered-subsets expectation maximization, two iterations, and eight subsets). Attenuation was corrected by mapping the CT Hounsfield units to the linear attenuation coefficients.

Image interpretation and analysis

PET, CT, and PET/CT acquired were interpreted as follows: CT and PET images were interpreted independently by one radiologist and one nuclear medicine specialist, respectively, who were blinded to any additional clinical and other imaging findings. PET/CT studies were read in consensus.

Quantitative analysis of fluorodeoxyglucose uptake

For the calculation of standard uptake value (SUV), circular regions of interest were placed on consecutive axial images of lesions visually identified to have abnormally increased FDG uptake. The SUV was calculated as: decay-corrected activity (kBq)/tissue volume (ml)/injected – FDG activity (kBq)/bodyweight (g). To minimize partial volume effects and assure reproducibility of measurements, the maximum SUV (SUVmax) was used.

Criteria for contrast-enhanced computed tomography (for locoregional recurrence)

Morphological changes such as the presence of an enhancing soft tissue mass as opposed to streaking of the fat in the postoperative/postradiotherapy bed, increase in size/shape of the mass on follow-up scans, regional lymph node metastases, and invasion of contiguous structures.

Criteria for contrast-enhanced computed tomography (for distant metastasis)

Hypoattenuating liver lesions with irregular margins and predominant peripheral contrast enhancement, with washout in delayed phases were considered as metastasis; multiple rounded randomly distributed predominantly peripheral/subpleural located pulmonary nodules, detection of soft-tissue masses outside the liver with contrast enhancement, or further suggestive signs (e.g., surrounding tissue infiltration and localization) were also considered as malignant, and the lymph node assessment used a size-based threshold of 1.0 cm (short axis) for malignancy. Furthermore, lymph nodes with fatty hilum or with calcifications were regarded as benign, whereas with central necrosis were considered malignant.

Criteria for positron emission tomography/computed tomography positive status

Soft-tissue masses in conjunction with focally increased glucose metabolism (FDG AVID) above the surrounding tissue level were regarded as malignant. A maximum standardized uptake value (SUVmax) of more than 2.5 (for extrahepatic lesions) and 3.5 (for intrahepatic lesions) supported the diagnosis of a malignant lesion but was always considered in conjunction with the qualitative appearance of the lesion (e. g., a liver lesion with a SUV max of 3.1, clearly demarcated from the background liver activity was considered malignant). Lymph nodes were assessed for metastatic spread on the basis of an increased glucose metabolism independent of their size. In cases of morphologically malignant appearance without increased glucose metabolism, the lymph nodes were evaluated on the basis of noncontrast-enhanced computed tomography criteria only.

Criteria for computed tomography negative status for recurrent disease

No obvious enhancing lesions detected on contrast-enhanced CT study.

Criteria for positron emission tomography/computed tomography negative status for residual/recurrent disease

No increased FDG uptake in lesions which were positive on CT.

Standard of reference

The standard of reference was histopathological examination or clinical and imaging follow-up evaluation for at least 6 months. Most of the patients underwent biopsy for histological diagnosis of residual/recurrent disease. For ethical reasons, systematic biopsies of all metastatic sites for restaging were not performed. Histopathological examination remained the gold standard of reference. A suspected tumor site was considered true positive if the histologic findings were positive or if the lesion exhibited progression on follow-up imaging after therapy. A lesion was considered true negative if the histologic findings were negative or the lesion regressed or remains unchanged at follow-up imaging and without clinical deterioration for at least 6 months.

Statistical analysis

Data collected were entered primarily into the Excel sheets and then transferred after data cleaning and rechecking to Epi Info software for analysis according to aims and objectives. Using the standard of reference, sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPVs) were calculated. In addition, comparison between groups was performed using the unpaired *t*-test and Pearson's Chi-square test. Correlations were sought using the Pearson correlation. $P < 0.05$ was considered statistically significant.

Ethical clearance

The study was submitted to the Institutional Scientific and Ethics Committee before the commencement of study and the permission was granted.

Results

Maximum number of cases in our study were in age group between 50 and 59 years [Table 1]. A comparison between posttreatment carcinoma cervix cases for detection of locoregional recurrence, pelvic node invasion, and distant metastasis by CT (positive and negative) and histopathological correlation/follow-up (positive and negative results) were statistically analyzed using Pearson's Chi-square and *P* values [Tables 2 and 3].

In the study population of 50 cases, 18 cases were identified positive on CT for locoregional recurrence, out of which 15 were positive on histological examination/follow-up scans. The remaining 3 false-positive cases were attributed to residual enhancing soft-tissue mass or thickening in the pelvic post-chemotherapy/radiotherapy with no active tumor cells. Out of the 32 CT-negative cases, 27 proved to be negative on histopathology, and remainder 5 cases turned positive on histological examination/follow-up scans. These false-negative cases in CT represented lesions that were isodense to the cervical stroma or masked by anatomic distortion or lesion too small to be appreciated on CT [Figure 1]. It was inferred from our study that CT imaging alone had a sensitivity and specificity of 75% and 90%, respectively, with a PPV of 83.3% and NPV of 84.4% for detection of locoregional recurrence. For locoregional recurrence, out of the study population of 50 cases, based on PET/CT criteria, 19 cases were identified as PET/CT positive and 31 cases as PET/CT negative. All PET/CT identified positive cases were positive on histological examination/follow-up scans as well [Figures 2-4]. However, out of the 31 PET/CT-negative cases, 30 were truly histological/follow-up negative cases, and 1 histologically positive case was missed by PET/CT which was explained by very small tumor burden in postchemoradiation patient. Thus, it could be inferred that PET/CT fusion imaging has a sensitivity and specificity of 95% and 100%, respectively, with a PPV of 100% and NPV of 96.8% for locoregional recurrence [Tables 2 and 3].

In our study, the evaluation of pelvic node involvement also was done by CT as well as PET/CT with histopathological/follow-up correlation. In our study population of 50 cases, 18 cases were identified as CT-positive cases for pelvic nodal involvement, out of which 16 were histologically positive for the malignancy. The false positivity in 2 cases could be explained by enlarged nodes due to infectious/inflammatory cause. Out of the 32 CT-negative reported cases, 6 histologically positive cases were missed by CT. This fact could be explained by metastatic tumor in subcentimeter lymph nodes. Thus, CT imaging alone had sensitivity and specificity of 72.7% and 92.9%, respectively, with a PPV of 88.9% and NPV of 81.3% for detection of pelvic nodal involvement. For pelvic node involvement by PET/CT, out of the study population of 50 cases, based on

Table 1: Distribution of study population on the basis of age groups

Age (years)	Number of cases (%)
33-39	2 (4.0)
40-49	10 (20.0)
50-59	22 (44.0)
60-69	11 (22.0)
70-79	5 (10.0)
Total	50 (100.0)

Table 2: Evaluation of locoregional recurrence in posttreatment carcinoma cervix cases by computed tomography and histopathological/follow-up correlation

Prognostic findings	Histopathology/follow-up		Total	χ^2 (*P*)
	Positive	Negative		
CT findings suggestive of locoregional recurrence				
Present	15	3	18	19.274
Absent	5	27	32	(0.000)
Total	20	30	50	
PET/CT findings suggestive of locoregional recurrence				
Present	19	0	19	45.96
Absent	1	30	31	(0.000)
Total	20	30	50	
CT findings suggestive of pelvic node involvement				
Present	16	2	18	23.000
Absent	6	26	32	(0.000)
Total	22	28	50	
PET/CT findings suggestive of pelvic node involvement				
Present	21	2	23	38.681
Absent	1	26	27	(0.000)
Total	22	28	50	
CT findings suggestive of distant metastasis				
Present	22	1	23	38.749
Absent	2	25	27	(0.000)
Total	24	26	50	
PET/CT findings suggestive of distant metastasis				
Present	23	0	23	46.142
Absent	1	26	27	(0.000)
Total	24	30	50	

P<0.05 considered as significant. PET: Positron emission tomography, CT: Computed tomography

Table 3: Evaluation of distant metastasis, locoregional recurrence, and pelvic node involvement in posttreatment carcinoma cervix cases by computed tomography versus positron emission tomography/computed tomography

Diagnostic parameters	CT	PET/CT
Locoregional recurrence		
Sensitivity	75 (57.0-85.4)	95 (80.9-95.0)
Specificity	90 (78.0-97.0)	100 (90.6-100)
PPV	83.3 (63.3-94.9)	100 (85.2-100)
NPV	84.4 (73.1-90.9)	96.8 (87.7-96.8)
Positive likelihood ratio	7.500 (2.587-28.011)	∞ (8.617-∞)
Negative likelihood ratio	0.278 (0.150-0.552)	0.050 (0.050-0.211)
Pearson's χ^2 (P)	19.274 (0.000)	45.96 (0.00)
Pelvic node involvement		
Sensitivity	72.7 (56.5-80.1)	95.5 (81.0-99.8)
Specificity	92.9 (80.1-98.7)	92.9 (81.5-96.2)
PPV	88.9 (69.1-97.9)	91.3 (77.4-95.4)
NPV	81.3 (70.1-84.3)	96.3 (84.5-99.8)
Positive likelihood ratio	10.182 (2.845-60.433)	13.364 (4.369-26.486)
Negative likelihood ratio	0.294 (0.201-0.543)	0.049 (0.003-0.234)
Pearson's χ^2	23.000 (0.000)	38.681 (0.000)
Distant metastasis		
Sensitivity	91.7 (78.4-95.6)	95.8 (84.0-95.8)
Specificity	96.2 (83.9-99.8)	100 (89.1-100)
PPV	95.7 (81.8-99.8)	100 (87.7-100)
NPV	92.6 (80.8-96.1)	96.3 (85.8-96.3)
Positive likelihood ratio	23.833 (4.861-455.627)	∞ (7.718-∞)
Negative likelihood ratio	0.087 (0.044-0.258)	0.042 (0.0042-0.179)
Pearson's χ^2	38.749 (0.000)	46.142 (0.000)

Sensitivity, specificity, PPV, NPV are expressed in percentage. Values in parenthesis represent CIs of estimates. CT: Computed tomography, PET: Positron emission tomography, PPV: Positive predictive value, NPV: Negative predictive value, CI: Confidence interval

PET/CT criteria, 23 cases were identified as PET/CT positive and 27 were identified as PET/CT negative [Figure 7]. Out of the 23 PET/CT-positive cases, 21 were histologically positive cases and 2 histologically negative cases were identified by PET/CT as falsely positive. These 2 (false positive) could be explained by the presence of FDG avid nodes which turned out to be of reactive etiology. Out of the 27 PET/CT-negative cases, 1 histologically positive case was missed in PET/CT criteria. This was explained by the presence of micrometastasis in subcentimetric node. In our study, it was inferred that PET/CT imaging had a sensitivity and specificity of 95.5% and 92.9%, respectively, with a

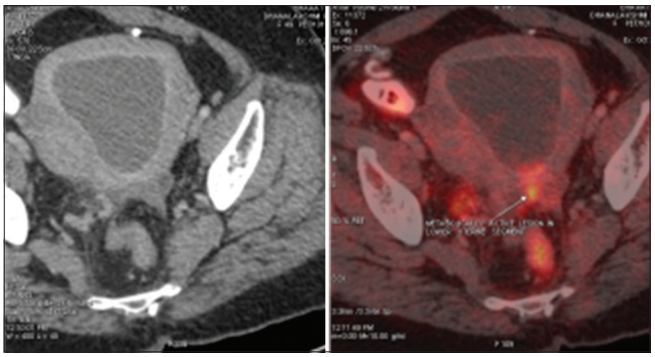

Figure 1: Axial contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images. There was no computed tomography detectable enhancing lesion in vaginal vault; however, there was abnormal fluorodeoxyglucose uptake in vaginal vault region, proved to be residual/recurrent malignancy on histopathology

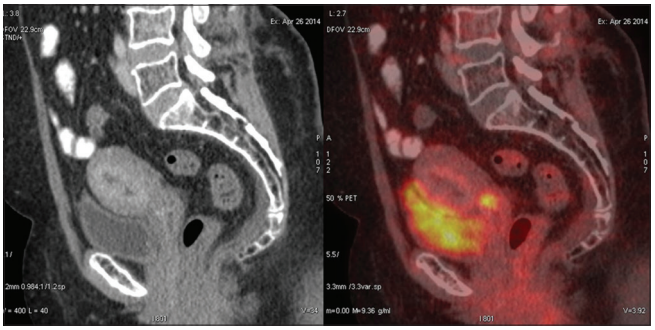

Figure 2: Reformatted sagittal contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images demonstrating small enhancing soft-tissue density focus in the posterior wall of the cervix with corresponding increased fluorodeoxyglucose uptake in positron emission tomography/computed tomography fusion images

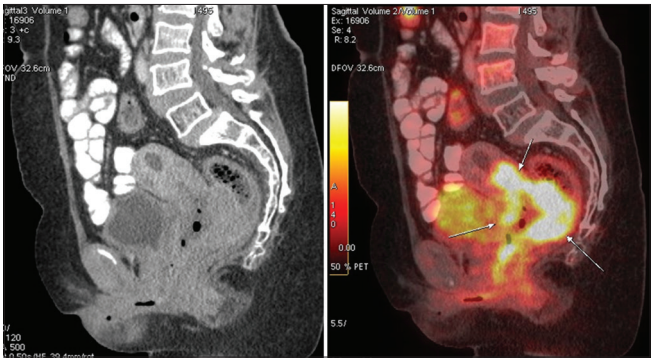

Figure 3: Reformatted sagittal contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images demonstrating enhancing mass in the cervix with corresponding increased fluorodeoxyglucose uptake. The arrows indicating extension of the lesion anteriorly into the posterior wall of the urinary bladder and posteriorly into the rectum

PPV of 91.3% and NPV of 96.3% for detection of pelvic node involvement [Tables 2 and 3].

In our study, we also demonstrated the evaluation of distant metastasis by CT as well as PET/CT with histopathological/follow-up correlation. In study population of 50 cases, out of 23 cases that were identified as CT positive,

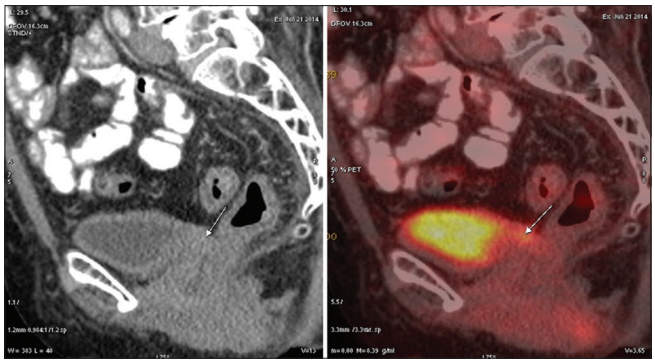

Figure 4: Reformatted sagittal contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images demonstrating enhancing mass in the vaginal vault with corresponding increased fluorodeoxyglucose uptake

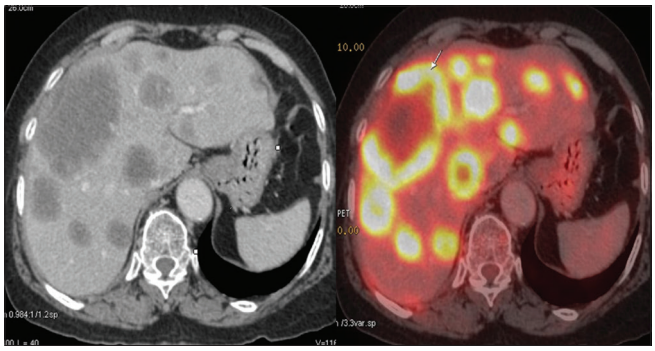

Figure 6: Axial contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images showing multiple varying size peripherally enhancing hypodense lesions in hepatic parenchyma with corresponding increased fluorodeoxyglucose uptake. Same patient's coronal reformatted images (below) show recurrence at postoperative bed in the pelvis with multiple metastatic foci including bilateral iliac, para-aortic, and mediastinal lymph nodes

22 were positive on histological/follow-up and 1 case was falsely positive. This false positivity could be again explained by enlarged infectious/inflammatory nodes. Out of 27 cases identified as CT negative for distant metastasis, 25 were true negative on follow-up/biopsy and 2 false-negative cases were attributed to spread into subcentimeter lymph node [Figure 5]. Thus, from our study, it could be inferred that CT imaging alone had a sensitivity and specificity of 91.7% and 96.2%, respectively, with a PPV of 95.7% and NPV of 92.6% for detection of distant metastasis. For distant metastasis by PET/CT, out of the study population of 50 cases, all 23 cases that were identified as PET/CT-positive cases were histologically positive. Thus, there was no false-positive cases for distant metastasis [Figures 6-9]. Thus, PET/CT imaging alone had a sensitivity and specificity of 95.8% and 100%, respectively, with a PPV of 100% and NPV of 96.3% for detection of distant metastasis [Tables 2 and 3].

Discussion

Accurate information is important in recurrent carcinoma cervix cases, for early detection of residual/recurrent disease and in posttreatment follow-up settings regarding the

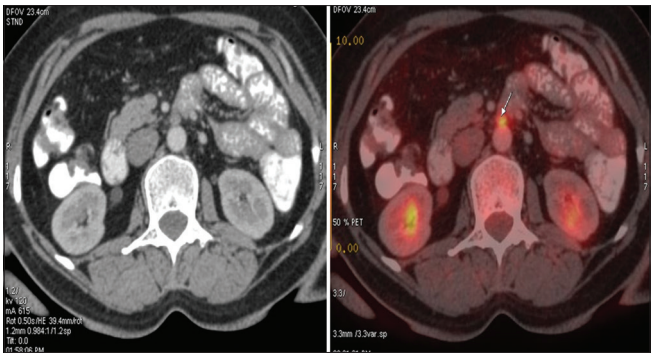

Figure 5: Axial contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images showing subcentimetric preaortic lymph node (computed tomography criteria negative) with corresponding increased fluorodeoxyglucose uptake (positron emission tomography/computed tomography criteria positive)

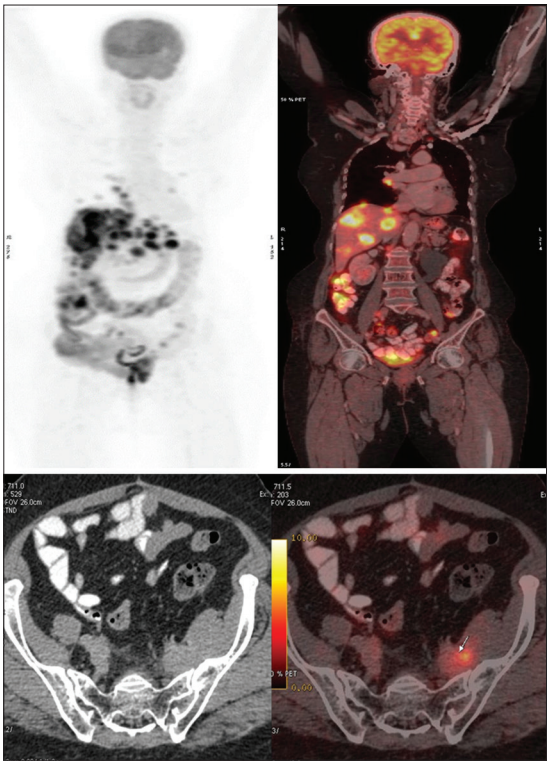

Figure 7: Axial contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images showing left common iliac lymphadenopathy with corresponding increased fluorodeoxyglucose uptake

effectiveness of radiotherapy and/or chemotherapy, to decide whether there is a need for continuation of the selected therapeutic regimen or switching to an alternative regimen.

Out of our study population of 50 patients, maximum number of cases were detected in age group between 50 and 59 years. This is the common spectrum of case distribution in posttreatment carcinoma cervix patients in the Indian scenario.

CT imaging alone has a low sensitivity and moderate specificity in the evaluation of local and pelvic recurrence

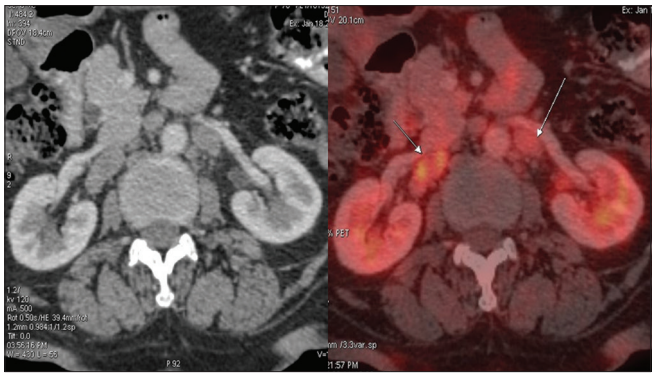

Figure 8: Axial contrast-enhanced computed tomography and positron emission tomography/computed tomography fusion images showing extensive retroperitoneal lymphadenopathy with corresponding increased fluorodeoxyglucose uptake

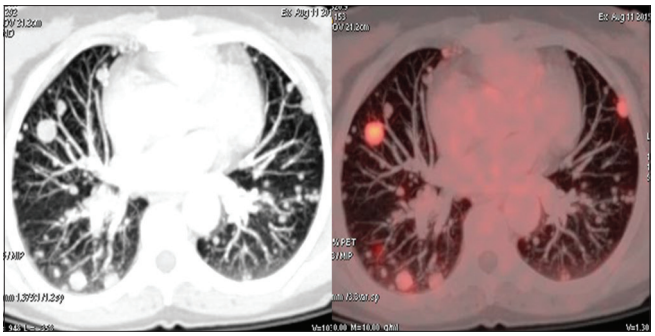

Figure 9: Contrast-enhanced axial maximum intensity projection computed tomography and positron emission tomography/computed tomography fusion images demonstrating multiple varying size predominantly subpleurally located rounded pulmonary nodules with increased fluorodeoxyglucose uptake – pulmonary metastatic nodules

in posttreatment carcinoma cervix cases. In our study, there were 3 falsely positive cases on CT evaluation for locoregional residual/recurrent disease with residual soft-tissue mass or thickening in the pelvic region after chemotherapy/radiotherapy where no active tumor cells were found on histological evaluation/follow-up and the lesion regressed in size as well as in enhancement pattern. There were 5 falsely negative cases as well on CT for locoregional residual/recurrent disease which were positive on histological/follow-up scans which represented lesions that were isodense to the cervical stroma or masked by anatomic distortion or lesion too small to be appreciated on CT.

All cases whose PET/CT was read as positive for locoregional residual/recurrent malignancy were positive on histological examination/follow-up scans as well. However, 1 histologically positive case was missed by PET/CT which was explained by very small tumor burden in postchemoradiation patient, which manifested in follow-up scan.

It was inferred from our study that CT imaging alone had a sensitivity and specificity of 75% and 90%, respectively, with a PPV of 83.3% and NPV of 84.4% for detection of locoregional recurrence. PET/CT fusion imaging had a sensitivity and specificity of 95% and 100%, respectively, with a PPV of 100% and NPV of 96.8% for locoregional recurrence.

Similar to our results, Cetina *et al*. in their study which included 16 patients demonstrated that the sensitivities of PET/CT and MDCT were 100% and 91.7%, respectively, and specificity of 50% for both PET/CT and CT considering the tumor site-based analysis for recurrence. FDG PET/CT has higher sensitivity but similar specificity to CT in the identification of recurrence in patients with suspected recurrence or persistent locally advanced carcinoma cervix in their study.[9] Park *et al*. studied 36 patients for recurrence in posttreatment carcinoma cervix and reported that PET/CT alone showed sensitivity and specificity of 100% and 94.4%, respectively.[10] However, in another study by Heron *et al*., in total study population of 64 cases, the sensitivity and specificity of CT for identifying recurrence was 92% and 95%, respectively.[11] Loft *et al*. in their study reported the diagnostic accuracy of FDG/CT in recurrent cervical cancer with sensitivity and specificity for local involvement about 75% and 96%.[12] Furthermore, a study by Mittra *et al*. reported the diagnostic accuracy of FDG/CT about 93% (both sensitivity and specificity), 86% (NPV), and 96% (PPV) for local recurrence.[13] A recent study by Kitajima *et al*. also reported the diagnostic accuracy of FDG PET/CT in recurrent cervical cancer with sensitivity and specificity for local recurrence 90.9% and 93.5%.[14]

In our study, the evaluation of pelvic node involvement by CT as well as PET/CT with histopathological/follow-up correlation was also done where PET/CT imaging had much better sensitivity with almost equal specificity. In our study, it was inferred that CT imaging alone had sensitivity and specificity of 72.7% and 92.9%, respectively, with a PPV of 88.9% and NPV of 81.3% for detection of pelvic nodal involvement. PET/CT imaging had a sensitivity and specificity of 95.5% and 92.9%, respectively, with a PPV of 91.3% and NPV of 96.3% for detection of pelvic node involvement. The false positivity in 2 cases on CT interpretation of nodal disease was explained by enlarged nodes due to infectious/inflammatory cause. However, histologically positive pelvic lymph nodes in 6 cases were missed by CT. This fact could be explained by metastatic tumor in subcentimeter lymph nodes. CT has inherent limitations in detection of invasion of pelvic lymph nodes, as it includes size and anatomy as the basic criteria for identifying pathology; thus, in our study also, CT has limited sensitivity in detecting pelvic node involvement. There were 2 false-positive cases in PET/CT interpretation of pelvic lymph nodal assessment also, which could be explained by the presence of FDG avid nodes which turned out to be of reactive etiology in follow-up imaging. Out of the 27 PET/CT-negative cases, 1 histologically positive case was missed in PET/CT

criteria, explained by the presence of small focus of tumor cells (micrometastasis) in subcentimetric node. Loft *et al*. also reported similar diagnostic accuracy of FDG/CT with sensitivity and specificity for pelvic node involvement about 75% and 96%.[12]

In our study, we also demonstrated the evaluation of distant metastasis by CT as well as PET/CT with histopathological/follow-up correlation. CT imaging alone had a sensitivity and specificity of 91.7% and 96.2%, respectively, with a PPV of 95.7% and NPV of 92.6% for detection of distant metastasis. For distant metastasis evaluation by PET/CT, we obtained sensitivity and specificity of 95.8% and 100%, respectively, with a PPV of 100% and NPV of 96.3% for detection of distant metastasis. Similar results were also reported previously by Loft *et al*. who in their study showed the diagnostic accuracy of FDG/CT in recurrent cervical cancer for distant metastasis with sensitivity, specificity, PPV, and NPV as 100%, 94%, 63%, and 100%, respectively.[12]

Furthermore, a study by Mittra *et al*. reported the diagnostic accuracy of FDG/CT about 96%(sensitivity), 95% (specificity), 96% (PPV), and 95%(NPV) for distant metastasis.[13] Similar to our findings, Amit Bhoil *et al*. previously reported the sensitivity, specificity, PPV, and NPV of FDG/PET about 97.5%, 63.6%, 90.9%, and 87.5% for recurrence (including local/distant both);[15] while on the other hand, Chung *et al*. reported the sensitivity and specificity about 90.3% and 81% for the same.[16]

Thus, it can be concluded that PET/CT has a fairly good sensitivity and specificity for detection and evaluation of locoregional as well as pelvic nodal recurrence in posttreatment carcinoma cervix cases. Sensitivity of PET/CT is better than CT in detecting locoregional recurrence, but for evaluation of pelvic node involvement and distant metastasis, the specificity of both PET/CT and CT are comparable. However, CT imaging alone has a lower sensitivity and moderate specificity in the evaluation of locoregional and pelvic nodal recurrence in posttreatment carcinoma cervix cases. However, for evaluation of distant metastasis in posttreatment carcinoma cervix cases, both PET/CT and CT were having fairly comparable high sensitivity and specificity with PET/CT imaging performing marginally better in the evaluation of distant metastasis in posttreatment carcinoma cervix cases. Thus, PET/CT fusion imaging in comparison to CT alone is the preferred imaging modality of choice in the evaluation of tumor recurrence in posttreatment carcinoma cervix patients. It should be recommended as the first-line diagnostic tool for assessing recurrence in posttreatment carcinoma cervix patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Nandakumar A, Ramnath T, Chaturvedi M. The magnitude of cancer cervix in India. Indian J Med Res 2009;130:219-21.
2. Rylander E. Cervical intraepithelial neoplasia. In: Kavanaugh JJ, editor. Cancer in Women. Malden, MA: Blackwell Science; 1998. p. 251-8.
3. American Cancer Society. Cancer Facts and Figures 2004. Atlanta, GA: American Cancer Society; 2004. Available from: http://www.pink-ribbon-pins.com/CancerRates2004.pdf. [Last accessed on 2017 Feb 14].
4. Friedlander M, Grogan M; U.S. Preventative Services Task Force. Guidelines for the treatment of recurrent and metastatic cervical cancer. Oncologist 2002;7:342-7.
5. Waggoner SE. Cervical cancer. Lancet 2003;361:2217-25.
6. Brooks RA, Rader JS, Dehdashti F, Mutch DG, Powell MA, Thaker PH, *et al.* Surveillance FDG-PET detection of asymptomatic recurrences in patients with cervical cancer. Gynecol Oncol 2009;112:104-9.
7. Gadducci A, Tana R, Fanucchi A, Genazzani AR. Biochemical prognostic factors and risk of relapses in patients with cervical cancer. Gynecol Oncol 2007;107:S23-6.
8. Grigsby PW, Siegel BA, Dehdashti F, Rader J, Zoberi I. Posttherapy [18F] fluorodeoxyglucose positron emission tomography in carcinoma of the cervix: Response and outcome. J Clin Oncol 2004;22:2167-71.
9. Cetina L, Serrano A, Cantú-de-León D, Pérez-Montiel D, Estrada E, Coronel J, *et al.* F18-FDG-PET/CT in the evaluation of patients with suspected recurrent or persistent locally advanced cervical carcinoma. Rev Invest Clin 2011;63:227-35.
10. Park DH, Kim KH, Park SY, Lee BH, Choi CW, Chin SY, *et al.* Diagnosis of recurrent uterine cervical cancer: Computed tomography versus positron emission tomography. Korean J Radiol 2000;1:51-5.
11. Heron CW, Husband JE, Williams MP, Dobbs HJ, Cosgrove DO. The value of CT in the diagnosis of recurrent carcinoma of the cervix. Clin Radiol 1988;39:496-501.
12. Loft A, Berthelsen AK, Roed H, Ottosen C, Lundvall L, Knudsen J, *et al.* The diagnostic value of PET/CT scanning in patients with cervical cancer: A prospective study. Gynecol Oncol 2007;106:29-34.
13. Mittra E, El-Maghraby T, Rodriguez CA, Quon A, McDougall IR, Gambhir SS, *et al.* Efficacy of 18F-FDG PET/CT in the evaluation of patients with recurrent cervical carcinoma. Eur J Nucl Med Mol Imaging 2009;36:1952-9.
14. Kitajima K, Murakami K, Yamasaki E, Domeki Y, Kaji Y, Sugimura K, *et al.* Performance of FDG-PET/CT for diagnosis of recurrent uterine cervical cancer. Eur Radiol 2008;18:2040-7.
15. Bhoil A, Mittal BR, Bhattacharya A, Santhosh S, Patel F. Role of F-18 fluorodeoxyglucose positron emission tomography/computed tomography in the detection of recurrence in patients with cervical cancer. Indian J Nucl Med 2013;28:216-20.
16. Chung HH, Jo H, Kang WJ, Kim JW, Park NH, Song YS, *et al.* Clinical impact of integrated PET/CT on the management of suspected cervical cancer recurrence. Gynecol Oncol 2007;104:529-34.