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Original Article

Role of F-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Staging of Colorectal Carcinoma

Authors
Anurag Jain[1], Aniruddha G Pandit[2], Maj Braj Kishore[3], Arun Ravi John[4], Lt Col Amit Sharma[5], Abhinav Jaimini[6]
[1]MBBS, DNB in Nuclear Medicine, Graded Specialist Nuclear Medicine, Army Hospital R and R, Delhi 110010
[2]MBBS, MD, DRM, Senior Advisor Nuclear Medicine, Army Hospital R and R, Delhi 110010
[3]Graded Specialist Nuclear Medicine, Army Hospital R and R, Delhi 110010
[4]MBBS, DNB Resident, Army Hospital R and R, Delhi 110010
[5]MO Nuclear Medicine, Army Hospital R and R, Delhi 110010
[6]MBBS, DRM, DNB Resident, Army Hospital R and R, Delhi 110010
Corresponding Author
Aniruddha G Pandit MBBS, MD, DRM
Senior Advisor Nuclear Medicine, Army Hospital R and R, Delhi 110010
Email: *agpandit@yahoo.com, Mobile: 09958028030*

Abstract
Colorectal cancer shows an increasing trend in the incidence in Asian country like India.Complex clinical decisions for management of such patients depends on early diagnosis and correct clinical staging imaging findings, thus reducing the morbidity. Accurate determination of the anatomy and morphology of tumors with extent, tumor size, lymph node involvement, and distant metastasis are valuable. F-18 fluorodeoxyglucose positron emission tomography/computed tomography in Staging of Colorectal carcinoma that provide information about metabolic activity of tumor and distant metastases can change the management protocols Our study showed that whole body PET/CT should be done as part of protocol in cases of colorectal carcinoma, for staging work up as well as for evaluating local invasiveness, metastases, recurrence and treatment monitoring.

Keywords: *Colorectal carcinoma, FDG PET-CT, Staging.*

Introduction

Colorectal carcinoma is one of the leading cancers amongst western world. It is third most common cancer in terms of incidence in United States.[1,2] Although colorectal cancer is less common in India,[3] recent studies have shown an increasing trend in the incidence. Early diagnosis and correct staging of colorectal cancer can reduce the morbidity and mortality. Complex clinical decisions about treatment of oncologic patients are largely guided by imaging findings, among other factors. Most radiological procedures including Computed Tomography (CT) scan map the anatomy and morphology of tumors with little information about their metabolism.

Positron Emission Tomography technology (PET) introduced in '70s, is a non invasive modality that uses radiotracers to detect and quantify cellular biochemical processes. 18F-2-Fluoro-2-Deoxy-D-Glucose (18F-FDG) is a common radiotracer with glucose analogue attached to positron emitting radionuclide 18F and is preferentially taken by malignant cells. Positron annihiliation after 18 F decay intracellularly is detected by PET scanner and this data reconstructed to a 3D image. Semi quantitative analysis of FDG-PET images in terms of Standardized Uptake Value (SUV) represents the metabolic activity for the tumor compared with that in surrounding tissue, corrected for injected dose and patient weight. With introduction of fusion technology PET-CT, now anatomical details are better appreciated.

Accurate determination of the extent of local invasion, tumor size, lymph node involvement, and distant metastasis provides valuable information for treatment selection. In case of locally advanced disease without distant metastases, hemicolectomy after neoadjuvant chemotherapy and radiotherapy is the treatment of choice. Hence, in all patients with potentially resectable disease, accurate staging is important as it has both prognostic and therapeutic importance.

In the present study, patients with histological diagnosis of colorectal carcinoma (primary) were evaluated with both CECT (Chest, Abdomen and Pelvis) and whole body 18F-FDG PET/CT for staging of the disease in order to compare the two techniques and correlate the findings with the histo-pathologic findings. To the best of our knowledge till date, there is limited data in the Indian population on this subject. This study may help in assessing the impact of 18F-FDG PET/CT findings in Indian patients suffering from colorectal carcinoma.

Material and Methods

Fifty nine patients with preoperatively proven colorectal carcinoma underwent CECT and 18 F FDG PET/CT scan within an interval of 2 weeks. Complete history and detailed clinical examination was done in every case. Routine laboratory investigations along with liver function tests and CEA, Chest X-ray, USG abdomen and pelvis, and Colonoscopy with biopsy were done. Staging was done on the basis of TNM (Tumor, Node, and Metastases) staging method. A Whole body PET/CT scan was acquired after injection of 8-10 mCi of 18 F-FDG and was evaluated for areas of increased focal uptake. CECT scan of chest, abdomen and pelvis was done after injection of iodinated non-ionic contrast media.

Staging accuracy of 18F-FDG PET/CT in comparison to CECT, and its impact on further management was evaluated. All results were compared with histopathological examination and in few cases with cytological examination (for metastasis).

All the data was recorded in specified Performa and statistical analysis of the data done by Non parametric test (Chi- Square Test) and using SPSS software to find out the staging accuracy and the impact of 18F-FDG PET/CT findings on treatment strategy.

Observations

59 patients were included in the study and observations of this study are presented here.

Staging

Staging of the tumor was done by CECT (chest, abdomen, and pelvis), 18F-FDG PET/CT, and results were compared with available histopathology. Out of 59 patients 47 patients underwent surgery and final histopathological staging was available in 47 patients and T and N staging by CECT and PET/CT was compared with histopathological T and N Staging. 12 patients could not be evaluated for T and N staging by histopathological examination as 5 patients underwent NACCRT, 2 patients were found to have disseminated disease at laparotomy and in another 5 patients metastatic disease was diagnosed pre operatively and these patient received Chemotherapy and/or palliative bypass/colostomy. M staging was evaluated in all the 59 patients.

T Staging on CECT, PET/CT and Histopathology

Out of 59 patients 9 were staged as T2, 42 as T3, and 8 as T4 by CECT**.** PET/CT staged 13 patients as T2, 41 as T3 and 5 patients as T4**.**

On histopathological examination 47 patients were evaluated for T staging out of which 12 patients were staged as T2, 34 as T3, and 1 patient as T4.**(Figure 1).**

CECT findings for T stage when compared with Histopathological T stage in 47 patients shows that 7/12 T2 lesions, 30/34 T3 lesions, and 1/1 T4 lesion was correctly staged and CECT correctly identified T stage in 38/47 (80.1%) patients. CECT over staged T stage in 7 patients and under staged in 2 patients.

PET/CT findings for T stage when compared with Histopathological T stage in 47 patients shows that 8/12 T2 lesions, 31/34 T3 lesions, and 0/1 T4 lesion was correctly staged and PET/CT correctly identified T stage in 39/47 (82.9%) patients. PET/CT over staged T stage in 5 patients and under staged in 3 patients. Mean SUV value for T stage was 6.75 and it was 4.33 in mucinous type adenocarcinomas.

PET/CT correctly identified one patient more than CECT as far as T staging is concerned.

N Staging on CECT, PET/CT and Histopathology

Out of 59 patients, 22 (37.3%) patients were staged as N0 and 37 (62.7%) patients as N1 on CECT, while 26(44%) patients were staged as N0 and 33 (56%) patients as N1 on PET/CT. On histopathological examination 47 patients were evaluated for N staging out of which 21(44.6 %)patients were staged as N0, 23 (48.9%) as N1, and 3 (6%) patients as N2 **(Figure-2).**

CECT findings for N stage when compared with histopathological N stage in 47 patients shows that 19/26 N0 patients and 13/21 N1 lesions were correctly staged with a CECT sensitivity of 73%, specificity of 61.9%, and overall accuracy of 68.1%. CECT under staged N stage in 8 patients and over staged in 7 patients.

PET/CT findings for N stage when compared with Histopathological N stage in 47 patients shows that 20/26 N0, and 19/21 N1 lesions were correctly staged and sensitivity, specificity and overall accuracy of PET/CT in detection of nodal metastasis was 76.9%, 90.5%, and 83% respecti-vely. PET/CT under staged N stage in 5 patients and over staged in 3 patients and 2 of these patients have granulomatous lymphaden-opathy. Mean SUV value for N stage was 3.5.

M Staging on CECT, PET/CT and Histopathology

Out of 59 patients 45 patients were staged as M0 and 14 patients as M1 on CECT. While, 45 patients were staged as M0 and 14 patients as M1 on PET/CT. On histopathological examination all the 59 patients were evaluated for M staging out of which 45 patients were staged as M0 and, 14 as M1 **(Figure-3).**

CECT findings for M stage when compared with Histopathological M stage in 59 patients shows that 40/45 M0 patients and 9/14 M1 lesions were correctly staged with a CECT sensitivity of 64.3%, specificity of 88.9% , and overall accuracy of 83.1%.

PET/CT findings for M stage when compared with Histopathological M stage in 59 patients shows that 43/45 M0, and 12/14 M1 lesions were correctly staged and sensitivity, specificity and overall accuracy of PET/CT in detection of distant metastasis was 85.7%, 95.6%, and 93.2% respectively. **Peritoneal carcinomatosis was not picked up by both CECT and PET/CT in 2/2 patients.** On histopathological examination all the 59 patients were evaluated for M staging and 47 patients for T and N staging as 9 patients were metastatic and 5 patients received neo adjuvant concurrent chemotherapy **(Figure-4).**

TNM Staging by CECT, PET/CT and Histopathological examination

Out of 54 patients 31 patients were correctly staged on CECT and 39 patients were correctly staged on PET/CT. On CECT scan 4/6 patients of stage I, 6/15 of stage IIA, 3/4 of stage IIIa, 9/13 of stage IIIB, 0/2 of stage IIIC, and 9/14 0f stage IV

were correctly staged, whereas on PET/CT scan 4/6 patients of stage I, 12/15 of stage IIA, 2/4 of stage IIIa, 9/13 of stage IIIB, 0/2 of stage IIIC, and 12/14 0f stage IV were correctly staged. CECT over staged 14 patients and under staged 9 patients as compared to PET/CT which over staged 9 patients and under staged 6 patients.

CECT (Chest, Abdomen, and Pelvis) correctly identify overall (TNM) stage in 57.4% (31/54) of patients and PET/CT correctly identifies overall (TNM) stage in 72.2% (39/54) of patients and the difference was statistically significant. (P value < 0.006).

PET/CT findings changed the management strategy in 7 patients. PET/CT picked up metastasis in 3 patients which were not picked up by CECT, one in Left supraclavicular lymph node, and in two patients in the liver. In 4 patients diagnosed as metastatic on CECT, PET/CT picked up additional metastatic lesions which changed the intent and primary management of these patients.

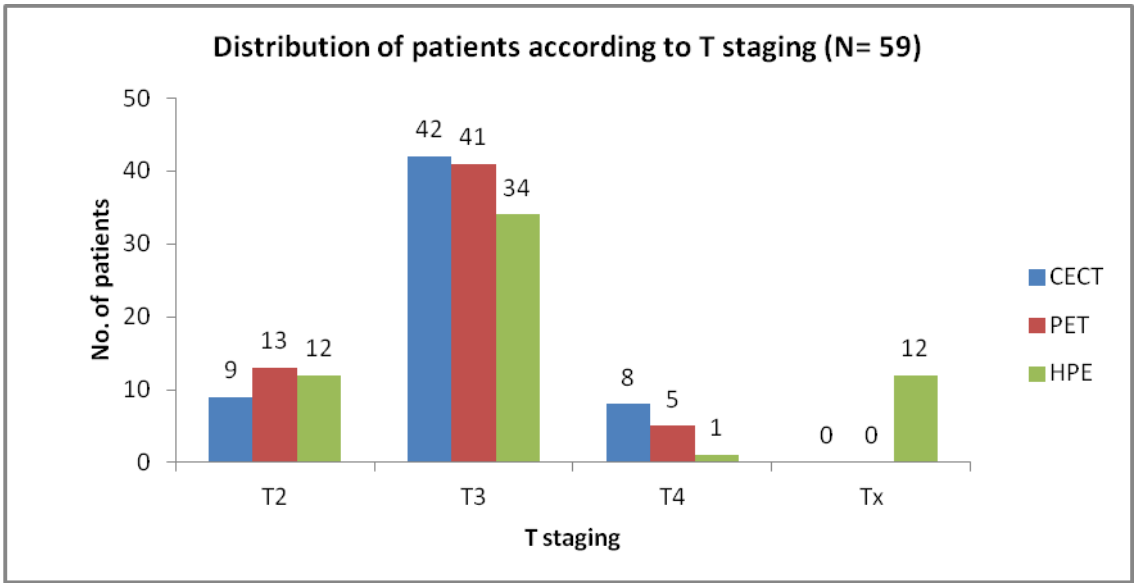

Figure 1 – Distribution of patients according to T staging

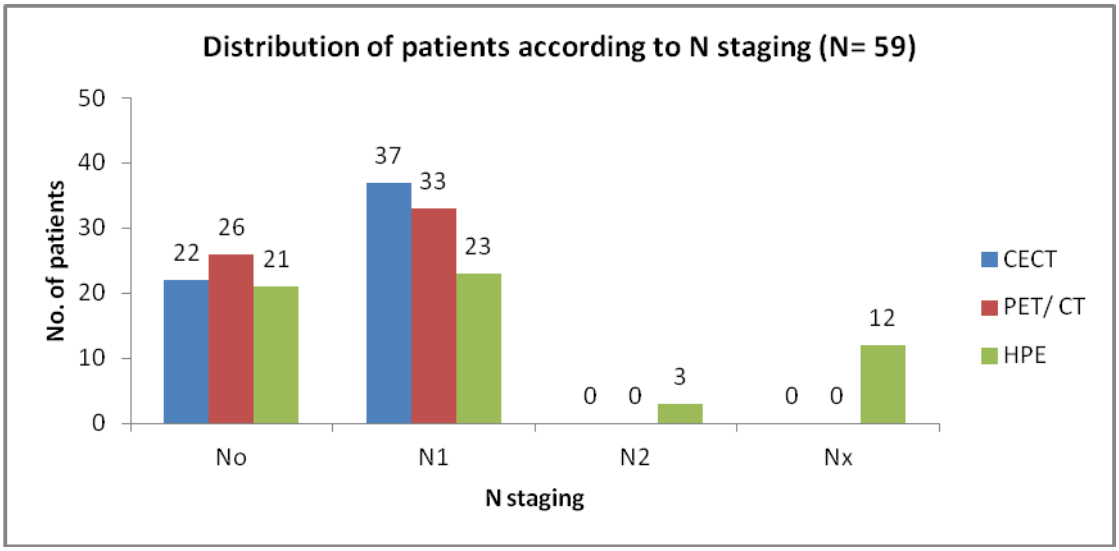

Figure 2 – Distribution of patients according to N staging

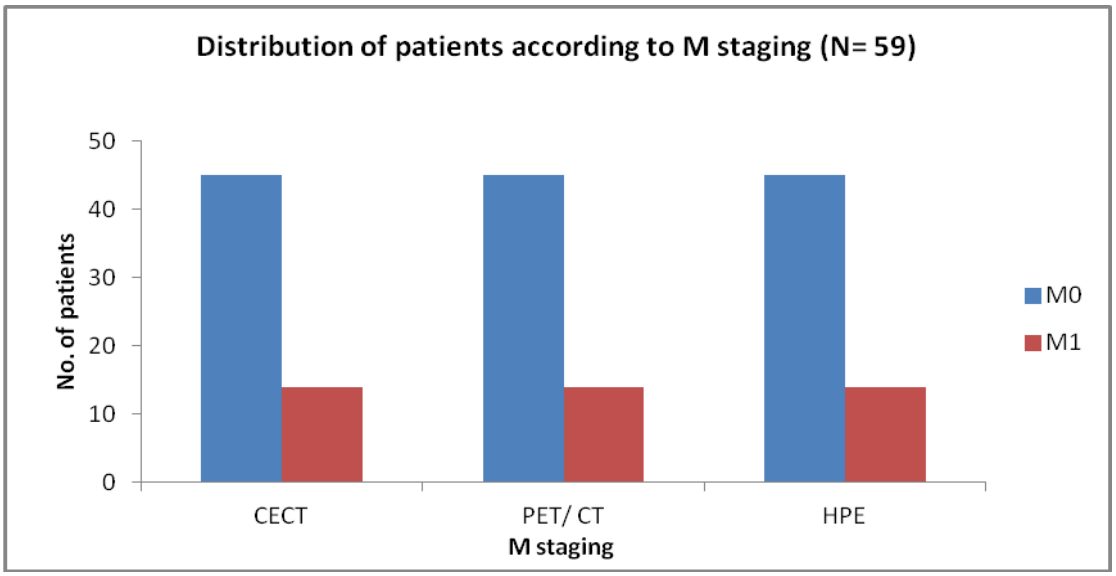

Figure 3 – Distribution of patients according to M staging

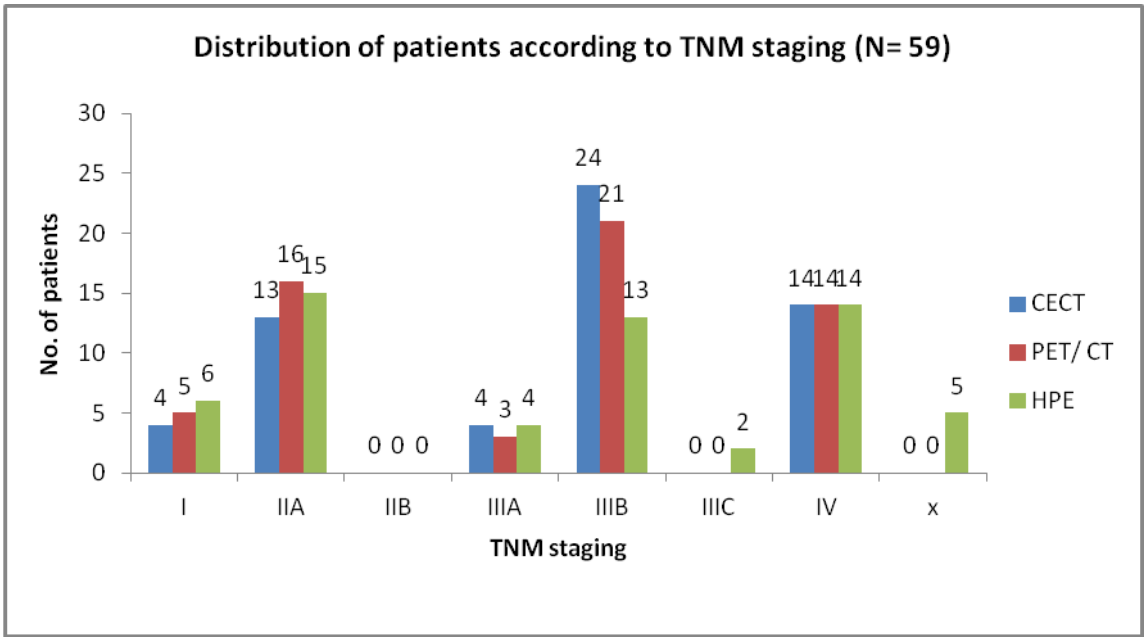

Figure 4 – Distribution of patients according to TNM staging

Discussion

In terms of T staging, the tumor detection rate in our study was similar to the study conducted by Furukawa H et al, who evaluated 44 patients of colorectal carcinoma with preoperative multidetector CT(MDCT) and FDG PET. The tumor detection rate in their study was 95 % (42/44) for MDCT and 100 %(44/44) for FDG – PET.[4] In our study the tumor detection by CECT was 80.1% (38/47) and by FDG PET/CT was 82.9 %(39/47). CECT over staged T stage in 7 patients and under staged in 2 patients. PET/CT also over staged T stage in 7 patients and under staged in 2 patients. PET/CT correctly identified only one patient more than CECT as far as T staging is concerned**.** The reasons for false T-staging of tumor by PET/CT may be physiological metabolic activity in the bowels, low resolution of PET/CT as compared to CECT and partial volume effect.

In our study , CECT findings for N stage when compared with histopathological N stage in 47 patients shows that 19/26 N0 patients and 13/21 N1 lesions were correctly staged with a CECT sensitivity of 73%, specificity of 61.9% , and overall accuracy of 68.1%. CECT under staged N stage in 8 patients and over staged in 7 patients.

PET/CT findings for N stage when compared with histopathological N stage in 47 patients shows that 20/26 N0, and 19/26 N1 lesions were correctly staged and sensitivity, specificity and overall accuracy of PET/CT in detection of nodal metastasis was 76.9%, 90.5%, and 83% respectively. PET/CT under staged N stage in 5 patients and over staged in 3 patients and 2 of these patients have granulomatous lymphadenopathy. Mean SUV value for N stage was 3.5. For nodal staging the overall sensitivity, specificity and accuracy of PET/CT was more than CECT. Yoo JJ et al studied 76 patients of colorectal cancer. His study shows the sensitivity and specificity for N staging were 76.9% and 35.1% for abdominal CT and 61.8% and 66.7% for PET/CT. His study shows low diagnostic accuracy i.e. CT 57.9% and PET/CT 61.8%. [5] The results of our study are in contradiction with Yoo JJ et al.

All the patients in our study underwent CECT chest, abdomen and pelvis while patients that were studied by Yoo JJ et al underwent only abdominal CT. In PET/CT the regional lymph nodes may get masked by the high metabolic activity of tumor itself or the bowel activity. They can be false positive due to non malignant inflammatory response, as we have observed in our study, that 02 patents were over staged, showed granulomatous lymphadenopathy on histopathological confirmation.

In our study, CECT findings for M stage when compared with Histopathological M stage in 59 patients shows that 40/45 N0 patients and 9/14 M1 lesions were correctly staged with a CECT sensitivity of 64.3%, specificity of 88.9%, and overall accuracy of 83.1%. PET/CT findings for M stage when compared with Histopathological M stage in 59 patients shows that 43/45 M0, and 12/14 M1 lesions were correctly staged and sensitivity, specificity and overall accuracy of PET/CT in detection of distant metastasis was 85.7%, 95.6%, and 93.2% respectively. Peritoneal carcinomatosis was not picked up by both CECT and PET/CT in 2/2 patients.

In a study by Abdel-Nabi H et al 48 patients were evaluated with biopsy proven colorectal cancer or high clinical suspicion for colorectal cancer, underwent whole-body PET after intravenous administration of 10mCi (370MBq) of FDG. FDG PET results were correlated with computed tomographic (CT), surgical, and histopathologic findings. 37 patients with intraluminal carcinoma were depicted in PET. FDG PET commented positive for liver metastases in seven of eight patients and was superior to CT that showed three patients positive for liver metastases (sensitivity of 88% and 38 %). FDG PET and CT, respectively, correctly depicted the absence of liver metastases in 35 and 32 patients (specificity, 100% and 97%; negative predictive value, 97% and 86%). FDG PET has a high sensitivity and specificity for detection of colorectal carcinoma (primary and liver metastases) and appears better than CT in the staging of primary colorectal carcinoma. [6] However, our study does not correlate with Abdel-Nabi H et al. This disagreement may be because our study was conducted with contrast enhanced computed tomography as compared to non-contrast computed tomography of Abdel-Nabi H et al.

A retrospective review carried out by Kong G et al for 65 patients of metastatic colorectal carcinoma to determine comparative efficacy of 18F-FDG PET/CT and CECT in identifying extra hepatic disease. They concluded in finding PET/CT having incremental benefit over conventional CECT in identifying extra hepatic disease. PET/CT also showed high sensitivity and specificity for liver metastases. The recommendations also supported inclusion of 18F-FDG PET/CT in pre-surgical evaluation.[7] Selzner M et al compared CECT and PET/CT in patients with colorectal cancer metastatic to the liver and concluded for sensitivities of 95% and 91%, respectively. Hybrid imaging was potentially superior at the diagnosis of disease recurrence at the site of or in close proximity to previous hepatic surgery, with as specificity of 100% (vs. 50% for contrast-enhanced CT), as well as for the diagnosis of recurrence at the primary site of the

tumor. PET/CT detected more hepatic dissemination, with a sensitivity of 89%, compared with 64% sensitivity for CT. The surgeons (coauthors of Selzner et al.) indicated that PET/CT was their preffered imaging modality of choice for assessment of the resectability of liver metastases in patients with colorectal cancer. [8] We also found incremental benefit of PET/CT over CECT regarding M Staging and agree with the study conducted by Selzner M et al and Kong G et al.

Soyka JD et al evaluated 54 patients referred for restaging of colorectal carcinoma, and carried out Contrast Enhanced(CE) PET/CT. Retrospective analysis done by 2 experienced readers with consensus: first, CECT alone; second, non-CE PET/CT; and third, CE PET/CT. The number, localization, diagnostic certainty of lesions and the therapeutic impact of the findings was determined. Non-CE PET/CT added correct additional information in 20 of 30 patients, where CECT was inconclusive. In 7 of 24 patients with conclusive CECT, non-CE PET/CT added new lesions, leading to a change in treatment in 5 patients. In comparision to non-CE PET/CT, CE PET/CT had potentially added information in 39 of 54 patients (72%), with therapeutic relevance in 23 patients, due to correct segmental localization of liver metastases that is crucial for planning surgery. Authors suggested that CE PET/CT might be considered as the first-line diagnostic tool for restaging of patients with colorectal cancer. [9] We totally agree with the study conducted by Soyka JD et al that corroborates with an added benefit of CE PET/CT over non CE PET/CT seen in our study.

In our study, CECT (Chest, Abdomen, and Pelvis) correctly identified overall (TNM) stage in 57.4% (31/54) of patients and PET/CT correctly identified overall (TNM) stage in 72.2% (39/54) of patients. The difference was statistically significant. (P value < 0.006). PET/CT findings changed the management strategy in 7 patients. PET/CT picked up metastasis in 3 patients which were not picked up by CECT, one in Left supraclavicular lymph node, and two in the liver. In 4 patients diagnosed as metastatic on CECT, PET/CT picked up additional lesions which changed intent and primary management of these patients. The alteration in management plan in our study is in agreement with Park IJ et al who evaluated 100 patients with primary colorectal carcinoma during 2004. PET/CT detected 15 intra-abdominal metastatic lesions more than abdomino-pelvic CT scan. PET/CT showed true negative findings in 13 patients and false positive or negative findings in 10. Due to PET/CT results, management plans were altered in 27 patients; 9 had inter-modality changes, 10 received more extensive surgery, and 8 avoided unnecessary procedures. PET/CT altered management plan in 24% of patients with colorectal carcinoma in correct direction.[10] These findings suggest that PET/CT should be considered a part of standard work up for preoperative evaluation in a subset of patients with colorectal carcinoma.

Conclusion

FDG PET/CT scan can improve preoperative staging work up and the disease status in colorectal carcinoma along with the conventional modalities. It can improve the accuracy in determining the invasiveness of disease. This can further result in avoidance of unnecessary surgical intervention as well as help in determining the line of management. Our study also compared the effectiveness of PET/CT with CECT in colorectal liver metastases. Resectability of liver metastases in colorectal malignancies is of prognostic importance. The results of our studies suggested that PET/CT is more sensitive and specific for hepatic as well as extra-hepatic disease. CT with contrast appears to be sufficient to identify intrahepatic disease. The added effective radiation dose of 13 to 30 mSv with (PET/CT) compared with 7 mSv (CT) and 10 mSv (PET) is marginal for patients with metastatic cancer. Our study showed that whole body PET/CT should be done as part of protocol in cases of colorectal carcinoma, preferably in developing Asian countries like India, where the incidence of

colorectal carcinoma is rising. Whole body 18F-FDG PET/CT has the potential to be one stop platform for staging work up in colorectal cancer, as well as for evaluating local invasiveness, metastases, recurrence and treatment monitoring.

Acknowledgements
Department of oncology

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