Original Article

Role of ^{18}F-Fluorodeoxyglucose Positron-Emission Tomography/Computed Tomography Scan in Primary Staging of Breast Cancer Compared to Conventional Staging

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Abstract

Aim: In newly diagnosed carcinoma breast cancer patients, comparing conventional staging and 18F-fluorodeoxyglucose positron-emission tomography–computed tomography (^{18}F-FDG PET/CT) staging. **Materials and Methods:** This was a retrospective observational study. A total of 171 new diagnosed carcinoma breast patients who underwent staging ^{18}F-FDG PET/CT scan and routine conventional imaging including mammosonography of breast and axilla, chest X-ray, ultrasound sonography abdomen, and bone scan were included in the study. Staging was done according to the American Joint Committee on Cancer staging (tumor-node-metastasis). Changes in staging and management with ^{18}F-FDG PET/CT scan were assessed. **Results**: Overall PET/CT upstaged in 22.2% of cases and changed management in 15.78% of cases. PET/CT upstaged in three of eight cases in Stage IA patients but changed management in only one case. In Stage IIA, of 31 patients PET/CT upstaged in two patients (6.45%). In Stage IIB, of 45 patients PET/CT upstaged in six patients (13.3%). In Stage IIIA, of 22 patients PET/CT upstaged in six patients (27.2) and in five patients there is a change in management. In Stage IIIB, of 43 patients PET/CT upstaged in 21 patients (48.8%) with change in management in 13 patients (25.5%). **Conclusion:** ^{18}F-FDG PET/CT scan can be helpful in a significant number of patients with Stage IIB and above in upstaging and changing management.

Keywords: *Fluorodeoxyglucose, positron-emission tomography/computed tomography, stage IIB, upstaging*

Introduction

Breast cancer is the most common cancer in females worldwide.[1] Even in India, breast cancer is the most common cancer in females, and the incidence is increasing.[2] Stage of cancer and lymph node positivity were the important factors in treatment planning and prognostication. For the detection of primary tumor, magnetic resonance imaging is the gold standard but ultrasonography is routinely performed.[3] For axillary lymph node status, ultrasonography and intraoperative sentinel node examination are done. Intraoperative sentinel lymph node biopsy is superior in identifying axillary lymph node metastases and is the current standard of care.[4] For detection of distant metastases, chest X-ray, ultrasound sonography (USG) abdomen, and bone scan were usually done.

18F fluorodeoxyglucose positron-emission tomography–computed tomography (^{18}F FDG PET/CT) scan is a very sensitive modality in staging of breast cancer. Many studies have shown that ^{18}F FDG PET/CT scan was not superior to conventional methods for delineating primary and detecting axillary lymph node metastases but was superior for detection of extra-axillary lymph node and distant metastases.[5-10]

According to the NCCN guidelines, there was role of ^{18}F FDG PET/CT scan in patients with Stage IIIA and above.[11] Recently, some studies showed the role of ^{18}F FDG PET/CT scan in breast cancer with Stage II.[12-14]

The aim of this retrospective study was to evaluate the role of ^{18}F FDG PET/CT scan in staging breast cancer patients compared to conventional staging, especially in Stage II and how it helped in changing the management.

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Materials and Methods

This study was approved by the local Institutional Ethics Committee.

This was a retrospective study including 171 patients referred for the whole body ^{18}F FDG PET/CT scan. All were newly diagnosed breast cancer patients confirmed with trucut biopsy. All patients underwent staging with conventional methods which include USG of breast and axilla, Chest X-ray, USG abdomen, and bone scan in few cases.

Tumor-node-metastasis staging using the American Joint Committee on Cancer classification was done with conventional methods and after the whole body ^{18}F FDG PET/CT scan and was compared.

Imaging protocol

Patient preparation includes fasting for minimum of 6 h. All patient's blood sugar levels were <150 mg/dl. Patients were injected 10–15 mCi of ^{18}F-FDG and allowed to rest for about 60 min. Patients were instructed to avoid muscular activity. Whole body FDG PET/CT scan acquired from vertex of the skull to mid-thigh using GE discovery STE scanner with 16 slices CT.

The patient was given around 100 ml of omnipaque contrast (nonionic contrast, 350 mg iodine/ml) with an automated injector at a rate of 1.5 ml/s and CT scan started after a delay of about 100 s. Whole body CT scan from the vertex of the skull to midthigh was performed in a single step followed by breath-hold limited imaging of chest to avoid respiratory motion artifacts. CT was acquired with 330 mA and 120 KeV and slice thickness of 3.75 mm. The matrix used was 512 × 512.

Crystal used was bismuth germanium oxide. PET acquisition was done with beds ranging from six to eight beds with 3 min per bed. Axial field of view was 15.7 cm. PET image matrix used was 128 × 128. CT images were resized to match with PET images and fused. Iterative reconstruction was used in PET reconstruction using optimum subset-expectation maximization algorithm. CT transmissions maps were used for attenuation correction. Images were displayed and interpreted in ADW 4/4.5 workstations.

^{18}F FDG PET/CT scans were interpreted by two experienced nuclear medicine physicians. Visual inspection and FDG uptake of the tumor by measuring SUV_{max} value were taken into consideration to differentiate malignant and benign lesions. Uptake was correlated with corresponding CT lesions to differentiate benign conditions such as degenerative bone changes and fractures. In suspicious cases, histopathological confirmation of metastases was made. Staging of each case was done according to scan findings. PET/CT scan stage was compared to staging with conventional method. Changes in stage and management with PET/CT scan were noted.

Results

A total of 171 female patients were included in the study. Mean age of the patients was 53.52 ± 11.62 years. Among histopathology types of 171, 155 were of invasive ductal type carcinoma (IDC), 15 patients IDC with lobular, papillary, and spindle-cell differentiation and one patient was of lobular type. In histopathological grading, seven patients were of Grade-1, 146 patients of Grade 2, and 18 patients of Grade 3.

Overall PET/CT upstaged in 38 (22.2%) cases and changed management in 27 (15.78%) cases. PET/CT upstaged in three of eight cases in Stage IA patients but changed management in only one case. In Stage IIA, of 31 patients PET/CT upstaged in two patients (6.45%). In Stage IIB, of 45 patients PET/CT upstaged in six patients (13.3%). In Stage IIIA, of 22 patients PET/CT upstaged in six patients (27.2%) and in five patients there is a change in management. In stage IIIB, of 43 patients, PET/CT upstaged in 21 patients (48.8%) with change in management in 13 patients (25.5%).

New sites of metastases in ^{18}F FDG PET/CT scan compared to conventional staging are summarized in Table 1. Stage-wise number and percentage of cases who had change in staging are summarized in Tables 2 and 3 and Bar Chart 1. Stage-wise percentage of cases who were upstaged and change in management are summarized in Table 3.

Discussion

The accurate staging was very crucial in proper treatment planning of carcinoma breast patients. We analyzed 171 newly diagnosed carcinoma breast patients who had not received any kind of neoadjuvant therapy or surgery. ^{18}F FDG PET/CT scan had limited role in T staging of the tumor. Several studies showed that sensitivity of ^{18}F FDG PET/CT scan was low in detecting axillary nodes in patients who were clinically negative. Hence, sentinel lymph node biopsy was the standard of care.[15,16]

Extra-axillary lymph node detection will change the stage and management of the patient. Extra-axillary lymph node involvement was an important prognostic factor.[17] Several

Table 1: New sites of metastases in 18F-fluorodeoxyglucose positron-emission tomography/computed tomography scan stage wise

	IA	IIA	IIB	IIIA	IIIB
Ipsilateral axillary nodes	3	1	-	-	-
Contralateral axillary nodes	-	-	-	1	2
Internal mammary nodes	-	-	4	-	10
Cervical and mediastinal lymph nodes	-	1	1	3	9
Liver and other abdominal metastases	-	-	1	2	1
Lung metastases	-	-	1	1	2
Bone metastases	-	-	-	4	5

Table 2: Cross table comparing conventional staging and positron-emission tomography/computed tomography staging

	PET/CT staging								
	IA	IB	IIA	IIB	IIIA	IIIB	IIIC	IV	Total
Conventional staging									
IA	5	0	2	1	0	0	0	0	8
IB	0	0	0	0	0	0	0	0	0
IIA	0	0	29	1	0	0	1	0	31
IIB	0	0	1	38	0	0	4	2	45
IIIA	0	0	0	1	14	0	1	6	22
IIIB	0	0	0	0	0	23	8	12	43
IIIC	0	0	0	0	0	0	3	0	3
IV	0	0	0	0	0	0	0	19	19
Total	5	0	31	42	14	23	17	39	171

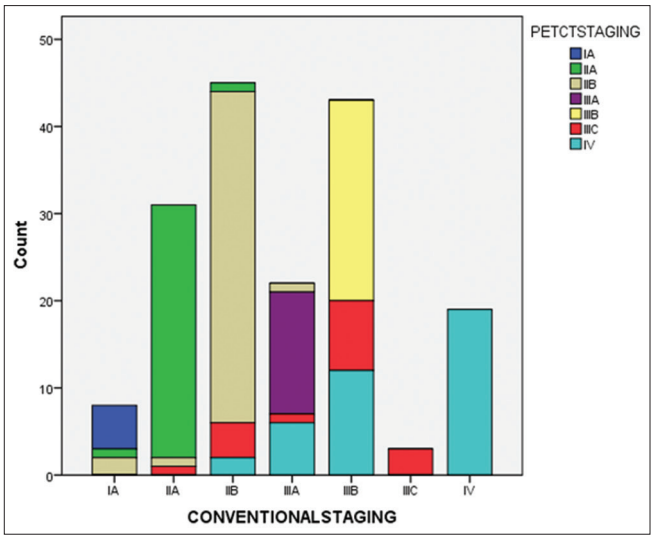
PET: Positron-emission tomography, CT: Computed tomography

studies showed that ^{18}F FDG PET/CT scan was the most sensitive test to detect extra-axillary lymph node metastases and distant organ metastases.[5,12-14,18] The NCCN guidelines recommend ^{18}F FDG PET/CT scan in breast cancer for Stage IIIA and above.

Few studies showed the role of ^{18}F FDG PET/CT scan in early breast cancer in changing management of patients.[12,14,15] A study done by Yararbas *et al*. showed that over all PET/CT upstaged in 35% of cases. They also showed that 18.6% and 30.3% of patients with Stage IIA and IIB were upstaged. Groheux *et al*. in their prospective study including 254 patients showed that ^{18}F FDG PET/CT scan upstaged in 30.3% of patients overall. They also showed that ^{18}F FDG PET/CT scan upstaged in 2.3% and 10.7% of patients with Stage IIA and IIB, respectively. Sergeant also showed that ^{18}F FDG PET/CT scan was superior to conventional methods in detection of extra-axillary lymph nodes and distant metastases for Stage IIB and stage III breast cancer patients.

In the present study, ^{18}F FDG PET/CT scan upstaged in 6.45% and 13.30% of cases with Stage IIA and IIB breast cancers, respectively. Among two cases which were upstaged in Stage IIA, one was upstaged to IIB and management had changed from simple mastectomy to modified radical mastectomy. In other case with identification of extra-axillary lymph node metastases, it was upstaged to IIIC and patient was given neoadjuvant chemotherapy. In Stage IIB of six cases who were upstaged, four cases upstaged to Stage IIIC, and two cases upstaged to Stage IV. In four cases who were upstaged to stage IIIC, neoadjuvant chemotherapy was given. In two cases who were upstaged to Stage IV, the intent of treatment was changed from curative to palliative. Figure 1 shows a case of breast cancer with breast mass and ipsilateral axillary lymph nodes. Chest X-ray, USG abdomen, and bone scan were normal. PET/CT scan showed internal mammary lymph nodes and solitary liver lesion. The patient was treated with neoadjuvant chemotherapy and follow-up PET/CT scan in Figure 2 showed showed resolution of the liver lesion. Two cases were down staged with ^{18}F FDG PET/CT scan, one from IIB to IIA and other from IIIA to IIB.

This was one of the few studies with good sample size to establish the role of ^{18}F FDG PET/CT scan in Stage



Bar Chart 1: Bar diagram representing change in staging with 18F-fluorodeoxyglucose positron-emission tomography–computed tomography scan compared to conventional staging

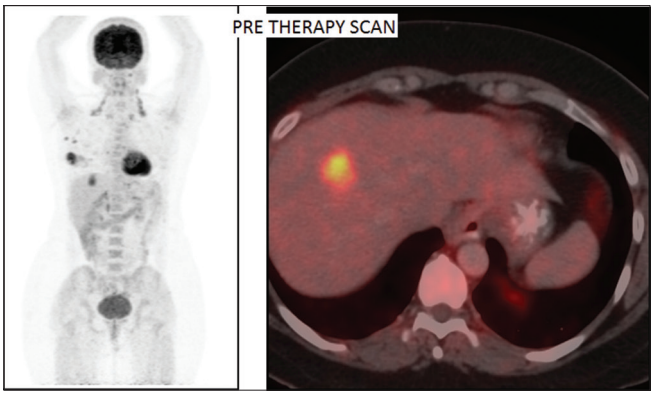


Figure 1: Pretherapy 18F-fluorodeoxyglucose positron-emission tomography–computed tomography detecting additional internal mammary lymph nodes and liver metastases. Upstaged to stage IV from IIB

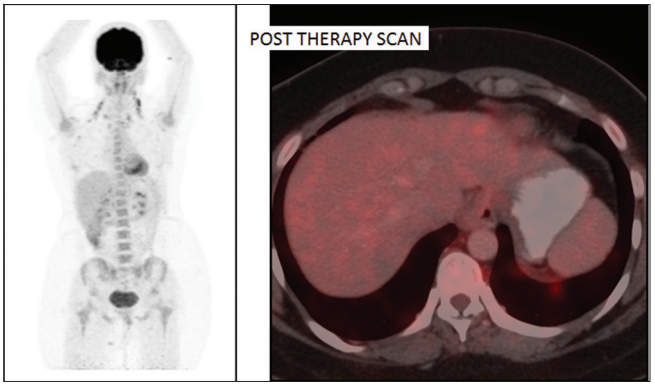


Figure 2: Post 4 cycles neoadjuvant chemotherapy, there is complete resolution of liver lesion

Table 3: Cases upstaged and change in management with positron-emission tomography/computed tomography scan

	PET/CT staging				
	Total	**Upstaged**	**Percentage upstaged**	**Change in management**	**Percentage change in management**
Conventional staging					
IA	8	3	37.50	1	12.50
IB	0	0	0	0	0
IIA	31	2	6.45	2	6.45
IIB	45	6	13.30	6	13.30
IIIA	22	6	27.20	5	22.72
IIIB	43	21	48.80	13	30.20
IIIC	3	0	0	0	0
IV	19	0	0	0	0
Total	171	38	22.22	27	15.78

PET: Positron-emission tomography, CT: Computed tomography

IIB breast cancer management. Limitations of the study include, it was a retrospective study and subjected to referral bias, and sample size in each stage was different. In Stage I and IIA, the sample size was very less to be statistically significant.

Conclusion

^{18}F FDG PET/CT scan was a valuable investigation in staging breast cancer even in Stage IIB. ^{18}F FDG PET/CT scan detected multiple new metastatic lesions compared to conventional staging. Hence, ^{18}F FDG PET/CT scan may be indicated in all breast cancer patients with Stage IIB and above.

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Conflicts of interest

There are no conflicts of interest.

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