Original Research Article

Correlation of primary tumor FDG uptake with clinicopathologic prognostic factors in invasive ductal carcinoma of the breast

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Abstract

Introduction: 18F-fluoro-2-deoxyglucose positron emission tomography/ computed tomography (18F-FDG PET/CT) has become an important tool in the evaluation of patients with invasive breast cancer by revealing the functional properties of breast tumors[1]. The maximum standardized uptake value (SUVmax) measured with FDG PET is a sensitive indicator for metabolic activity in breast cancer[2-10], which can be used to assess tumor aggressiveness and is associated with prognostic factors, such as the histological type, histological grade, immunohistochemical factors, and proliferation index[11,2-10]. PET with F-18 FDG has been widely used in clinical practice for the diagnosis, staging, treatment monitoring, and detection of disease recurrence in breast cancer patients[12]. **Aim/purpose:** To correlate clinicopathologic variables (tumor size, histologic grade, TNM stage, status of the hormonal receptor (ER, PR, HER2 expression) with PET-CT parameters such as maximum standardized uptake value(SUVmax). **Materials and methods:** This was a hospital based prospective cross sectional analytical study conducted for 19 months at Apollo Hospitals, Hyderabad. In the total of 70 participants after explanation of the procedure study and taking written informed consent who were diagnosed with invasive ductal carcinoma of the breast during the study period undergoing FDG PET CT scan, 55 participants were included for the study in accordance to inclusion and exclusion criteria. 15 participants were excluded. Patient was assessed for age, menopause status, tumor size (T), tumor grade (G), hormone receptor status (ER, PR, Herer2neu) and stage. Patient undergoes FDG PET CT for diagnostic evaluation. Measurement and assessment of FDG pSUVmax (mean + S.D.) in primary tumor of ductal carcinoma of the breast and correlation with clinicopathologic variables was done. **Results:** SUVmax was higher in the participants with higher tumor stage andhighertumorgrade.TheSUVmaxvaluesforT4stage, pTNMstageIVandGrade3 tumors were respectively 20.4 ± 2.0; 17.1 ± 3.5; and 13.2 ± 3.2. SUV max was also higher i nparticipants who were ER and PR negative(13.2±3.0; ±5.4), premenopausal women, patients with higher tumor stage, higher histological grade - poorly differentiated tumors, ER and PR negativity, triple negative receptor status and positive axillary lymph node status. Conclusion**:** The study demonstrates that SUVmax values are related to the recognized histopathologic and immuno histochemical prognostic factors in breast cancer predictability of predictive and prognostic factors before treatment is of importance in terms of deciding the therapeutic approach. In preoperative assessment of patients with breast cancer, PET/CT scanning is inadequate in examining axillary lymph nodes; however,it may prove beneficial in displaying the biologic characteristics and behavior of a tumor.

Keywords: PET CT, SUVmax, ER, PR

Introduction

Breast cancer is a heterogeneous disease with a broad range of therapeutic responses, recurrence risk, and overall prognosis[1]. Predicting the prognosis of breast cancer is very important to determine the direction of treatment. Most factors (tumor size, lymph node metastasis, pathological determination of the tumor size, histological tumor grade, axillary lymph node (LN) involvement, endocrine (hormonal) receptor status, and human epidermal growth factor receptor 2 (HER2) status) can be assessed only after surgery or invasive procedures for a definite tissue diagnosis[13].The immunohistochemical prognostic factors include hormone receptors, such as estrogen receptor (ER), progesterone receptor (PR) and HER2 and the Ki-67 proliferation index[13]. By using this, tumors are classified into the following five clinicopathologic subtypes: luminal A, luminal B (ERBB2-negative), luminal B (ERBB2-positive), (ERBB2- positive) (non-luminal and triple-negative.

18F-fluoro-2-deoxyglucose positron emission tomography/ computed tomography (18F-FDG PET/CT) has become an important tool in the evaluation of patients with invasive breast cancer by revealing the functional properties of breast tumors[1].

The maximum standardized uptake value (SUVmax) measured with FDG PET is a sensitive indicator for metabolic activity in breast cancer [14-22], which can be used to assess tumor aggressiveness and is associated with prognostic factors, such as the histological type, histological grade, immunohistochemical factors, and proliferation index[11,2-10]. PET with F-18 FDG has been widely used in clinical practice for the diagnosis, staging, treatment monitoring, and detection of disease recurrence in breast cancer patients[12].

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The detection rate of breast cancer by FDG-PET is lower when the tumor diameter is less than 1 cm owing to a partial volume effect.
Variable metabolic activity intrinsic to each specific tumor type represents one of the most significant limitations for the routine diagnostic application of PET in breast carcinoma. These variations can lead to a wide array of SUV readings after administration of 18F-FDG. To combat this issue, the technique of dual point imaging has been proposed.
FDG-PET using the dual point method, may be helpful because of its high positive predictive value in selected patients and in certain instances, such as false negative SLN, or inflammatory breast cancer, PET/CT can provide accurate staging information[30-32].
FDG-PET and PET/CT seem to detect much more distant metastatic lesion compared with conventional imaging methods in locally advanced and inflammatory breast cancers. However, current PET devices have a lower sensitivity in assessing lung nodules smaller than 1 cm, because of partial volume effect and respiratory motion. In such cases, CT images on PET/CT can be very helpful in the assessment of small nodules arising from metastatic pulmonary disease[14]. Dynamic CECT (DCECT) can measure the regional blood flow and volume along with mean transit time of blood through the capillaries. Therefore, combined FDG-PET/DCECT can assess not only glucose metabolism of tumors but also tumor vascularity. Both of these parameters can be used to differentiate between malignant and benign tumors, evaluate tumor aggressiveness, determine tumor response to therapy and occult residual tumors, and delineate the tumor during radiotherapy planning. Therefore, FDG-PET/DCECT can improve the diagnosis, prognosis, treatment selection, and therapy monitoring of various cancers[14].
The intensity of FDG uptake on PET/CT in the primary tumor and in metastatic lesions also serves as an important prognostic factor. High FDG uptake in the primary breast tumor has been associated with poor prognostic factors, including high histologic grade, triple negative status, and p53 mutation.

Aim/Purpose of the study

To correlate clinicopathologic variables (tumor size, histologic grade, TNM stage, status of the hormonal receptor (ER, PR, HER2 expression) with PET-CT parameters such as maximum standardized uptake value(SUVmax).

Materials and methods

This was a hospital based prospective cross sectional analytical study conducted between October 2016 to March 2018 (1 year and 7 months) at Apollo Hospitals. Patients diagnosed with invasive ductal carcinoma of the breast cancer referred for initial assessment (freshly diagnosed cases) were included. Patients who are pregnant andlactating, < 18 years ofage, those who have undergone any treatmentmodality and follow-up, recurrence, treatment response andrestaging cases are excluded. In the total of 70 participants after explanation of the procedure studyandtakingwritteninformedconsent who were diagnosed with invasive ductal carcinoma of the breast during the study period undergoing FDG PET CT scan, 55 participants were included for the study in accordance to inclusion and exclusion criteria. Fifteen participants were excluded.

Study Methods and Procedure

Complete detailed history pertaining to the clinicopathologic variables were taken prior to study. The standard clinico pathological and radiological methods were followed in this study during test as per hospital protocols and guidelines. The study was performed 4 weeks post biopsy.

Pet-CT scanner - imaging protocol

FDG PET/CT was performed on PET CT machine (Siemens Biograph 16 slice PET CT). The patients were required fasting>6 hrs., blood glucose level<200mg/dl , bladder emptying priorto the F-18 FD G injection. Images were acquired 60 min after intravenous injection of 5-10 mCi of F-18 FDG. Contrast enhanced CT scan was performedonlyforvenousphase.PET scan was acquired from the base of the skull to the proximal thigh High-resolution multi planar reformations were reconstructed for viewing. ThePETandCECT data were reconstructed and images fused with the help of fusion software. Image interpretation was done by experienced radiologist and nuclear medicinephysician.

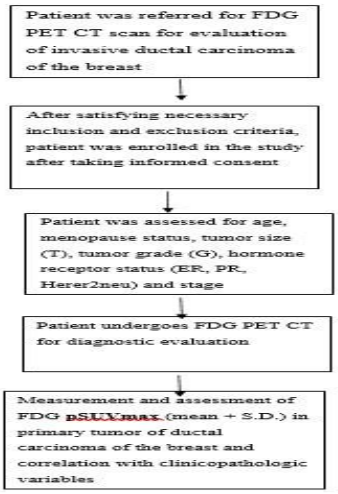
Study Outcomes measured

Patient age, family history, age of men arche, age of men opause, marital history, child birth history, clinical examination findings such tumor size and TNM stage, pathological findings such as tumor size, tumor grade, hormone receptor status have been assessed. Primary tumor FDG PET CT SUV max (mean +S.D.) – expressed as continuous variable was assessed after the completion of the scan.

Study Statistical Analysis Plan

All study data were entered into master chart excel sheet and data was analyzed using “Microsoft excel sheet” and SSPS software. The relationship between levels of primary tumor SUV (pSUVmax) and clinicopathological parameters were evaluated using the student’s t-test or Mann-Whitney U-test. It was regarded as statistically significant when p-values are less than 0.05 with a confidence interval of95%.

Study Flow chart



Results

This was a hospital based cross sectional analytical study and assessment done-

I. **Clinical variables**

a) Agecharacteristics: The Age range was 40 to 56 years with mean age of 48.4 ± 8.5 years.

b) Menopause and menarchestatus:Menopause was observed in 29 participants constituting 52.7 % of the total, the mean age of menopause in those participants was 46 ± 2.3 years, ranging from 44 to 49years. The mean age of menarche was 14 + 2 years.

Table 1 – showing mean age of menopause and menarche in the participants

Clinical variable	mean age
menopause	46 ± 2.3 years
menarche	± 2 years

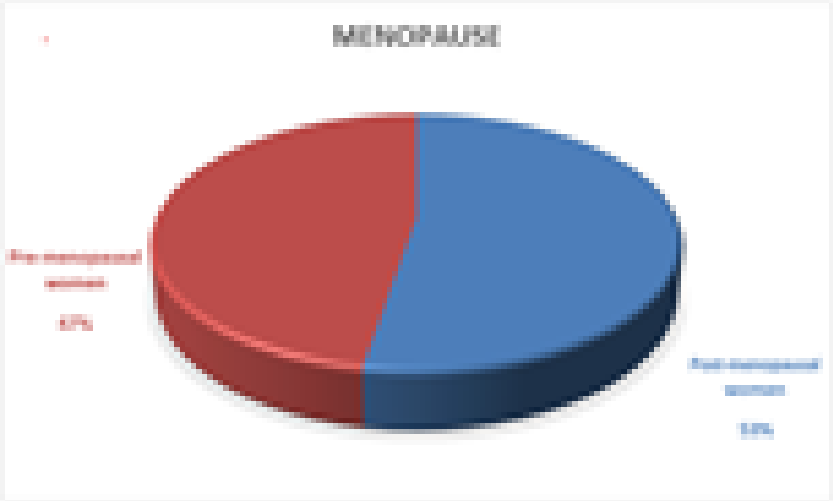


Figure 1 - Pie Diagram depicting distribution of post-menopausal and pre- menopausal participants

c)Child birthhistory: 39 participants (70.9%) had history of child birth before being diagnosed with carcinoma of the breast.

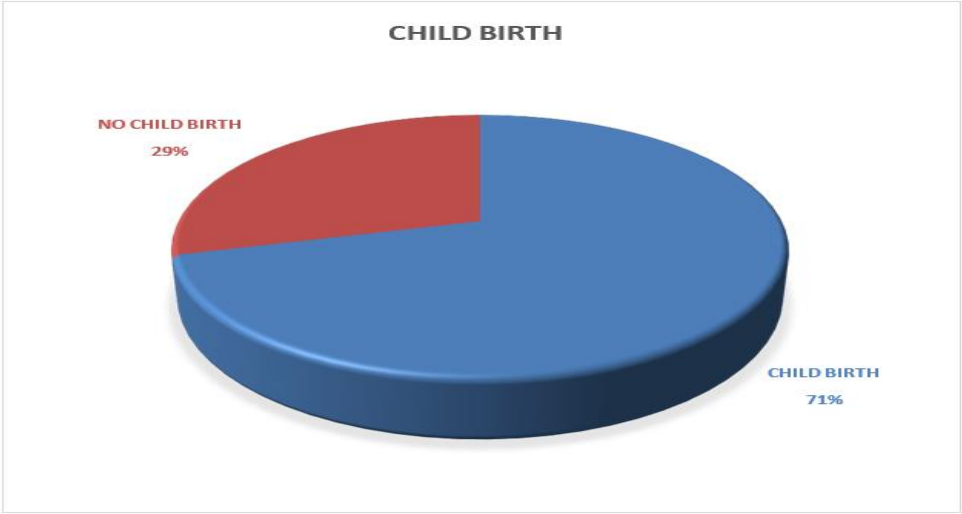


Figure 2 - Pie Diagram depicting distribution of participants with and without childbirth

d) Familyhistory: of breast cancer was seen in 33 participants (60%), of which 11 participants (20%) had first degree relatives diagnosed with carcinoma of the breast and the rest 22 participants (40%) had other than first degree relatives diagnosed with carcinoma of the breast.

II.Pathologicvariables

a) Tumor stage(T)

Tumor stage was categorized by the size of primary tumor (T). 7 patients belonged to T1b (0.5 cm<size≤1.0 cm), comprising 10.9 % of the total. 15 belonged to T1c (1.0 cm<size≤2.0 cm), constituting to 27.27 % , 20 cases belonged to T2 (2.0 cm<size≤5.0 cm), constituting 36.36 % , 8 cases belonged to T3 (5.0 cm<size), constituting 14.5% , 5 belonged to T4 constituting to 9.09% of the total.

Table 2– showing distribution of tumor stage T in the participants

Demographics of tumor stage -T		
Tumor stage	**Frequency**	**Percentage (%)**

T1b	7	12.7 %
T1c	15	27.27 %
T2	20	36.36 %
T3	8	14.5 %
T4	5	9.09 %

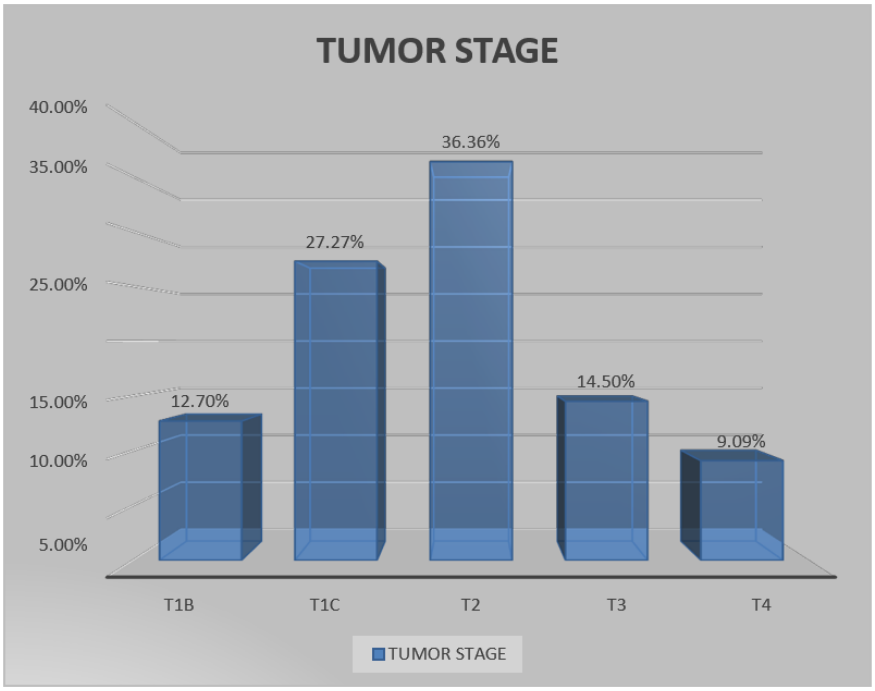


Figure 3- Column diagram depicting distribution of tumor stage in the participants

HISTOLOGICAL GRADE(G): Histological grade of the tumor was assessed with the help of Modified Nottingham Scarff - Bloom - Richardson grading system. 18 cases belonged to Grade 1, constituting 32.7% ,17 belonged to Grade 2, constituting 30.9%, 20 belonged to Grade 3, constituting to 36.36 % .

Table 3 – showing distribution of tumor grade in the participants

Demographics of tumor grade		
Tumor grade	**Frequency**	**percentage (%)**
GRADE 1	18	32.7 %
GRADE 2	17	30.9 %
GRADE 3	20	36.36 %

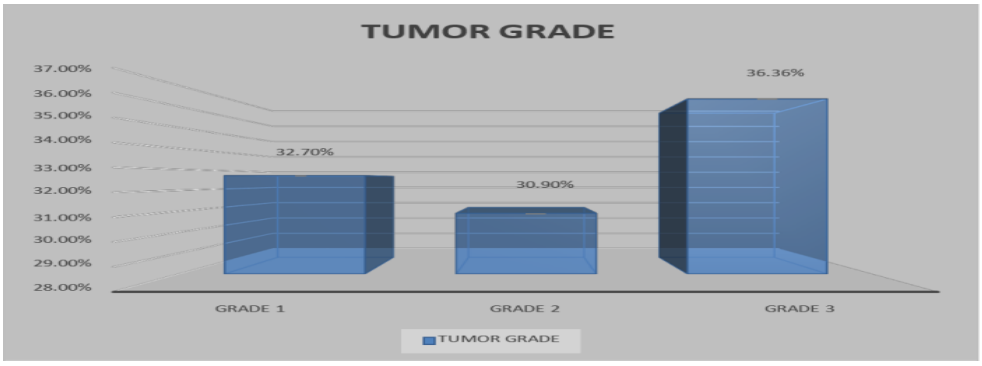


Figure 4- Column diagram depicting distribution of tumor grade in the participants.

Axillary lymph nodestatus : Axillary lymph node involvement at pathology was observed in 39 patients comprising 70.9% of the total. 18 cases belonged to stage II, constituting to 32.7 % , 10 belonged to stage III, constituting 18.18 % , 11 cases belonged to stage IV, constituting 20 % .

Table 4 – showing distribution of axillary lymph node involvement in the participants

Demographics of axillary lymph node status		
	Frequency	**Percentage (%)**
STAGE II	18	32.7 %

STAGE III	10	18.18 %
STAGE IV	11	20 %
TOTAL	39	70.9 %

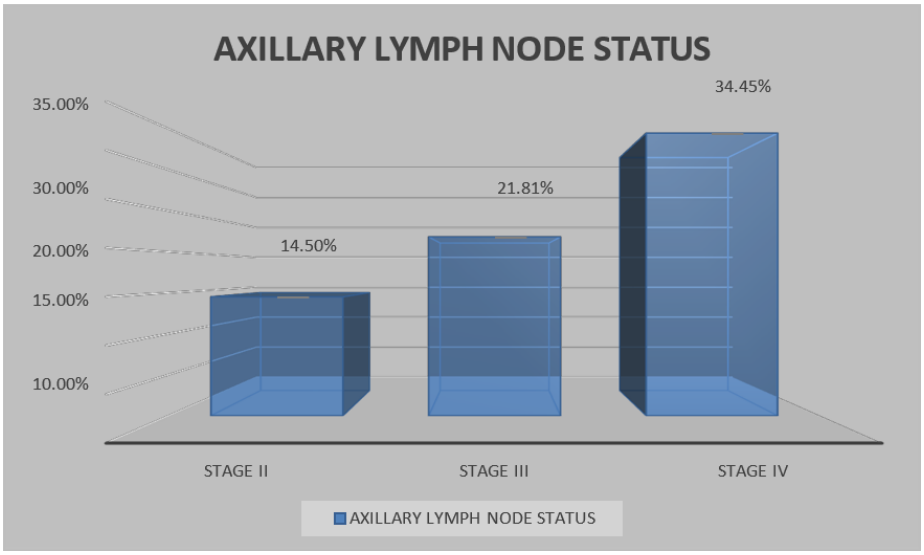


Figure 5 - Column diagram depicting distribution of axillary lymph node status in the population

Hormone receptorstatus: ER was positive in 35 cases , comprising 63.63 % , Negative in 20 cases constituting of 36.36 % , PR was positive in 39 participants, constituting 70.9 % , Negative in 16 patients, constituting of 29.1 % , HER2-neu receptor was positive in 17 cases, constituting 30.9 % , Negative in 38 participants, constituting of 69.1 % of the total.

Table 5 – showing distribution of receptor positivity in the participants

Demographics of receptor positivity		
Variable	**Positive**	**Negative**
ER	35 (63.63 %)	20 (36.36 %)
PR	39 (70.9 %)	16 (29.1 %)
HER2/NEU	17 (30.9 %)	38 (69.1 %)

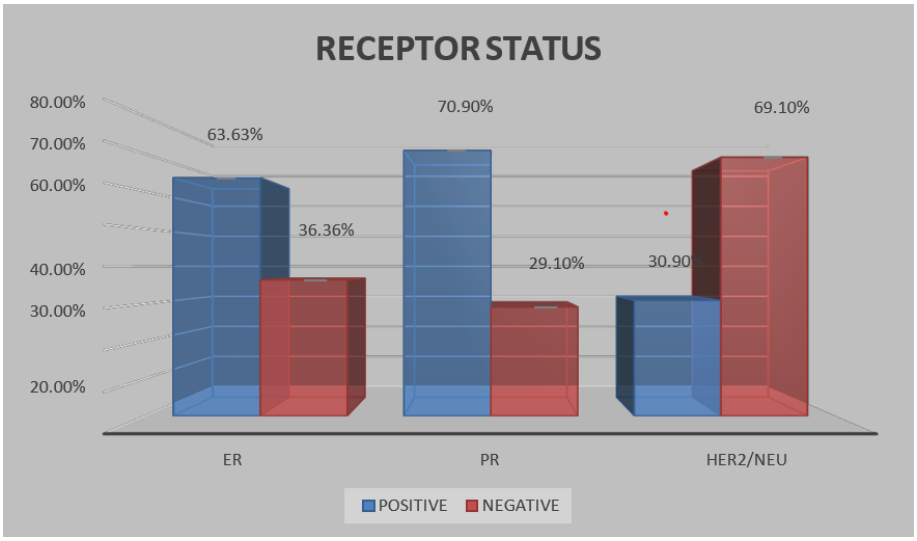


Figure 6 - Column diagram depicting distribution of receptor node status.

Nine participants were negative for all the receptors, i.e. triple negative, which constitute to about 16.3 % of the total.

TNMSTAGE : Pathological pTNM staging according to AJCC cancer staging manual 8th edition was performed. 16 cases belonged to stage I, constituting 29.1 % , 18 belonged to stage II, constituting 32.7 % , 10 cases belonged to stage III, constituting 18.18 % , 11 belonged to stage IV, constituting 20.0 % of the total.

Table 6 – showing distribution of TNM stage in the participants

Demographics of pTNM staging

Stage	Frequency	Percentage (%)
I	16	29.1 %
II	18	32.7 %
III	10	18.18 %
IV	11	20.0 %

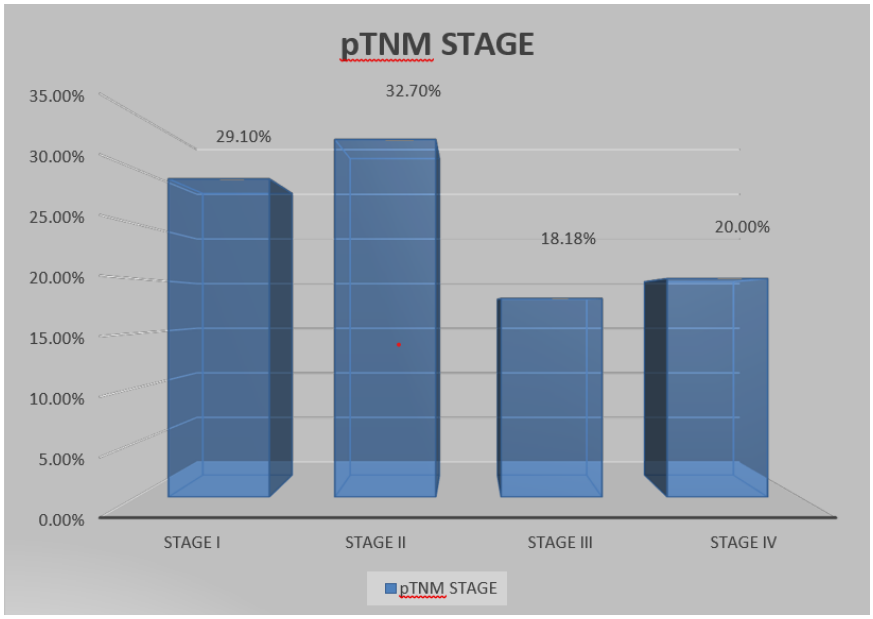


Figure 7- Column diagram depicting distribution of TNM stage in the population

III .relationship between psuvmax and clinicopathological parameters

Mean pSUVmax of the 55 participants was 7.1 ± 2.5 (range, 1.5–20.4).

A. Psuvmax and menopausestatus

Mean pSUVmax in pre-menopausal women, who were 26 cases of the total 55 (47.3%) was 12.03 ± 4.5 and in post-menopausal women was 4.3 ± 2.3.

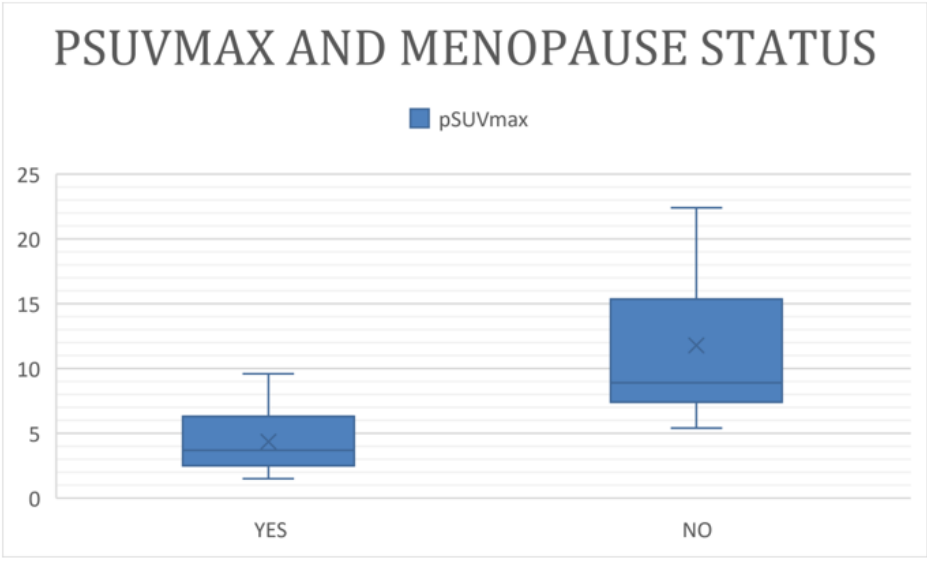


Figure 8 - Box and whisker plot depicting correlation between mean pSUVmax and menopause status.

B. Psuvmax and tumor stage (T)

Mean pSUVmax of the participants with tumor stage T1b was 1.9 ± 0.4, with tumor stage T1c was 3.9 ±1.2,with tumor stage T2 was 7.5 ± 2.1, with tumor stage T3 was 14.4 ± 3.0 and with tumor stage T4 was 20.4 ± 2.0.

Table 7 – showing correlation between tumor stage - T and pSUVmax

Correlation between tumor stage -T and pSUVmax		
Tumor Stage	**pSUVmax**	**p value**

T1b	1.9±0.4	~ 0.015
T1c	3.9±1.2	
T2	7.5±2.1	
T3	14.4±3.0	
T4	20.4±2.0	

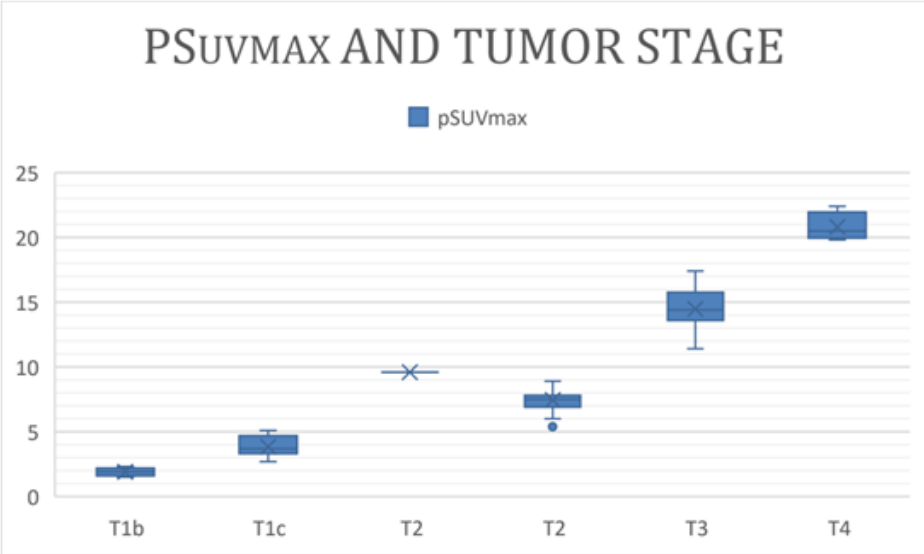


Figure 8 - Box and whisker plot depicting correlation between mean pSUVmax and tumor stage.

C. **Psuvmax and axillary lymph nodestatus**: Mean pSUVmax of the participants with lymph node negativity was 3.0 ± 1.5 and in participants with lymph node positivity was 10.1 ± 5.2.

Table 8 – showing correlation between Axillary Lymph Node status and pSUVmax

Correlation between axillary lymph node status and pSUVmax		
ALN STATUS	**pSUVmax**	**p value**
POSITIVE	3.0±1.5	~0.005
NEGATIVE	10.1±5.2	

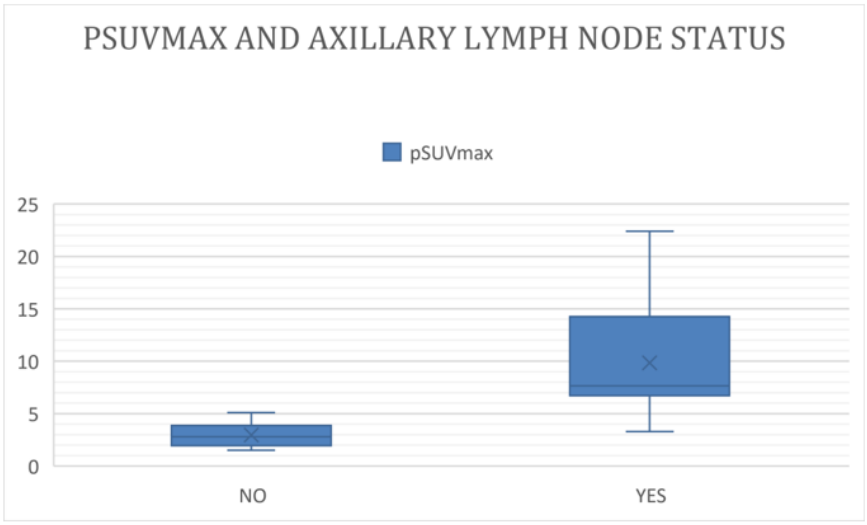


Figure 9 - Box and whisker plot depicting correlation between mean pSUVmax and axillary lymph node status.

D. **PSUVmax and tumor grade(g):** Mean pSUVmax of the participants with Grade 1 was 3.6 ± 0.4, with Grade 2 was 7.0 ± 1.9 and with Grade 3 was 13.2 ± 3.2.

Table 9 – showing correlation between tumor grade and pSUVmax

Correlation between tumor grade and pSUVmax		
TUMOR GRADE	**pSUVmax**	**p value**
GRADE 1	3.6±0.4	<0.001
GRADE 2	7.0±1.9	

GRADE 3	13.2±3.2	

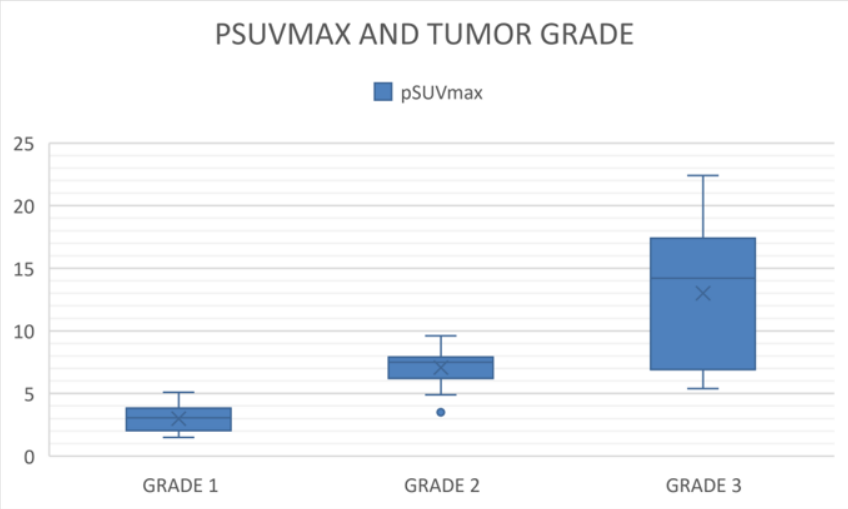


Figure 10- Box and whisker plot depicting correlation between mean pSUVmax and tumor grade.

E. PSUVmax and hormone receptor status

PSUVmax and erstatus: Mean pSUVmax of the participants with ER positivity was 4.9 ± 2.4 and in participants with ER negativity was 13.2 ± 3.0.

Table 10 – showing correlation between Estrogen receptor and pSUVmax

Correlation between ER status and pSUVmax		
ER STATUS	**pSUVmax**	**p value**
POSITIVE	4.9±2.4	<0.001
NEGATIVE	13.2±3.0	

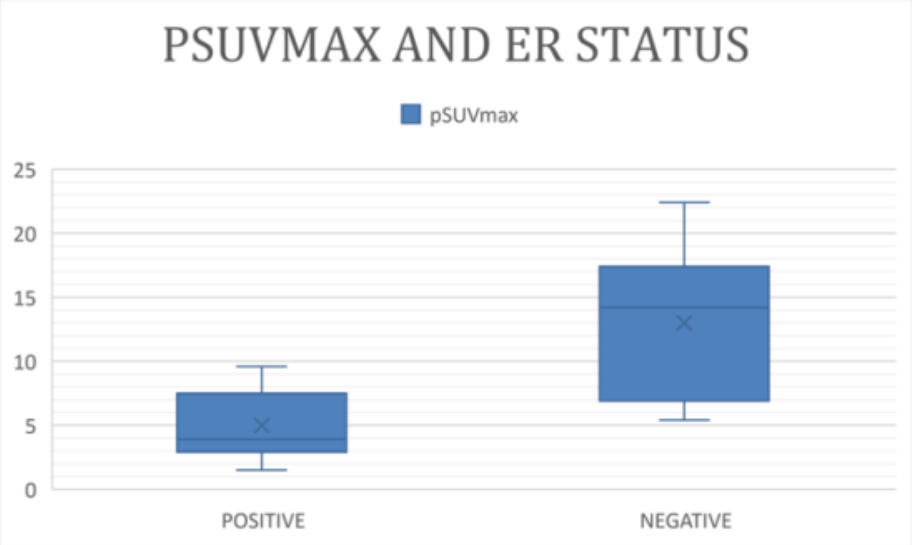


Figure 11- Box and whisker plot depicting correlation between mean pSUVmax and ER status.

I. PSUVmax and prstatus: Mean pSUVmax of the participants with PR positivity was 5.1 ± 2.3and in participants with PR negativity was 13.8 ± 5.4.

Table 11 – showing correlation between Progesterone receptor and pSUVmax

Correlation between pr status and pSUVmax		
PR STATUS	**pSUVmax**	**p value**
POSITIVE	5.1±2.3	<0.001
NEGATIVE	13.8±5.4	

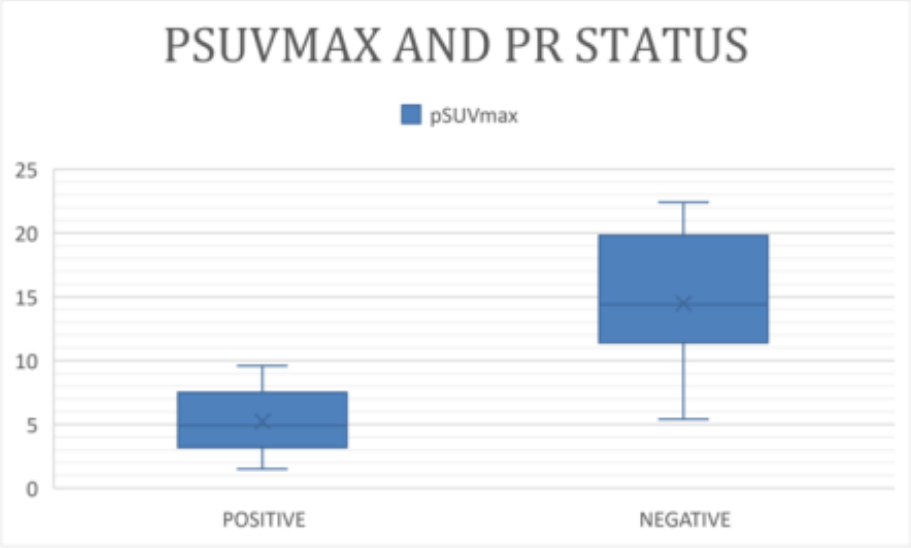


Figure 12- Box and whisker plot depicting correlation between mean pSUVmax and PR status

PSUVMAX AND HER2/NEUSTATUS: Mean pSUVmax of the participants with Her2/neu positivity was 8.4 ± 5.9and in participants with Her2/neu negativity was 7.9 ± 5.2

Table 12 – showing correlation between Her2/neu receptor and pSUVmax

Correlation between HER2/NEU STATUS AND pSUVmax		
HER2/NEU STATUS	**pSUVmax**	**p value**
POSITIVE	8.4±5.9	~0.212
NEGATIVE	7.9±5.2	

The mean pSUVmax in participants with triple negative receptor status (participants who were negative for estrogen, progesterone and Her2/neu status) was 15.2 ±4.9.

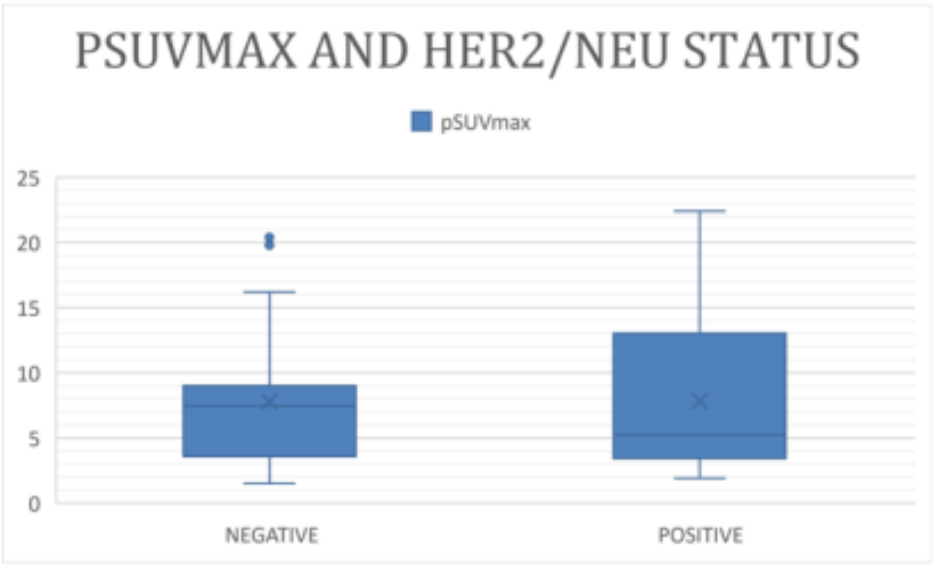


Figure 13- Box and whisker plot depicting correlation between mean pSUVmax and HER2/NEU status

PSUVMAX and TNM stage

The mean pSUVmax was 3.3 ± 1.2 in pTNM stage I, 6.5±2.5in stage II, 8.5±3.1 in stage III, and 17.1 ± 3.5 in stage IV, respectively, which are significantly different between each group (P<0.001).

Table 13 – showing correlation between TNM STAGE and pSUVmax

Correlation between TNM STAGE AND pSUVmax		
Tumor stage	**pSUVmax**	**p value**
STAGE I	3.3±1.2	<0.001
STAGE II	6.5±2.5	

STAGE III	8.5±3.1	
STAGE IV	17.1±3.5	

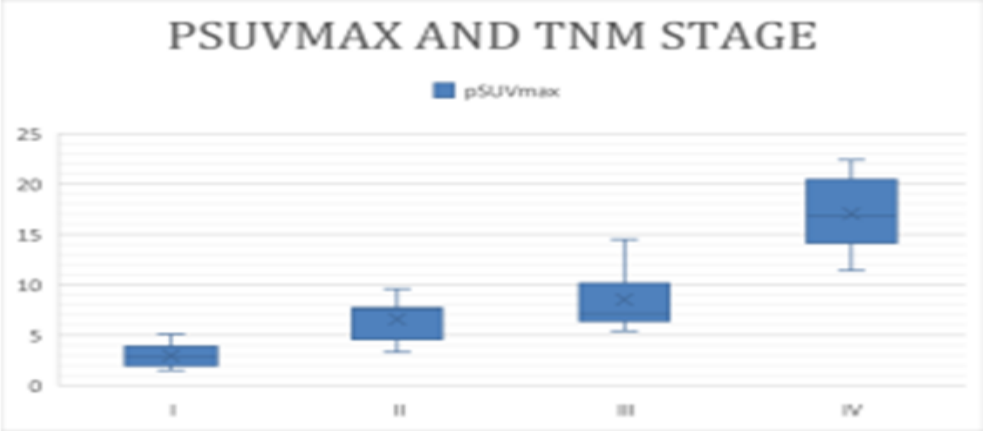


Figure 14- Box and whisker plot depicting correlation between mean pSUVmax and TNM stage.

Characteristic images from study cases

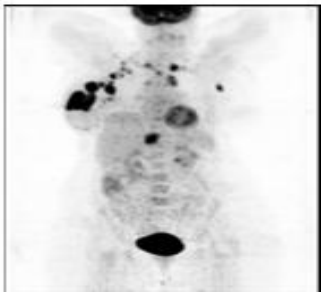
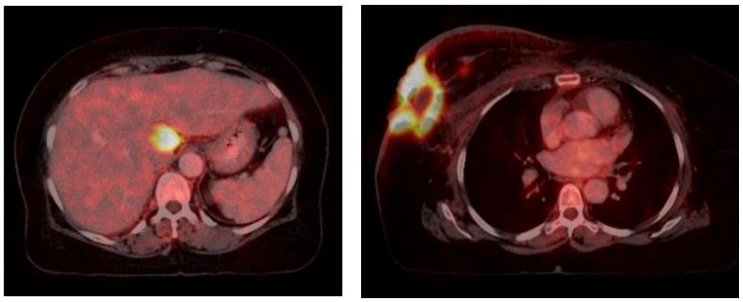
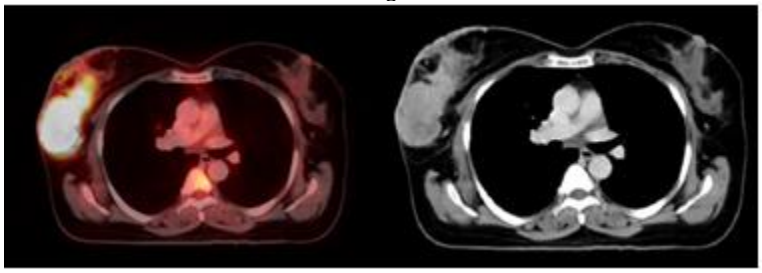


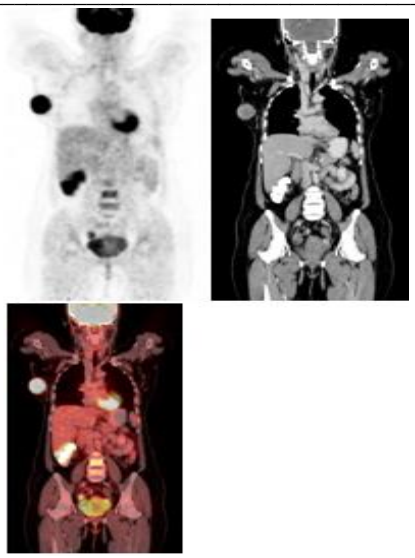
Figure 15 - Maximum intensity projection (MIP) image of FDG PET showing a stage IV invasive ductal carcinoma of right breast tumor stage T4 with nodal and liver metastasis. The pSUVmax of the primary tumor was 20.4. It was triple negative breast cancer.



Figures 16 PET-CECT images showing FDG avid liver metastasis in the left image and necrotic T4 mass in right breast in the right image.



Figures 17 PET-CECT image of chest on the left, showing FDG avid primary right breast carcinoma and right-side image of CECT thorax, showing heterogenous enhancing ill-defined mass lesion.



Figures 18 – PET Maximum intensity projection (MIP), CECT whole body and PET CECT whole body images showing a FDG avid heterogeneously enhancing tumor stage III and TNM stage III right breast invasive ductal carcinoma.

The pSUVmax of the primary tumor was 14.2. It was triple negative breast cancer.

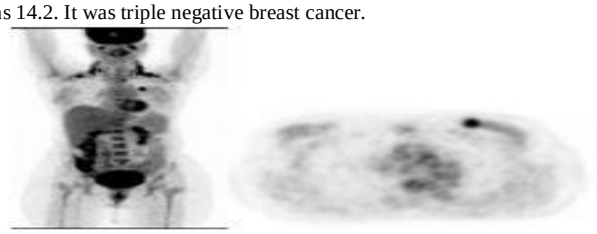


Figure19 - PET Maximum intensity projection (MIP) and axial PET thorax showing a FDG avid mass which was tumor stage II and TNM stage II left breast invasive ductal carcinoma. The pSUVmax of the primary tumor was 7.5. It was ER and PR positive and negative for Her2/Neu receptor. Note is made of incidental uptake in brown fat in the neck on bothsides.

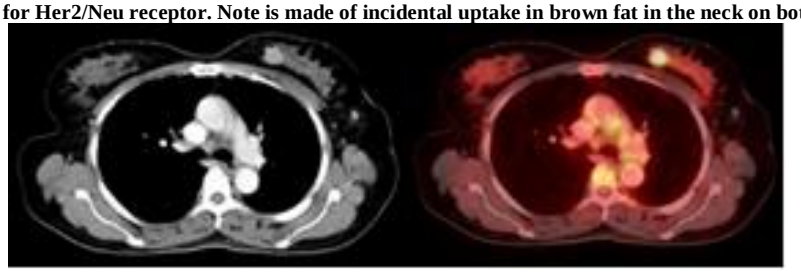


Figure 20 CECT image of chest on the left, showing heterogeneously enhancing ill-defined mass lesion of left breast and right- side image of PET-CECT thorax, showing FDG avid primary left breast invasive ductal carcinoma.

Discussion

Pathological predictors can only be obtained post- surgery, which is frequently associated with significant morbidity and mortality. On the other hand, F-18 FDG PET can provide quantitative information about tumor glucose metabolism, which represents the aggressiveness of the malignant lesion. FDG uptake can be evaluated noninvasively and be measured with good inter- test reproducibility[15]. Therefore, quantitative FDG-PET can be a valuable adjunct to conventional preoperative clinical assessment.

Distribution of different clinicopathologic variables mentioned in the study varied as follows. Regarding tumor stage-T, majority of participants belonged to tumor stage T2 followed by T1c, T3, T1b and T4 in the decreasing order. Regarding histological tumor grade–G, majority belonged to Grade3, followed by Grade1 and 2. Axillary lymph node positivity was seen in the participants from stage II to stage IV, none of the participants in stage I have shown positive ALN. Majority of the participants who have shown ALN positivity belonged to stage II, followed by stage IV and stage III. Regarding hormone receptor status distribution majority were showing ER positivity, PR positivity and her2neu receptor negativity. Regarding patient profile of hormone receptor status, majority of the patients were having ER PR positivity with her 2 neu negativity, followed by triple receptor positivity, triple receptor negativity, ER&PRnegativeandher2neureceptorpositive;andleastwith PR positivity only. Regarding pTNM staging, majority were stage II, followed by stage I, stage IV and stage II in decreasing order.

Inthepresentstudy, SUV max was higher in pre men opausal women (12.03±4.5), patients with tumor stage IV(20.4±2.0), histological grade3(13.2±3.2),ER and PR negativity (13.2± 3.0; 13.8 ± 5.4), ALN positivity (10.1±5.2) and TNM stage IV status(13.2±3.2). Her 2 neu receptor status in the study did not affect SUV max. These results were similar to the findings published by Osborne et al, Humbertetal, Miyakeetal, Jungetal, Mavietal, Basuetal, Groteuxetal, Kajary et al, Uğurluer et al, Seo et al, Lorca et al and Jo et al[13,12,17,16,20].

The mean SUV max in the premen opausal women was 12.03±4.5. These findings were similar to the study done by Gro heux et al[16].

In the present study, the SUV max was higher in participants with ER negativity(13.2±3.0) and lower in participants with ER positivity (4.9±2.4), higher in participants with ER and PR negativity (13.2 ± 3.0; 13.8 ± 5.4) and lower in patients with
ER and PR positivity (4.9 ± 2.4; 5.1 ± 2.3). The relationship between ER PR status with SUVmax was similar to the study by Humbert et al and Mavi et al[17].
In the present study, the SUV max was higher in participants with axillary lymph node positivity (10.1±5.2) and lower in the participants who were negative for axillary lymph nodes (3.0 ± 1.5). The relationship between axillary lymph node status and SUVmax was similar to the study by Hyun et al.
The SUVmax in participants with triple negative receptor status (participants who were negative for ER, PRand Her2/neu status) was 15.2 ± 4.9.The relationship between triple negative receptor status and SUVmax was similar to the study by Basu et al, Groheux et al, Koo et al, Kajary et al, Lorca et al and Jo et al[16,18,19].
ER and PR hold a crucial place in determining prognosis for patients with breast cancer and establishing whether they would benefit from hormonal therapy. HER2 status is an important predictive factorthatdeterminestherthepatientscanstartgoal-directedtherapy(trastuzumab)[20].
LuminalAtumors(positiveERandPR,negativeHER2,Ki-67<1%)isthesubtype with the best prognosis, triple-negative tumors show more biologically aggressive behavior[20].Inourstudy,negativeERandPR,positiveHER2andtriple-negative patients had higher SUVmax values. High values of SUV have also been reported in patients with negative hormone receptors by previous researchers[1-11].

Table 14– showing comparison between previous similar studies and current study

Comparison of previous studies with the current study				
First author	**Groheux et al**	**Jo et al**	**Uğurluer et al**	**Current study**
Year of study	2011	2015	2016	2016-2018
Mean/median age of Participants	50 YEARS (RANGE 26– 81)	53 YEARS	48±10.2 YEARS	48 YEARS
Number of participants	132	136	139	55
MEAN(±SD)/MEDIAN SUVMAX IN TNM STAGE I		6.1±4.4	IA- 5.1 ± 1.0 IB - 3.7 ± 2.9	3.3 ± 1.2
Mean(±SD)/median SUVMAX in TNM stage II		8.8±5.7	IIA- 6.4 ± 0.6 IIB- 6.9 ± 0.7	6.5 ± 2.5
MEAN(±SD) /median SUVMAX IN TNM stage III		10.3±6.0	IIIA- 6.1 ±0.8 IIIC- 6.2±0.9	8.5±3.1
MEAN(±SD) /median SUVMAX IN ER+/-	5.5 (3.7–8.2) 7.6(5.3–13.1)	6.0 ± 6.0 11.6 ± 5.9	5.4 ± 0.4 8.7 ± 0.7	4.9 ± 2.4 13.2 ± 3.0
MEAN(±SD)/median SUVMAX IN PR+/-	5.2 (3.7–7.7) 7.0(5.0–11.8)	6.3 ± 5.7 10.2 ± 6.0	5.4 ± 0.4 8.0 ± 0.6	5.1 ± 2.3 13.8 ± 5.4
MEAN(±SD)/median SUVMAX in her 2 NEU+/-	6.7 (5.1–9.7) 6.2 (4.2–9.7)	9.2 ± 5.0 7.6 ± 5.7	6.8 ± 0.6 5.9 ± 0.4	8.4 ± 5.9 7.9 ± 5.2
Mean(±SD) /median SUVMAX IN ALN status +/-	6.6 (4.5–9.6) 5.7(3.6-12.5)	8.6 ± 5.0 8.1 ± 5.8	5.9 ± 0.5 6.6 ± 0.6	3.0 ± 1.5 10.1 ± 5.2
Mean(±SD)/median SUVMAX IN grade I tumors	4.8 (3.4–6.4)	4.9 ± 1.7	3.3 ± 1.5	3.6 ± 0.4
Mean(±SD) /median SUVMAX IN grade II Tumors	4.8 (3.4–6.4)	5.3 ± 2.9	5.4 ± 0.6	7.0 ± 1.9
Mean(±SD)/median SUVMAX IN grade III tumors	9.7(7.0-15.3)	9.2 ± 5.7	7.0 ± 0.5	13.2 ± 3.2
Mean(±SD) / median SUVMAX IN T stage I		6.5 ± 4.4	4.5 ± 0.8	T1b- 1.9±0.4 T1c- 3.9±1.2
Mean(±SD)/median SUVMAX IN T stage II	6.3 (4.0–9.2)	10.2 ± 5.7	6.7 ± 0.4	7.5±2.1
Mean(±SD) /median SUVMAX IN T stage III	5.3 (3.4–8.6)	8.8 ± 6.6	6.7 ± 0.4	14.4 ± 3.0
Mean(±SD) /median SUVMAX IN T stage IV				20.4 ± 2.0

Significant correlation was found between 18F-FDG uptake and clinicopathologic variables. In preoperative assessment of patients with breast cancer, PET/CT using 18-FDG/ SUV max has an important role in providing proper staging, risk stratification, prediction of tumor biology and prognostication. PET indices enable better follow-up of patients with operable breast cancer and aid in making appropriate treatment decisions for thesepatients.

Conclusion

The study demonstrates that SUV max values are related to the recognized histopathologic and immune histochemical prognostic factors in breast cancer. Predictability of predictive and prognostic factors before treatment is of importance in terms of deciding the therapeutic approach. In preoperative assessment of patients with breast cancer, PET/CT scanning is inadequate in examining axillary lymph nodes; however, it may prove beneficial in displaying the biologic characteristics and behavior of a tumor and has an important role in providing proper staging, risk stratification, prediction of tumor biology and prognostication. PET indices enable better follow-up of patients with operable breast cancer and aid in making appropriate treatment decisions for these patients.

Limitations and future directions

First, the glucose metabolism of breast tumors was determined by SUV max; however, such indirect determination of FDG uptake using SUV is greatly affected by partial volume effects. Using anatomically

guided reconstruction and post reconstruction methods may overcome this effect. Post reconstruction methods include regional simultaneous estimation methods, voxel-based additive and multiplicative methods, purely multiplicative methods, wavelet-transform methods, deconvolution methods and segmentation-free methods. Reconstruction methods include spatial prior methods, intensity prior methods, diffusion priormethods and level set method [59]. The study included relatively small tumors (< 1 cm). Underestimation of FDG uptake in small tumors could not be ruled out. Advances should be made in the PET technology to detect the smaller tumors at an early stage, thereby improving diagnosis and thereby improving treatment options. SUVmax being a semiquantitative analysis does not 100% reflect the true value of metabolism of a tumor. In future, better quantitative parameters such as total lesion glycolysis (TLG) in place of SUVmax should be encouraged, to quantify the FDG uptake in the primary tumor. Another major limitation of SUVmax of FDG PET/CT is its reproducibility. As there is a long list of factors that affect SUV max, uniformity in scan acquisitions between patients and successive scans in the same patient should be maintained with utmost priority. SUV max calculation should be made more independent of external factors and error free, so that it can quantify tumor proliferation with high fidelity. No correlation was done between arobust proliferative marker such asKi-67andSUVmax. More studies should be done to correlate between proliferative marker such as Ki-67 and FDG uptake as they reflect tumor proliferation with more fidelity. There should be proper stratification based on receptor status and each group should be analyzed separately.

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Conflicts of interest
There are no conflicts of interest.

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