The effect of preoperative ^{18}F-FDG PET on the surgical decision in early breast cancer: 5-Year follow-up

Sina Ferahman[1,2] **MD,**
Mehmet Velidedeoglu[1] **MD,**
Yasin Tosun[1] **MD,**
Gurcan Albeniz[1] **MD,**
Kivilcim Ulusan[1] **MD,**
Varol Celik[1] **MD,**
Mehmet Ferahman[1] **MD,**
Ertugrul Gazioglu[1] **MD**

1. Cerrahpasa Medical Faculty, Istanbul University Cerrahpasa, General Surgery, Istanbul, Turkey
2. Bakirkoy Dr. Sadi Konuk Research and Training Hospital, General Surgery, Istanbul, Turkey

Keywords: Early breast cancer - ^{18}F-FDG PET - 5-year follow-up - Surgical decision - Metastasis

Corresponding author:
Sina Ferahman MD
Bakirkoy Dr. Sadi Konuk Egitim ve Arastirma Hastanesi,
Genel Cerrahi 4. Kat Zuhuratbaba Mah. Tevfik Sağlam Cd. No:11
Bakirkoy / Istanbul / Turkey
Orcid ID: 0000-0003-1160-9156
Phone: 0090533 612 0201
sinaferahmantr@hotmail.com

Received:
21 July 2020
Accepted revised:
23 November 2020

Abstract

Objective: The diagnosis, treatment, and management of the breast cancer (BC) require a multidisciplinary approach. In newly diagnosed BC, fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET) can detect extra-axillary regional nodal and distant lesions. **Subjects and Methods:** Between 2010 and 2015, this study included 101 patients with early-stage BC who were examined with ^{18}F-FDG PET before surgery. Patients were divided into two groups: Group 1 consisted of patients with suspected ^{18}F-FDG uptake and Group 2 with the remaining ^{18}F-FDG-negative patients. Differences between these groups were tested using the Pearson chi-square test, Fisher's exact test, Mann Whitney-U test, independent t-test and ROC analysis. They could be followed-up after 2015 for 5 years. All patients were then rediscussed either neoadjuvant therapy or surgery in the oncology board in 2020 with changing neoadjuvant criteria and oncoplastic surgery techniques. **Results:** Fluorine-18-FDG PET was found to have a sensitivity of 77.8% and a specificity of 90.8% in detecting axillary lymph node metastasis. During the minimum 5-year follow-up, one patient had bone metastasis, 2 patients had a local recurrence, and 3 patients had metastatic lymph nodes in the axilla. In the re-evaluation of the same patients over 5 years, the decrease in mastectomy decision was remarkable (P-value 0.01). **Conclusion:** We observed that we could not achieve a significant difference in 5-year metastasis/recurrence between the groups. Moreover, due to ^{18}F-FDG PET high false positivity, it significantly extended the time to surgery (P-value 0.01). In early-stage BC, ^{18}F-FDG PET demonstrated better performance in axillary lymph nodes metastases detection in comparison with other diagnostic imaging methods, even if SLNB remains the gold standard technique.

Hell J Nucl Med 2020; 23(3): 256-263 *Epub ahead of print: 14 December 2020* *Published online: 28 December 2020*

Introduction

Breast cancer (BC) is the most common form of cancer among women worldwide and the most common cause of cancer-related deaths as well. It is noteworthy that the incidence of BC has increased from past to present, while cancer-related deaths have gradually decreased [1]. As a result, it has been observed that each year the newly diagnosed BC cases are on average 3.6% more, compared with the year before [2]. The diagnosis, treatment, and management of disease require a multidisciplinary approach. Imaging methods such as mammography (MMG), ultrasonography (USG), magnetic resonance imaging (MRI), fluorine-18-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET), and bone scintigraphy are used in the diagnosis of BC [3].

In the newly diagnosed BC cases, ^{18}F-FDG PET can detect extra-axillary regional nodal and distant lesions. However, the role of ^{18}F-FDG PET in assessing nodal staging is uncertain due to its variable sensitivity and specificity values [4, 5].

Treatment decision of patients with BC is affected by many factors. The age of the patient, tumour size, hormone status, multicentricity, family history, and size of the patient's breast are among these factors [6, 7]. Our knowledge and BC guidelines change over time. More minimal conservative procedures are desired with developing chemotrophic drugs, imaging techniques, and surgical methods [8, 9]. However, the increase in mastectomy rates in the literature is remarkable [10]. While axillary dissection was performed 5 years ago in BC patients with axillary metastasis, neoadjuvant chemotherapy is currently recommended [11, 12]. In studies conducted in the last decade, axillary dissection rates decrease after neoadjuvant chemotherapy in patients with axillary metastasis. It has become more important to detect axillary lymph node (LN) metastasis in early stage breast cancer to reduce the morbidity of patients [10].

Although ^{18}F-FDG PET is not recommended for early stage BC, it could detect axillary

LN metastasis with higher specificity and sensitivity than all radiological imaging methods [4, 13, 14]. Therefore, the ^{18}F-FDG PET result has become more valuable before the surgical decision than in the past, for evaluating both BC mass and its relationship to metastatic axillary LN [15, 16].

In our study, we evaluated the effect of preoperative ^{18}F-FDG PET imaging on our surgical decision, in terms of local recurrence or metastasis. In addition, we examined if surgical decisions have changed over the past 5 years.

Subjects and Methods

Patients who applied to the breast diseases outpatient clinic between 2010 and 2015 were retrospectively examined. Those who were examined with ^{18}F-FDG PET, USG, MMG, and MRI before surgery were found. All of the patients were diagnosed by biopsy. Patients were staged radiologically according to TNM classification. Patients with early-stage BC (stage I-II) were included in the study.

Fluorine-18-FDG PET results of the patients were examined. Patients were divided into two groups: Group 1 consisted of patients with suspected ^{18}F-FDG uptake, Group 2 consisted of the remaining ^{18}F-FDG-negative patients. We used the cut-off value of maximum standardized uptake value (SUVmax) as 4.0 for suspicious lesions in ^{18}F-FDG PET [17, 18].

Patients of group 1 were re-evaluated with additional methods (bone scintigraphy, computer tomography and biopsy) for metastasis. After the examination, patients with metastases were referred to neoadjuvant chemotherapy and the patients without metastases were reserved for surgery (Figure 1). All of the patients were reassessed by the oncology team, which consisted of a general surgeon, radiologist, oncologist, pathologist, radiation oncologist, and nuclear medicine staff in 2020. First of all, the ^{18}F-FDG PET results were hidden from the board and the patients were evaluated. Afterward, the ^{18}F-FDG PET results were reported and the decisions were revised.

The patients' files contained data including the American Society of Anaesthesiologists (ASA) grade, body mass index (BMI), age, gender, additional diseases, and type of surgery results. The patients' follow-up continued for at least 5 years. Histological diagnosis, tumour size, hormone receptor status, surgical margin positivity, and axillary node status were obtained from pathology reports. Chemotherapy and radiotherapy treatments were questioned. All information was transferred to the computer system. Patients were invited to general surgery outpatient clinic, and were examined with USG at 6-month intervals and 1-year MMG and ^{18}F-FDG PET. The patients who failed to come to their follow-up appointments were interviewed by phone. Patients diagnosed with advanced BC before ^{18}F-FDG PET, patients who could not be reached during their follow-up, and patients who died due to BC were excluded from the study.

All procedures performed in this study involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants of the study. The authors also declare that they have no competing financial interests, and they do not have any conflict of interest.

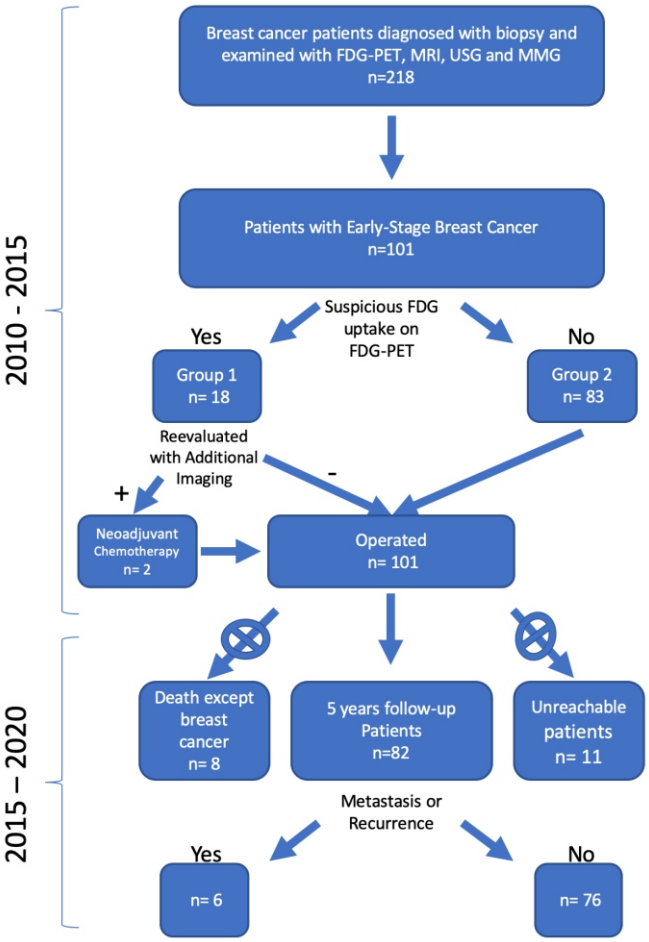

Figure 1. Patients who received ^{18}F-FDG PET preoperatively between 2010 and 2015 were found. Those with early-stage breast cancer were included in the study. The patients were followed up for 5 years. The study was completed in 2020, with 82 patients who continue their follow-up and/or can be reached by phone. Metastasis/recurrence was observed in 6 patients.

Descriptive statistics were used to present the demographic characteristics of the study population. Differences between the two groups were tested using the Pearson chi-square test or Fisher's exact test for categorical variables, and Mann Whitney-U test or independent t-test for continuous variables. Receiver operating characteristic (ROC) analysis was performed to calculate the sensitivity and specificity values of ^{18}F-FDG PET in relation to axillary LN metastasis detection. All analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA). A P-value <0.05 was considered statistically significant.

Institution review board (IRB) number

There is ethical approval from the Cerrahpasa-Istanbul University ethics committee (Ref. Nr: 2016-396164).

Results

It was determined that 218 patients diagnosed with BC were scanned with USG, MRI, MMG, and ^{18}F-FDG PET methods between 2010 and 2015. One hundred and seventeen patients with advanced BC were excluded from the study. The beginning of the study started with 101 patients.

The doctors were not apprised about the ^{18}F-FDG PET results of the patients. In the oncological committee, the files of the patients were re-evaluated with the current information of 2020. It was decided to perform breast-conserving surgery in 63 patients and mastectomy in 30 patients. Eight patients were considered to take neoadjuvant chemotherapy. Fluorine-18-FDG PET results and additional imaging were submitted to the oncology board and the patients were re-evaluated. Sixty one patients had breast preservation surgery, while 28 patients had mastectomy. Twelve patients were planned to receive neoadjuvant chemotherapy. There was not statistically significant difference between the surgical decisions based on ^{18}F-FDG PET results and surgical decisions without ^{18}F-FDG PET results (P-value 0.95).

However, after re-evaluating the same patients with the updated information and oncoplastic surgery techniques over the past 5 years, we can see that there is a remarkable decrease in mastectomy numbers (P-value 0.01), independently from ^{18}F-FDG PET results (Table 1).

Sentinel lymph node biopsy was accepted as the gold standard for lymph node metastasis [13]. Fluorine-18-FDG PET was found to have 77.8% sensitivity and 90.8% specificity in detecting axillary lymph node metastasis and the positive predictive value was 82.4%, while the negative predictive value was determined as 88.1%. The comparison of the sensitivity and specificity of MRI, USG, and ^{18}F-FDG PET in finding axillary lymph node metastasis and sentinel lymph node biopsy can be seen in Figure 2.

Table 1. *When comparing the council decisions between 2015 and 2020, there was a statistically significant difference (P-value 0.01). There was no statistically significant difference in which ^{18}F-FDG PET results were evaluated by hiding and explaining from the oncological council (P-value 0.95).*

	2010-2015 Decisions		2020 Decisions	
	Before ^{18}F-FDG PET	**After ^{18}F-FDG PET**	**Before ^{18}F-FDG PET**	**After ^{18}F-FDG PET**
Breast conserving surgery	60 (59,4%)	59 (58,4%)	63 (62,4%)	61 (60,4%)
Mastectomy	41 (40,6%)	40 (39,6%)	30 (29,7%)	28 (27,7%)
Axillar dissection	16 (14,9%)	15 (14,9%)	8 (7,9%)	4 (4%)
SLNB*	85 (84,2%)	84 (83,1%)	85 (84,2%)	85 (84,2%)
Neoadjuvant chemotherapy	0	2 (2%)	8 (7,9%)	12 (11,9%)

**SLNB: sentinel lymph node biopsy*

		Sentinel Lymph Node Biopsy			Sensitivity	Specificity
		Positive	Negative	Mean		
FDG-PET	Positive	28	6	34	77.8%	90.8%
	Negative	8	59	67		
MRI	Positive	26	9	35	72.2%	86.2%
	Negative	10	56	66		
USG	Positive	26	16	42	72.2%	75.4%
	Negative	10	49	59		

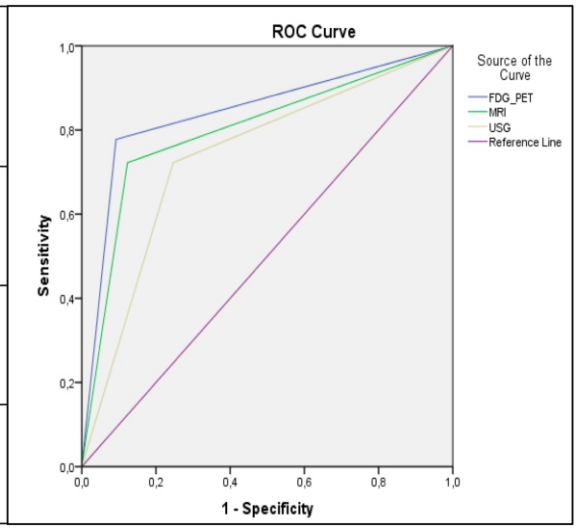

Figure 2. Condition of suspicious lymph nodes seen on ^{18}F-FDG PET, MRI and USG examinations compared with sentinel lymph node biopsies. Sensitivity and specificity of ^{18}F-FDG PET, MRI and USG were calculated.

After the preoperative ^{18}F-FDG PET examination, suspicious ^{18}F-FDG uptake was observed in 18 patients localized: 12 in the lung, 1 in the skull soft tissue (Figure 3), 2 in the thyroid, 1 in the humerus, 1 in the mediastinal lymph node and 2 in the stomach. Additional examinations (USG, bone scintigraphy, computed tomography, MRI, endoscopy and biopsy) were performed to clarify patients with suspected ^{18}F-FDG uptake.

Bone metastasis was detected in 1 patient and mediastinal LN metastasis in 1 different patient. Also, 1 patient was diagnosed with lymphoma and was excluded from the study. The patients with mediastinal LN and bone metastasis were directed to neoadjuvant chemotherapy.

The intervals between ^{18}F-FDG PET and the operation were evaluated. It was observed that there were 46.5 (±53.53) days in Group 1 and 17.8 (±10.75) days in Group 2. There was 28.7 days difference between the two groups. The comparison of the time between the ^{18}F-FDG PET and the surgery date suggests that the operation time was significantly extended due to the false positivity (P-value 0.01). In particular, the time taken for additional examinations had an impact on the treatment of the patients.

The patients were followed up for an average of 87 (±13.21) months. Five patients from Group 1, and 14 patients from Group 2 were excluded from the study because they could not be reached during this follow-up period (missing data and death from causes other than BC or its effects). The study proceeded with the remaining 82 patients.

The mean age of the patients was 59.3 (±13.16), and the mean BMI was 31.9 (±5.15). It was observed that there were 7 patients with ASA score 1, 39 patients with 2, and 36 patients with 3. There was no difference between BC breast's sides. Bilateral BC was observed in 2 patients. Cancer tissue was most common in the upper outer quadrant. Multicentric BC was seen in 10 patients. Invasive ductal carcinoma was the most common tumour type in both groups. Luminal A tumours were most common. The mean tumour size was 22.4 (±25.16) mm (Table 2).

Statistically, there was no significant difference between Group 1 and Group 2 regarding age, ASA score, BMI, comorbidities, cancerous breast, BIRADS, histological diagnosis, hormonal subgroup, tumor size, histological grade.

During the 5-year follow-up, 1 patient had bone metastasis, 2 patients had local recurrent tumor, and 3 patients had metastatic LN in the axilla, where 2 patients belonged to Group 1 and 4 patients to Group 2. Lymph nodes were confirmed by biopsy. These patients were re-operated. In group 1, LN metastasis in the axilla was observed after 34th months, and bone metastasis after 24th months. In Group 2, LN metastasis was seen in the axillary at 21st and 38th months, and recurrence in the breast at 43rd and 56th months (Table 3).

There was no statistically significant difference between the follow-up time (P-value 0.915) and the number of metastases/recurrences seen (P-value 0.177).

Discussion

In literature, there are many studies on BC and ^{18}F-FDG PET for the characterization of primary tumors, LN staging, and the post-surgery, chemotherapy, and/or external radiotherapy patient follow-up [19-21]. However, a study that examined the effect of ^{18}F-FDG PET on surgical decision-making and proceeded with a 5- year follow-up is new. Also, during

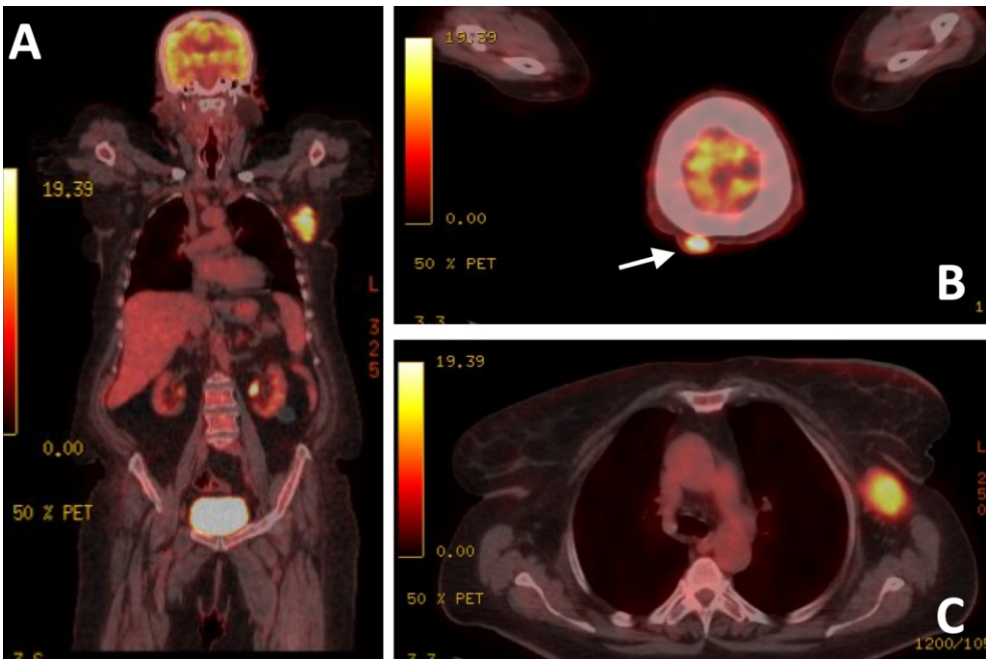

Figure 3. Fluorine-18-FDG PET in a patient with breast cancer. Fluorine-18-FDG uptake (SUVmax 8.2) in the LN in the left axilla in the coronal (A) and axial (C) planes; ^{18}F-FDG uptake (SUVmax 12.6) in the skull soft tissue (B, arrow). An infected cyst was detected by the additional USG in the skull area. Conversely, the metastasis of the axillary LN was proven by SLNB in surgery.

Table 2. *Demographic data of patients, ASA grades, BIRADS, tumour localization, histological types and grades, multicentric, tumour sizes, hormones subgroups.*

	Group 1	Group 2	Total	P-value
N	13	69	82	
Gender				
Female	13 (100%)	69 (100%)	82 (100%)	
Age (year)	59,8 (±12,5)	59,2 (±13,36)	59,3 (±13,16)	0.884
ASA*				
I	0 (0%)	7 (10,1%)	7 (8,5%)	
II	9 (69,2%)	30 (43,5%)	39 (47,6%)	0.178
III	4 (30,8%)	32 (46,4%)	36 (43,9%)	
BMI (kg/m^2)**	32,4 (±5,99)	31,8 (±5,03)	31,9 (±5,15)	0.744
Comorbidity†				
DM	3 (23,1%)	10 (14,5%)	13 (15,9%)	0.456
HT	2 (15,4%)	8 (11,6%)	10 (12,2%)	0.709
COPD/Asthma	0 (0%)	2 (2,9%)	2 (2,4%)	0.403
Malignancy	0 (0%)	2 (2,9%)	2 (2,4%)	0.403
Others	2 (15,4%)	15 (21,7%)	17 (20,7%)	0.593
Breast‡				
R/L/B	7 / 6 / 0	34 / 33 / 2	41 / 39 / 2	0.69
BIRADS††	3,3 (±2,05)	3,7 (±1,76)	3,7 (±1,8)	0.506
The localization of Tumor††				
UOQ	8 (61,5%)	27 (39,1%)	35 (42,7%)	
LOQ	3 (23,1%)	7 (10,1%)	10 (12,2%)	
UIQ	1 (7,7%)	18 (26,1%)	19 (23,2%)	0.101
LIQ	1 (7,7%)	8 (11,6%)	9 (11%)	
PA	0 (0%)	9 (13%)	9 (11%)	

(Continued)

Histological Type‡‡				
IDC	7 (53,8%)	50 (72,5%)	57 (69,5%)	
ILC	2 (15,4%)	6 (8,7%)	8 (9,8%)	0.627
Mixed	3 (23,1%)	9 (13%)	12 (14,6%)	
Others	1 (7,7%)	4 (5,8%)	5 (6,1%)	
Multicentric	3 (23,1%)	7 (10,1%)	10 (12,2%)	0.074
Tumor size (mm)	23,9 (±8,61)	22,2 (±9,57)	22,5 (±9,4)	0.535
Histological Grade	2,5 (±0,88)	2,4 (±0,55)	2,4 (±0,61)	0.175
Hormones				
Luminal A	9 (69,2%)	41 (59,4%)	50 (61%)	
Luminal B	1 (7,7%)	12 (17,4%)	13 (15,9%)	0.419
Triple Negative	1 (7,7%)	12 (17,4%)	13 (15,9%)	
HER-2 positive	2 (15,4%)	4 (5,8%)	6 (7,3%)	

Age, BMI, BIRADS, Tumour size, histological grade (n, Mean±SD), Gender, ASA, comorbidity, Tumour localization, histological Type, multicentric, Hormones subgroup (n/%)
**ASA: American Society of Anaesthesiologists grade **BMI: Body mass index †DM: Diabetes Mellitus, HT: Hyper tension, COPD: Chronic obstructive pulmonary disease, Malignancy includes Lymphoma and gastric cancer, Others include thyroid, familial Mediterranean fever, ‡R: Right, L: left, B: bilateral ††The Breast Imaging Report and Data System ‡‡UOQ: Upper outer quadrant, LOQ: Lower outer quadrant, UIQ: Upper inner quadrant, LIQ: Lower inner quadrant, PA: Periareolar quadrant ‡‡IDC: Invasive Ductal carcinoma, ILC: Invasive lobular carcinoma, Others includes squamous cancer, neuroendocrine tumor, papillary carcinoma*

these 5 years the continuously changing and developing medical knowledge were taken into account with the surgical preference.

Fluorine-18-FDG PET was found to be superior to MRI and computed tomography in detecting cancer and organ metastases in a single session [22]. Especially, it has an important role in the evaluation and staging advanced BC [23]. Few publications show that it can be used in axillary LN evaluation in early-stage BC [19].

Current evidence does not support the use of ^{18}F-FDG PET for staging locoregional disease because of its limited sensitivity compared to the gold standard sentinel LN biopsy (SLNB) and axillary LN dissection [24]. However, the superiority of ^{18}F-FDG PET in detecting axillary LN metastasis compared to other radiological imaging (USG, MRI) was found to be consistent with other studies in the literature [4, 13, 14]. Hubner et al. (2000) reported a ^{18}F-FDG PET sensitivity and specificity of 96% and 91%, respectively [25]. Contrary, there are other publications where the superiority of MRI is seen [26]. In our study, the ^{18}F-FDG PET specificity was found to be 90.8% in detecting the axillary LN metastasis, and superior compared to USG and MRI.

Among women with TNM stage I and II, there is limited evidence for the effect of prolonged waiting to affect survival and lead to disease progression [27]. The average waiting time for primary surgery was 24 days (maximum 62 days) and was significantly affected by the hospital volume with additional imaging and diagnostic biopsies [28]. It is a common belief in many studies that ^{18}F-FDG PET prolongs the time to surgery due to its high false positivity rate [29-33].

In the study of Chung et al. (2006) [18], it was seen that the lowest false positive value was reached when the SUVmax cut-off value was taken as 4.0 in BC. For this reason, we chose the SUVmax cut-off value as 4.0 in our study. Our breast and axillary lymph node results were consistent with Chung's study. We found high false positivity in distant organ metastasis (15 patients). Fluorine-18-FDG uptake varies according to tissue type. However, the SUVmax value of 4.0 is sufficient to cast doubt on all tissue types. The most important reason

Table 3. *Time between ^{18}F-FDG PET and surgery, follow-up time, axillary metastasis, number of breast recurrence and distant metastases and development time after surgery. Comparing the time between ^{18}F-FDG PET and the date of surgery shows that the operation time is significantly extended in Group 1 P-value 0.01).*

	Group 1	Group 2	Total	P-value
Time ^{18}F-FDG PET to Operation (days)	46,5 (±53,53)	17,8 (±10,75)	22,4 (±25,16)	0.01
Follow-up time (months)	86,6 (±13,91)	87,1 (±13,18)	87 (±13,21)	0.915
Metastasis or Recurrence (n)				
Axillary	1 (7,7%)	2 (2,9%)	3 (3.7%)	
Breast	n/a	2 (2,9%)	2 (2.4%)	0.177
Bone	1 (7,7%)	n/a	1 (1.2%)	
Time to Metastasis or Recurrence (months)				
Axillary	34	21,38	31 (±8.89)	
Breast	n/a	43,56	49.5 (±9.19)	
Bone	24	n/a	24	

for high false positivity may be suspected ^{18}F-FDG uptake in infections, trauma and benign lesions [17, 18]. In many instances, these false-positive lesions can be differentiated from cancer by correlation with characteristic imaging appearances on conventional breast imaging modalities and by biopsy for tissue diagnosis when needed. However, additional procedures increased the duration of the patient's treatment. In our study, we saw that ^{18}F-FDG PET significantly delayed the time to surgery due to their high false positivity. On average there was 28.7 days delay in patients' surgery dates.

Changes in mastectomy rates are still confusing in literature. Studies are suggesting that the mastectomy rates are increasing with the changes by age in BC incidence and the widespread use of implants. However, there are centers with reduced mastectomy rates [34]. While these studies were conducted with different patients, distinctively our study re-evaluates the same patients. In the last 5 years, there are many publications in the literature showing that the rates of neoadjuvant chemotherapy have increased [35, 36]. In our study, patients were re-assessed with changing neoadjuvant chemotherapy criteria and oncoplastic surgery techniques over 5 years. We have seen that patients reserved for mastectomy or axillary dissection were rather directed towards neoadjuvant therapy especially for axillary downstaging.

Fluorine-18-FDG PET is seen as an extra cost for early stage BC, as has been proven in many publications [13, 24, 31, 32]. Also, our results demonstrated that ^{18}F-FDG PET did not impact on surgical decision strategy, even if it is found to be superior compared to other diagnostic imaging methods (USG and MRI) in axillary lymph node metastases detection.

The most important limitation of our study is that it is a retrospective study. In addition, it was studied with a small sample group. Another important limitation is that patients are not classified according to biological characteristics.

In conclusion, there was no significant difference in a 5-year metastasis/recurrence in early-stage BC with preoperative positive ^{18}F-FDG PET or not. Due to its high false positivity rate, it significantly extended the time to surgery. However, ^{18}F-FDG PET is found to be superior compared to other radiological methods in axillary LN metastasis detection.

Although it is unthinkable to give up sentinel LN biopsy today, further studies on a larger sample size, are needed in order to consider in the future ^{18}F-FDG PET as a non-invasive pre-operative imaging method in early BC patients.

The authors declare that they have not conflicts of interest.

Bibliography

1. Jemal A, Bray F, Center MM et al. Global cancer statistics. *CA Cancer J Clin* 2011; 61(2): 69-90.
2. Leung G, Thach T, Lam T et al. Trends in breast cancer incidence in Hong Kong between 1973 and 1999: an age-period-cohort analysis. *Br J Cancer* 2002; 87(9): 982-8.

3. Cook GJ, Houston S, Rubens R et al. Detection of bone metastases in breast cancer by ^{18}F-FDG PET: differing metabolic activity in osteoblastic and osteolytic lesions. *J Clin Oncol* 1998; 16(10): 3375-9.
4. Greco M, Crippa F, Agresti R et al. Axillary lymph node staging in breast cancer by 2-fluoro-2-deoxy-D-glucose–positron emission tomography: clinical evaluation and alternative management. *J Natl Cancer Inst* 2001; 93(8): 630-5.
5. Wahl RL, Siegel BA, Coleman RE et al. Prospective multicenter study of axillary nodal staging by positron emission tomography in breast cancer: a report of the staging breast cancer with PET Study Group. *J Clin Oncol* 2004; 22(2): 277-85.
6. Rosenberg SM, Greaney ML, Patenaude AF et al. Factors affecting surgical decisions in newly diagnosed young women with early-stage breast cancer. *J Adolesc Young Adult Oncol* 2019; 8(4): 463-8.
7. Parker PA, Peterson SK, Bedrosian I et al. Prospective study of surgical decision-making processes for contralateral prophylactic mastectomy in women with breast cancer. *Ann Surg* 2016; 263(1): 178.
8. Crown A, Wechter DG, Grumley JW. Oncoplastic breast-conserving surgery reduces mastectomy and postoperative re-excision rates. *Ann Surg Oncol* 2015; 22(10): 3363-8.
9. Bowen ME, Mone MC, Buys SS et al. Surgical outcomes for mastectomy patients receiving neoadjuvant chemotherapy: a propensity-matched analysis. *Ann Surg* 2017; 265(3): 448.
10. Susini T, Renda I, Giani M et al. Changing Trends in Mastectomy and Breast Reconstruction. Analysis of a Single-institution Experience Between 2004-2016. *Anticancer Res* 2019; 39(10): 5709-14.
11. Caresia Aroztegui AP, García Vicente AM, Alvarez Ruiz S et al. ^{18}F-FDG PET/CT in breast cancer: Evidence-based recommendations in initial staging. *Tumor Biol* 2017; 39(10): 1010428317728285.
12. Gradishar WJ, Anderson BO, Abraham J et al. Breast Cancer, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2020; 18(4): 452-78.
13. Riegger C, Koeninger A, Hartung V et al. Comparison of the diagnostic value of ^{18}F-FDG-PET/CT and axillary ultrasound for the detection of lymph node metastases in breast cancer patients. *Acta Radiol* 2012; 53(10): 1092-8.
14. You S, Kang DK, Jung Y et al. Evaluation of lymph node status after neoadjuvant chemotherapy in breast cancer patients: comparison of diagnostic performance of ultrasound, MRI and ^{18}F-FDG PET/CT. *Br J Radiol* 2015; 88(1052): 20150143.
15. Orsaria P, Chiaravalloti A, Caredda E et al. Evaluation of the usefulness of ^{18}F-FDG PET/CT for nodal staging of breast cancer. *Anticancer Res* 2018; 38(12): 6639-52.
16. Ko H, Baghdadi Y, Love C et al. Clinical Utility of ^{18}F-FDG PET/CT in Staging Localized Breast Cancer Before Initiating Preoperative Systemic Therapy. *J Natl Compr Canc Netw* 2020; 18(9): 1240-6.
17. Groheux D, Espié M, Giacchetti S et al. Performance of ^{18}F-FDG PET/CT in the clinical management of breast cancer. *Radiology* 2013; 266(2): 388-405.
18. Chung A, Liou D, Karlan S et al. Preoperative ^{18}F-FDG-PET for axillary metastases in patients with breast cancer. *Arch Surg* 2006; 141(8): 783-9.
19. Raghavan B, Sivaramalingam G, Singh S et al. editors. PET/CT upstaging of unilateral operable breast cancer and its co-relation with molecular subtypes2019: European Congress of Radiology 2019.
20. Ravina M, Saboury B, Chauhan MS et al. Utility of ^{18}F-FDG PET/CT in pre-surgical risk stratification of patients with breast cancer. *Hell J Nucl Med* 2019; 22(3): 165-71.
21. Groheux D, Cochet A, Humbert O et al. ^{18}F-FDG PET/CT for staging and restaging of breast cancer. *J Nucl Med* 2016;57(Suppl 1): 17S-26S.
22. Gaeta C, Vercher-Conejero J, Sher A et al. Recurrent and metastatic breast cancer PET, PET/CT, PET/MRI: FDG and new biomarkers. *Q J Nucl Med Mol Imaging* 2013; 57(4): 352-66.
23. Bernsdorf M, Graff J. Clinical application of ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography in breast cancer. *Clin Physiol Funct Imaging* 2014; 34(6): 426-33.
24. Cardoso F, Kyriakides S, Ohno S et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019; 30(8): 1194-220.
25. Hubner KF, Smith GT, Thie JA et al. The potential of F-18-FDG PET in breast cancer: detection of primary lesions, axillary lymph node metastases, or distant metastases. *Clin Positron Imaging* 2000; 3(5): 197-205.
26. Meng Y, Ward S, Cooper K et al. Cost-effectiveness of MRI and PET imaging for the evaluation of axillary lymph node metastases in early stage breast cancer. *Eur J Surg Oncol* 2011; 37(1): 40-6.
27. Redaniel M, Martin R, Cawthorn S et al. The association of waiting times from diagnosis to surgery with survival in women with localised breast cancer in England. *Br J Cancer* 2013; 109(1): 42-9.
28. Zhang M, Sun S, Mesurolle B. The impact of pre-operative breast mri on surgical waiting time. *PLoS One* 2017; 12(1): e0169756.
29. Ong E. Preoperative imaging for breast conservation surgery-do we need more than conventional imaging for local disease assessment? *Gland Surg* 2018; 7(6): 554.
30. Robertson IJ, Hand F, Kell MR. ^{18}F-FDG PET/CT in the staging of local/regional metastases in breast cancer. *The Breast* 2011; 20(6): 491-4.
31. Pellet AC, Erten MZ, James TA. Value analysis of postoperative staging imaging for asymptomatic, early-stage breast cancer: implications of clinical variation on utility and cost. *Am J Surg* 2016; 211(6): 1084-8.
32. Lind P, Igerc I, Beyer T et al. Advantages and limitations of FDG PET in the follow-up of breast cancer. *Eur J Nucl Med Mol Imaging* 2004; 31(1): S125-S34.
33. Jung NY, Yoo IR, Kang BJ et al. Clinical significance of ^{18}F-FDG-PET/CT at the postoperative surveillance in the breast cancer patients. *Breast Cancer* 2016; 23(1): 141-8.
34. Wapnir IL, Kurian AW, Lichtensztajn DY et al. Rising Bilateral Mastectomy Rates Among Neoadjuvant Chemotherapy Recipients in California, 1998–2012. *Ann Surg* 2017; 266(2): 353.
35. Nirhale DS, Sooraj R, Rawat A. Role of neoadjuvant chemotherapy in downstaging locally advanced breast carcinoma, selection of surgical procedure and its outcome. *Intern Surg J* 2020; 7(2): 526-34.
36. Benderra M, Richard S, Antoine M et al. Breast cancer prognosis after neoadjuvant chemotherapy for breast cancers: molecular downstaging, proliferation, and endocrine sensitivity importance. *Ann Oncol* 2016; 27(suppl_6): 43-67.