ARCHIVES OF HELLENIC MEDICINE: ISSN 11-05-3992

ORIGINAL PAPER
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

Factors affecting the accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci in breast cancer

ARCHIVES OF HELLENIC MEDICINE 2021, 38(2):207–214
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2021, 38(2):207–214

A. Simsek,[1]
K. Kutluturk,[1]
A. Comak,[2]
A. Akatli,[3]
E. Kekilli,[2]
B. Unal[1]

[1]Department of General Surgery, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya
[2]Department of Nuclear Medicine, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya
[3]Department of Pathology, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya, Turkey

OBJECTIVE **To evaluate the effectiveness of ^{18}F-FDG PET/CT for detecting additional tumor foci in breast cancer.** MATERIAL-METHOD **The data were reviewed retrospectively of 232 women who underwent ^{18}F-FDG PET/CT examination prior to breast cancer surgery between January 2013 and December 2018.** RESULTS **Additional tumor foci were suspected in 95 cases on ^{18}F-FDG PET/CT, which were confirmed by histopathological analysis in 81 cases. The sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of ^{18}F-FDG PET/CT in detection of additional tumor foci were 77.7%, 79.48%, 66.3%, 87.32%, and 79.23%, respectively. The false negative and false positive rates were 22.22% and 20.51%, respectively. In univariate analysis, only the patient's age was positively associated with accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci. The accuracy was lower in women aged ≤50 years, with a substantial increase in false positive findings in women in that age group.** CONCLUSIONS **^{18}F-FDG PET/CT alone cannot replace conventional diagnostic procedures for evaluating additional tumor foci in breast cancer, as a substantial increase in false positive findings is recorded with this method in women aged ≤50 years old.**

Παράγοντες που επηρεάζουν την ακρίβεια του ^{18}F-FDG PET/CT στην ανίχνευση επιπρόσθετων εστιών του όγκου στον καρκίνο του μαστού

Περίληψη στο τέλος του άρθρου

Key words

Breast cancer
Multicentricity
Multifocality
PET/CT
Tumor foci

Submitted 3.7.2020
Accepted 15.8.2020

Surgical treatment of breast cancer (BC) has evolved from radical mastectomy (RM) to breast conservation surgery (BCS), which has become the standard treatment for early stage BC.[1] Along with other factors (contraindications to radiotherapy, connective tissue disease, genetic mutation, large tumor size, etc.) the number and localization of tumor foci determine surgical strategy. Multicentricity (MC) has been accepted as a contraindication for BCS. Although multifocality (MF) is not a contraindication for BCS, it must be investigated thoroughly for suitability, because relevant studies have produced conflicting results.[2]

The implication of additional tumor foci for decision making in regard to BCS is of increasing importance. Researchers have been interested in comparing different imaging methods for detecting tumor extension and additional tumor foci in BC. Magnetic resonance imaging (MRI) was the most popular modality in this setting. One consequence of the advent of the MRI was an increase in the rate of mastectomy, partly related to increased suspicion of additional tumor foci on MRI. Although its detection rate was more extensive than that of conventional imaging, the surgical outcome was no superior in terms of reduction in reoperation rate, despite a significant increase in initial mastectomy.[3–5]

Consequently, new techniques including positron emission tomography (PET), positron emission tomography/

computerized tomography (PET/CT), PET/MRI, and breast specific positron emission mammography (PEM), have been investigated to further extend the imaging accuracy and optimize surgical strategy in BC. PET offers the advantage of identifying early metabolic changes in malignant tissue, but its low sensitivity and low positive predictive value (PPV) in detecting early-stage BC do not support its use as a primary screening method. In addition to the functional activity of PET, PET/CT has the advantage of detecting anatomical findings, thus providing more accurate results when compared to PET or CT alone.[6] It was postulated that if ^{18}F-FDG PET/CT could accurately detect the additional tumor foci, it would substantially alter the surgical planning, and could be a valuable alternative to conventional imaging modalities.

The present retrospective study was conducted to evaluate the accuracy of ^{18}F-FDG PET/CT for detecting additional tumor foci in BC.

MATERIAL AND METHOD

Patient selection

The data were reviewed retrospectively on 232 women with 236 index BC who underwent ^{18}F-FDG PET/CT examination prior to breast surgery (only total mastectomy, not BCS) between January 2013 and December 2018. Women with a history of excisional biopsy, neoadjuvant chemotherapy, recurrent BC and non-invasive types of BC were excluded. The histopathological examination of the mastectomy specimen was used as a reference to evaluate the ability of the ^{18}F-FDG PET/CT to detect additional tumor foci. Ethical committee approval was obtained from the institution where study was conducted. It was conducted according to the principles set forth by the Helsinki Declaration of 1975.

Diagnostic imagination

Mammography and or ultrasonography were used for routine imaging. The hospital where the study was conducted serves as a reference center for many urban and rural areas. A substantial number of patients living in the rural area do not grasp the importance of comprehensive imaging, and many do not have sufficient income to attend hospital follow-up appointments. Some of these patients ignore their breast cancer, since it takes a long time to schedule preoperative imaging, including chest X-ray, liver ultrasound and bone scan. For this reason, along with mammography and breast ultrasonography ^{18}F-FDG PET/CT was applied more liberally, because it took shorter time to perform, and was covered by medical insurance.

^{18}F-FDG PET/CT technique

Informed consent was obtained from all the women prior to application of ^{18}F-FDG PET/CT. The women fasted for at least 6 hours before F-18 FDG injection. Approximately 60 minutes after the injection of 0.1 mg/kg F-18 FDG intravenously, anatomical imaging with CT (140 kev, 80 mA, Siemens), and then PET (Siemens Biograph mCTS (20)-3R; Knoxville, TN, USA) was performed from vertex to the mid-thigh by PET/CT. Data were reconstructed by ordered-subset expectation maximization (OSEM). Images on coronal, sagittal, and transverse axes were evaluated using the software program Syngo.via/VB10B software version, Siemens Medical Solutions Inc. The CT data were acquired without contrast enhancement. Breast lesion and axillary lymph nodes were evaluated visually first in PET and CT images. The maximum standardized uptake values (SUVmax) of hypermetabolic breast lesion and SUVmax of hypermetabolic axillary lymph nodes were automatically calculated via previously mentioned software (Syngo.via/VB10B software version, Siemens Medical Solutions Inc).

Surgical planning

Total mastectomy was performed in cases with locally advanced disease, multicentric tumor foci, diffuse microcalcifications, and small breast volume, unsatisfactory from the cosmetic standpoint. It was also preferred in women unwilling to be treated with BCS.

Sentinel lymph node biopsy (SLNB) was performed intraoperatively for patients with clinically and or radiologically node-negative, early stage BC. Axillary dissection (AD) was performed in all patients with positive SLN.

Histopathological examination

MF was defined as two or more individual invasive tumors in the same quadrant of the same breast. MC was defined as two or more separate invasive tumors occupying more than one quadrant of the same breast. The diameter of the largest invasive tumor was used for T staging.

The histological type of the tumor was classified into three types; invasive carcinoma of no special type (invasive ductal carcinoma), invasive lobular carcinoma, and others. The histological grade was determined according to the modified Bloom-Richardson method. The limit value for the presence of hormone receptor was determined as 1%. Her2/neu amplification was considered positive if the Her2 receptor was stained 3+ and or if the Her2 receptor was stained 2+ along with Her2/neu amplification determined by fluorescence *in situ* hybridization (FISH).

Statistical analysis

Statistical Package for Social Sciences (SPSS), version 17.0 was used for statistical analysis of the data. The clinicopathological characteristics of the tumors were analyzed by Chi-square independence test and descriptive analysis. Data are expressed as n (%) and mean with standard deviation (SD). The Shapiro-Wilk test was used to analyze normality of the groups. Univariate analysis

(Chi-squared test for categorical variables and Mann-Whitney U test for continuous variables without normal distribution) was performed to identify factors associated with accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci. Univariate analysis was also used to identify factors associated with false positivity and false negativity of ^{18}F-FDG PET/CT in detecting additional tumor foci. Significant variables were included in multivariate binary logistic regression analysis. The p-value of 0.05 was accepted as the cut-off for significance.

RESULTS

This study involved 232 women (mean age 52.09±13.31 years, range 25–93 years) with 236 index breast tumors (mean size 2.63±2.006 cm, range 0.5–23.3 cm). Four women had bilateral BC. Axillary dissection was performed in 81.7% of the cases. The mean SUVmax value of 236 index tumors was 11.73±8.97 (range 2.1–81.2), and mean SUVmax value of additional tumor focus was 7.85±7.73 (range 2.2–42) (tab. 1). The molecular subtypes of the index tumors were Luminal A (66.5%), Luminal B (17.8%), Triple negative (7.6%) and HER2 positive (8.1%), for which the mean SUVmax values were 10.41, 12.56, 19.58, and 13.32, respectively.

Additional tumor foci were suspected in 40.2% of the cases on ^{18}F-FDG PET/CT scan, which was confirmed by histopathological analysis in 34.3% of the cases. The sensitivity, specificity, PPV, negative predictive value (NPV), and overall accuracy (OAA) of ^{18}F-FDG PET/CT in detection of additional tumor foci were 77.7%, 79.48%, 66.3%, 87.32%, and 79.23%, respectively. The false negative (FN) and false positive (FP) rates were 22.22% and 20.51%, respectively.

Table 1. Study of ^{18}F-FDG PET/CT in the diagnosis of additional tumor foci in women with breast cancer. Characteristics of the patients (n=232) and tumors (n=236).

Characteristics	Mean ± SD	Min-Max	Median
Age *(years)*	52.09±13.31	25.0–93.0	49.0
Index tumor size on PET/CT *(cm)*	2.63±2.006	0.5–23.3	2.3
Index tumor size on pathology *(cm)*	3.79±2.66	0.1–23.5	3.1
Index tumor SUVmax	11.73±8.97	2.1–81.2	9.75
Additional tumor size on PET/CT *(cm)*	1.66±1.001	0.5–6.7	1.4
Additional tumor size on patholgy *(cm)*	1.208±1.020	0.1–5.5	1.0
Additional tumor focus SUVmax	7.85±7.73	2.2–42.0	5.5

PET/CT: Positron emission tomography/computerized tomography, SUVmax: Maximum standardized uptake value, SD: Standard Deviation

In univariate analysis, none of the following variables was associated with accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci: Index tumor T stage, index tumor histological subtype, index tumor histological grade, index tumor hormone receptor status, index tumor HER2/neu amplification, index tumor molecular subtype, index tumor SUVmax (p=0.289), additional tumor foci histological subtype, additional tumor foci T stage, additional tumor foci SUVmax (p=0.673), ALN metastasis, lymphovascular invasion, presence of ductal/lobular carcinoma *in situ* component. Only the patient's age was positively associated with accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci (tab. 2). The accuracy was lower in women aged ≤50 years, and there was a substantial increase in false positive findings in women in that age group (tab. 3).

^{18}F-FDG PET/CT false positive cases

Additional tumor foci were suspected in 32 women on PET/CT, but not confirmed on histology. Overestimation of additional tumor foci was found to be secondary to enhancement of glandular fibrocystic changes, fibroadenomas, papillomas, radial scars, reactive lymph nodes, etc.

^{18}F-FDG PET/CT false negatives cases

In 18 women, unifocal disease was identified on PET/CT, but MF/MC disease was found on histology. Among those with false negative results, the second largest tumor foci ranged in size from 0.1 to 2.5 cm. In univariate analysis (when the histological type of the tumor was classified into two types; invasive lobular carcinoma [ILC] and others), ILC subtypes of both index tumor and additional tumor foci were associated with false negativity of ^{18}F-FDG PET/CT in detecting additional tumor foci (tab. 3). Multivariate analysis revealed histology of the additional tumor foci was the only factor affecting the false negative results (ILC; OR [odds ratio]: 3.6, 95% CI [confidence interval]: 0.96–13.8). Almost half of the ILC could not be detected on ^{18}F-FDG PET/CT.

DISCUSSION

According to the current guidelines, ^{18}F-FDG PET/CT is not a routine imaging modality in early stage (I–II), or even in operable stage III, breast cancer, but it is regarded optional for locally advanced (increased possibility of distant metastasis) and metastatic cases.[7–11] Although it has additional value in loco-regional and distant staging, its sensitivity in detection of primary lesions, especially small ones (T_1), appears to be suboptimal. The reasons

Table 2. Univariate analysis results for the variables assumed to be associated with accuracy of ^{18}F-FDG PET/CT in the diagnosis of additional tumor foci in women with breast cancer (n=232), and tumors (n=236).

Characteristics		^{18}F-FDG PET/CT (incorrect diagnosis) n (%)	^{18}F-FDG PET/CT (correct diagnosis) n (%)	p
Age (years)	≤50	35 (27.6)	92 (72.4)	*0.01*
	>50	15 (13.8)	94 (86.2)	
Index tumor T stage	T_1	9 (17.6)	42 (82.4)	
	T_2	32 (21.8)	115 (78.2)	0.758
	T_3	9 (23.7)	29 (76.3)	
Index tumor histology	IDC	34 (20.9)	129 (79.1)	
	ILC	5 (23.8)	16 (76.2)	0.953
	Others	11 (21.2)	41 (78.8)	
Index tumor histology	ILC	5 (23.8)	16 (76.2)	0.758
	Others	45 (20.9)	170 (79.1)	
Additional tumor foci histology	IDC	10 (20.8)	38 (79.2)	
	ILC	4 (36.4)	7 (63.6)	0.464
	Others	4 (18.2)	18 (81.8)	
Additional tumor foci histology	ILC	4 (36.4)	7 (63.6)	0.225
	Others	14 (20)	56 (80)	
Additional tumor foci T stage	T_1	17 (24.6)	52 (75.4)	0.210
	T_2	1 (8.3)	11 (91.7)	
Index tumor grade	1	5 (13.9)	31 (86.1)	
	2	29 (25)	87 (75)	0.323
	3	14 (19.4)	58 (80.6)	
Index tumor ER	Negative	7 (17.5)	33 (82.5)	0.531
	Positive	43 (21.9)	153 (78.1)	
Index tumor PR	Negative	13 (18.8)	56 (81.2)	0.571
	Positive	37 (22.2)	130 (77.8)	
Index tumor Cerb2	Negative	37 (21.1)	138 (78.9)	0.978
	Positive	13 (21.3)	48 (78.7)	
Index tumor molecular subtype	Luminal A	33 (21)	124 (79)	
	Luminal B	11 (26.2)	31 (73.8)	0.586
	Triple negative	4 (22.2)	14 (77.8)	
	Her2 positive	2 (10.5)	17 (89.5)	
LVI	No	7 (20)	28 (80)	0.852
	Yes	43 (21.4)	158 (78.6)	
DCIS and or LCIS	No	22 (26.2)	62 (73.8)	0.162
	Yes	28 (18.4)	124 (81.6)	
Axillary metastasis	No	11 (18.6)	48 (81.4)	0.581
	Yes	39 (22)	138 (78)	

IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, ER: Estrogen receptor, PR: Progesterone receptor, Cerb2: Human epidermal growth factor receptor 2, LVI: Lenfovascular invasion, DCIS: Ductal carcinoma *in situ*, LCIS: Lobular carcinoma *in situ*

Table 3. Univariate analysis of variables associated with false positivity and false negativity of ^{18}F-FDG PET/CT in the diagnosis of additional tumor foci in women with breast cancer (n=232), and tumors (n=236).

Characteristics		^{18}F-FDG PET/CT false positivity			^{18}F-FDG PET/CT false negativity		
		(–)	(+)	(p)	(–)	(+)	(p)
Age (years)	≤50	103 (81.1)	24 (18.9)	*0.01*	115 (90.6)	12 (9.4)	0.255
	>50	101 (92.7)	8 (7.3)		103 (94.5)	6 (5.5)	
Index tumor T stage	T_1	47 (92.2)	4 (7.8)	0.373	46 (90.2)	5 (9.8)	0.530
	T_2	124 (84.4)	23 (15.6)		138 (93.9)	9 (6.1)	
	T_3	33 (86.8)	5 (13.2)		34 (89.5)	4 (10.5)	
Index tumor histology	IDC	144 (88.3)	19 (11.7)	0.435	152 (93.3)	11 (6.7)	0.115
	ILC	17 (81.0)	4 (19.0)		17 (81.0)	4 (19.0)	
	Others	43 (82.7)	9 (17.3)		49 (94.2)	3 (5.8)	
Index tumor histology	ILC	17 (81.0)	4 (19.0)	0.441	17 (81.0)	4 (19.0)	*0.039*
	Others	187 (87.0)	28 (13.0)		201 (93.5)	14 (6.5)	
Additional tumor histology	IDC	41 (85.4)	7 (14.6)	0.939	38 (79.2)	10 (20.8)	0.109
	ILC	9 (86.4)	2 (18.2)		6 (54.5)	5 (45.5)	
	Others	19 (86.4)	3 (13.6)		19 (86.4)	3 (13.6)	
Additional tumor histology	ILC	9 (81.8)	2 (18.2)	0.735	6 (54.5)	5 (45.5)	*0.046*
	Others	60 (85.7)	10 (14.3)		57 (81.4)	13 (18.6)	
Index tumor grade	1	32 (88.9)	4 (11.1)	0.738	31 (86.1)	5 (13.9)	0.204
	2	98 (84.5)	18 (15.5)		106 (91.4)	10 (8.6)	
	3	63 (87.5)	9 (12.5)		69 (95.8)	3 (4.2)	
Index tumor ER	Negative	35 (87.5)	5 (12.5)	0.830	36 (90.0)	4 (10.0)	0.535
	Positive	169 (86.2)	27 (13.8)		182 (92.9)	14 (7.1)	
Index tumor PR	Negative	61 (88.4)	8 (11.6)	0.571	65 (94.2)	4 (5.8)	0.496
	Positive	143 (85.6)	24 (14.4)		153 (91.6)	14 (8.4)	
Index tumor Cerb2	Negative	151 (86.3)	24 (13.7)	0.906	161 (92.0)	14 (8.0)	0.715
	Positive	53 (86.9)	8 (13.1)		57 (93.4)	4 (6.6)	
Molecular subtype	Luminal A	136 (86.6)	21 (13.4)	0.656	144 (91.7)	12 (8.3)	0.946
	Luminal B	35 (83.3)	7 (16.7)		39 (92.9)	3 (7.1)	
	Triple negative	15 (83.3)	3 (16.7)		17 (94.4)	1 (5.6)	
	Her2 positive	18 (94.7)	1 (5.3)		18 (94.7)	1 (5.3)	
LVI	No	30 (85.7)	5 (14.3)	0.892	32 (91.4)	3 (8.6)	0.820
	Yes	174 (86.6)	27 (13.4)		186 (92.5)	15 (7.5)	
DCIS	No	70 (83.3)	14 (16.7)	0.300	79 (94.0)	5 (6.0)	0.471
	Yes	134 (88.2)	18 (11.8)		139 (91.4)	13 (8.6)	
Axillary metastasis	No	53 (89.8)	6 (10.2)	0.380	56 (94.9)	3 (5.1)	0.396
	Yes	151 (85.3)	26 (14.7)		162 (91.5)	15 (8.5)	

IDC: Invasive ductal carcinoma, ILC: Invasive lobular carcinoma, ER: Estrogen receptor, PR: Progesterone receptor, Cerb2: Human Epidermal Growth Factor Receptor 2, LVI: Lenfovascular invasion, DCIS: Ductal carcinoma *in situ*, LCIS: Lobular carcinoma *in situ*

for this reduced sensitivity may be the limited resolution of whole-body scanners, suboptimal patient positioning, and decreased FDG uptake found in different types and grades of BC.[12–16]

In this study of 236 index cases with newly diagnosed BC, sensitivity and specificity of ^{18}F-FDG PET/CT for detecting additional tumor foci were suboptimal. It had a sensitivity of 77.7%, a specificity of 79.48%, and an accuracy of 79.23% for detecting additional tumor foci. It may be speculated that, if surgical planning was based solely on ^{18}F-FDG PET/CT, our results might lead to 32 patients with false positive findings who might undergo mastectomy unnecessarily. Likewise, 18 patients might have local recurrence if BCS was preferred to mastectomy, based on the ^{18}F-FDG PET/CT results. The suboptimal specificity and PPV (66.3%) rule out immediate mastectomy instead of further evaluation with other imaging techniques and or tissue biopsy in cases of additional tumor foci according to the ^{18}F-FDG PET/CT results. The low sensitivity (77.7%) and low NPV (87.32%) necessitate further evaluation in the absence of additional tumor foci on ^{18}F-FDG PET/CT.

Tumors with unfavorable prognostic characteristics (larger tumors, higher stage, higher grade, metastatic nodes, triple negative subtype) show a higher degree of FDG uptake.[12,17–19] One study reported that ^{18}F-FDG PET/CT detected all primary lesions with tumor size >2 cm, but its sensitivity was reduced to 81% in cases with T_1 lesion, and 70.8% in cases with tumor size <1 cm, while its overall sensitivity was 89.6%.[16] Another study reported that ^{18}F-FDG PET/CT had a primary lesion detection sensitivity of 93%, and sensitivity that varied according to tumor size: 42.8% in $T_{1a–b}$, 93.9% in T_{1c}, and 98% in T_2 tumors.[19] Similarly to previous studies concerning detection of primary tumor on PET/CT, the present study showed that the sensitivity of ^{18}F-FDG PET/CT in the detection of additional tumor foci varied according to the size of the different foci. It detected 91.7% of additional foci with size >2 cm. In 69 patients with a T_1 lesion, ^{18}F-FDG PET/CT detected only 52 (75.4%) (not statistically significant).

It is known that the considerably higher FDG uptake of invasive ductal carcinoma (IDC) compared to ILC makes its detectability easy.[20] In one earlier report it was stated that 95% of the IDC, but only one third of ILC were detected on PET/CT.[21] In the current study, correct diagnosis of additional tumor foci was higher in IDC (79.2%) than in ILC (63.6%). In univariate analysis, ILC subtypes of both index tumor and additional tumor foci were associated with false negativity of ^{18}F-FDG PET/CT in detecting additional tumor foci. In multivariate analysis, histology of the additional tumor foci was the only factor affecting false negative results. Almost half of the ILC could not be detected on ^{18}F-FDG PET/CT.

None of the unfavorable prognostic characteristics (larger tumors, higher stage, higher grade, metastatic node, triple negative subtype) was associated with accuracy of ^{18}F-FDG PET/CT in detecting additional tumor foci, but only the patient's age. The accuracy was lower in women aged ≤50 years, in who there was a substantial increase in false positive findings. Overestimation of additional tumor foci was found to be secondary to enhancement of glandular fibrocystic changes, fibroadenomas, papillomas, radial scars, reactive lymph nodes etc. ^{18}F-FDG PET offers the advantage of identifying early metabolic changes in malignant tissue compared to normal tissue. The degree of ^{18}F-FDG uptake in the glandular tissues of the normal breast may affect the identification of BC. As the majority of researchers have focused solely on imaging of malignant tissue, few studies have investigated the factors affecting ^{18}F-FDG PET uptake in normal breast tissue. Some authors stated that ^{18}F-FDG uptake was higher in dense breast than fatty breast, and in the premenopausal state than in the menopausal state.[22] Some authors reported no effect of age and menopausal status on ^{18}F-FDG uptake,[23] and others demonstrated that age and breast density were independent factors affecting ^{18}F-FDG uptake in normal breast tissue.[24] Due to the retrospective nature of the current study, data including hormonal status and breast density could not be evaluated, but based on previous research, it can be concluded that the increased false positive results in women aged ≤50 years may be associated with increased ^{18}F-FDG uptake in younger patients.

A few other studies have investigated the role of ^{18}F-FDG PET/CT in detecting additional tumor foci. Relatively, ^{18}F-FDG PET/CT showed high specificity in those studies ranging from 91.7% to 99.1%, with a wide range of sensitivity, from 12% to 100%.[16,19,25,26] In the current study, the specificity of ^{18}F-FDG PET/CT in detecting multiple lesions (79.48%) was lower than that previously reported. Its sensitivity (77.7%) was lower than in some studies, while higher than in others. The differences in study design might be responsible for the disparate results. We thought that the differing volume of histological specimens, which was more qualified in the current study due to inclusion of the total mastectomy specimen, leads to a comprehensive analysis. Exclusion of patients treated by neoadjuvant chemotherapy, in which regressed tumor foci after neoadjuvant chemotherapy were eliminated, made the current study superior. Exclusion of patients with non-invasive tumor has also made the study more specific.

One of the limitations of the present study was its ret-

rospective design, due to which data on hormonal status and breast density could not be evaluated. The ^{18}F-FDG PET/CT technique was not specific for breast examination, it did not have standardization of interpretation, and was not feasible in women with diabetes mellitus (DM). We could not compare the effect of ^{18}F-FDG PET/CT with other imaging methods.

Although ^{18}F-FDG PET/CT has certain advantages in detecting local and distant metastasis, it alone cannot replace conventional diagnostic procedures for evaluating additional tumor foci in BC. The decreased FDG uptake found in ILC reduced its sensitivity, and its accuracy was lower in women aged ≤50 years, in whom a substantial increase in false positive findings was observed.

ΠΕΡΙΛΗΨΗ

Παράγοντες που επηρεάζουν την ακρίβεια του ^{18}F-FDG PET/CT στην ανίχνευση επιπρόσθετων εστιών του όγκου στον καρκίνο του μαστού

A. SIMSEK,[1] K. KUTLUTURK,[1] A. COMAK,[2] A. AKATLI,[3] E. KEKILLI,[2] B. UNAL[1]

[1]Department of General Surgery, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya,

[2]Department of Nuclear Medicine, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya,

[3]Department of Pathology, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya, Τουρκία

Αρχεία Ελληνικής Ιατρικής 2021, 38(2):207–214

ΣΚΟΠΟΣ Αξιολόγηση της αποτελεσματικότητας του ^{18}F-FDG PE/CT ως προς την ανίχνευση επιπρόσθετων εστιών του όγκου στον καρκίνο του μαστού. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Εξετάστηκαν αναδρομικά τα δεδομένα γυναικών που υποβλήθηκαν σε εξέταση ^{18}F-FDG PET/CT πριν από τη χειρουργική επέμβαση για καρκίνο του μαστού μεταξύ Ιανουαρίου 2013 και Δεκεμβρίου 2018. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Ανιχνεύτηκαν επί πλέον εστίες του όγκου σε 95 περιπτώσεις με το ^{18}F-FDG PET/CT. Η διάγνωση επιβεβαιώθηκε με ιστοπαθολογική εξέταση σε 81 περιπτώσεις. Η ευαισθησία, η ειδικότητα, οι θετικές προγνωστικές τιμές, η αρνητική προγνωστική τιμή και η συνολική ακρίβεια των ^{18}F-FDG PET/CT για την ανίχνευση επιπρόσθετων εστιών του όγκου ήταν 77,7%, 79,48%, 66,3%, 87,32% και 79,23%, αντίστοιχα. Τα ψευδώς αρνητικά και τα ψευδώς θετικά ποσοστά ήταν 22,22% και 20,51%, αντίστοιχα. Μόνο η ηλικία της ασθενούς συσχετίστηκε θετικά με την ακρίβεια του ^{18}F-FDG PET/CT για την ανίχνευση επιπρόσθετων εστιών του όγκου. Η ακρίβεια ήταν χαμηλότερη στις γυναίκες ηλικίας ≤50 ετών, ενώ βρέθηκε σημαντική αύξηση ψευδώς θετικών ευρημάτων στις εν λόγω γυναίκες. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Το ^{18}F-FDG PET/CT δεν μπορεί να αντικαταστήσει τη συμβατική διαγνωστική διαδικασία για την αξιολόγηση πρόσθετων εστιών του όγκου στον καρκίνο του μαστού. Υπάρχει σημαντική αύξηση των ψευδώς θετικών ευρημάτων του ^{18}F-FDG PET/CT σε γυναίκες ηλικίας ≤50 ετών σχετικά με την αξιολόγηση πρόσθετων εστιών του όγκου στον καρκίνο του μαστού.

Λέξεις ευρετηρίου: Εστίες όγκου, Καρκίνος του μαστού, PET/CT, Πολυεστίαση, Πολυκεντρικότητα

References

1. MECHERA R, VIEHL CT, OERTLI D. Factors predicting in-breast tumor recurrence after breast-conserving surgery. *Breast Cancer Res Treat* 2009, 116:171–177
2. HARRIS JR, LIPPMAN ME, MORROW M, OSBORNE CK (eds). *Diseases of the breast.* Lippincott Williams & Wilkins, Philadelphia, PA, 2004
3. TURNBULL L, BROWN S, HARVEY I, OLIVIER C, DREW P, NAPP V ET AL. Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial. *Lancet* 2010, 375:563–571
4. PETERS NHGM, VAN ESSER S, VAN DEN BOSCH MAAJ, STORM RK, PLAISIER PW, VAN DALEN T ET AL. Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET-randomised controlled trial. *Eur J Cancer* 2011, 47:879–886
5. HOUSSAMI N, TURNER R, MORROW M. Preoperative magnetic resonance imaging in breast cancer: Meta-analysis of surgical outcomes. *Ann Surg* 2013, 257:249–255
6. YANG SK, CHO N, MOON WK. The role of PET/CT for evaluating breast cancer. *Korean J Radiol* 2007, 8:429–437
7. GAVILÁ J, LOPEZ-TARRUELLA S, SAURA C, MUÑOZ M, OLIVEIRA M, DE LA CRUZ-MERINO L ET AL. SEOM clinical guidelines in metastatic breast cancer 2015. *Clin Transl Oncol* 2015, 17:946–955
8. GARCIA-SÁENZ JA, BERMEJO B, ESTÉVEZ LG, PALOMO AG, GONZALEZ-FARRE X, MARGELI M ET AL. SEOM clinical guidelines in early-stage breast cancer 2015. *Clin Transl Oncol* 2015, 17:939–945
9. SENKUS E, KYRIAKIDES S, OHNO S, PENAULT-LLORCA F, POORTMANS P, RUTGERS E ET AL. Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann On-*

col 2015, 26(Suppl 5):v8–v30
10. CARDOSO F, COSTA A, NORTON L, SENKUS E, AAPRO M, ANDRÉ F ET AL. ESO-ESMO 2nd International Consensus guidelines for advanced breast cancer (ABC2). *Ann Oncol* 2014, 25:1871–1888
11. NATIONAL COMPREHENSIVE CANCER NETWORK. NCCN clinical practice guidelines in oncology (NCCN guidelines). Breast cancer – version 1, 2016, www.NCCN.org. Available at: https://www.nice.org.uk/guidance/cg81/evidence/surveillance-review-decision-matrix-november-2015-pdf-2178658910
12. KOOLEN BB, VAN DER LEIJ F, VOGEL WV, RUTGERS EJT, VRANCKEN PEETERS MJTFD, ELKHUIZEN PHM ET AL. Accuracy of ^{18}F-FDG PET/CT for primary tumor visualization and staging in T_1 breast cancer. *Acta Oncol* 2014, 53:50–57
13. JEONG YJ, KANG DY, YOON HJ, SON HJ. Additional value of F-18 FDG PET/CT for initial staging in breast cancer with clinically negative axillary nodes. *Breast Cancer Res Treat* 2014, 145:137–142
14. FUSTER D, DUCH J, PAREDES P, VELASCO M, MUÑOZ M, SANTAMARÍA G ET AL. Preoperative staging of large primary breast cancer with [18F] fluorodeoxyglucose positron emission tomography/computed tomography compared with conventional imaging procedures. *J Clin* 2008, 26:4746–4751
15. KOOLEN BB, VALDÉS OLMOS RA, ELKHUIZEN PHM, VOGEL WV, VRANCKEN PEETERS MJTFD, RODENHUIS S ET AL. Locoregional lymph node involvement on ^{18}F-FDG PET/CT in breast cancer patients scheduled for neoadjuvant chemotherapy. *Breast Cancer Res Treat* 2012, 135:231–240
16. CHOI YJ, SHIN YD, KANG YH, LEE MS, LEE MK, CHO BS ET AL. The effects of preoperative $^{(18)}$F-FDG PET/CT in breast cancer patients in comparison to the conventional imaging study. *J Breast Cancer* 2012, 15:441–448
17. GROHEUX D, GIACCHETTI S, MORETTI JL, PORCHER R, ESPIÉ M, LEHMANN-CHE J ET AL. Correlation of high ^{18}F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. *Eur J Nucl Med Mol Imaging* 2011, 38:426–435
18. GIL-RENDO A, MARTÍNEZ-REGUEIRA F, ZORNOZA G, GARCÍA-VELLOSO MJ, BEORLEGUI C, RODRIGUEZ-SPITERI N. Association between [18F] fluorodeoxyglucose uptake and prognostic parameters in breast cancer. *Br J Surg* 2009, 96:166–170
19. GARAMI Z, HASCSI Z, VARGA J, DINYA T, TANYI M, GARAI I ET AL. The value of 18-FDG PET/CT in early-stage breast cancer compared to traditional diagnostic modalities with an emphasis on changes in disease stage designation and treatment plan. *Eur J Surg Oncol* 2012, 38:31–37
20. KOOLEN BB, VRANCKEN PEETERS MJTFD, WESSELING J, LIPS EH, VOGEL WV, AUKEMA TS ET AL. Association of primary tumour FDG uptake with clinical, histopathological and molecular characteristics in breast cancer patients scheduled for neoadjuvant chemotherapy. *Eur J Nucl Med Mol Imaging* 2012, 39:1830–1838
21. GROVES AM, SHASTRY M, BEN-HAIM S, KAYANI I, MALHOTRA A, DAVIDSON T ET AL. Defining the role of PET-CT in staging early breast cancer. *Oncologist* 2012, 17:613–619
22. VRANJESEVIC D, SCHIEPERS C, SILVERMAN DH, QUON A, VILLALPANDO J, DAHLBOM M ET AL. Relationship between ^{18}F-FDG uptake and breast density in women with normal breast tissue. *J Nucl Med* 2003, 44:1238–1242
23. KUMAR R, CHAUHAN A, ZHUANG H, CHANDRA P, SCHNALL M, ALAVI A. Standardized uptake values of normal breast tissue with 2-deoxy-2-[F-18]fluoro-D:-glucose positron emission tomography: Variations with age, breast density, and menopausal status. *Mol Imaging Biol* 2006, 8:355–362
24. MAVI A, CERMIK TF, URHAN M, PUSKULCU H, BASU S, CUCCHIARA AJ ET AL. The effect of age, menopausal state, and breast density on $^{(18)}$F-FDG uptake in normal glandular breast tissue. *J Nucl Med* 2010, 51:347–352
25. JUNG NY, KIM SH, KIM SH, SEO YY, OH JK, CHOI HS ET AL. Effectiveness of breast MRI and $^{(18)}$F-FDG PET/CT for the preoperative staging of invasive lobular carcinoma versus ductal carcinoma. *J Breast Cancer* 2015, 18:63–72
26. KALINYAK JE, BERG WA, SCHILLING K, MADSEN KS, NARAYANAN D, TARTAR M. Breast cancer detection using high-resolution breast PET compared to whole-body PET or PET/CT. *Eur J Nucl Med Mol Imaging* 2014, 41:260–275

Corresponding author:

A. Simsek, Department of General Surgery, Turgut Ozal Medical Center, School of Medicine, Inonu University, Malatya, Turkey
e-mail: draksimsek@yahoo.com.tr