HEALTH SCIENCES QUARTERLY

Volume: 3
Issue: 4
2023

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2023-08-01
Accepted: 2023-08-25

ORIGINAL ARTICLE

The relationship between 18F-FDG PET/CT parameters and histopathological-immunohistochemical properties in breast cancer

Ali Ozan Öner[1] **Şenay Yıldırım**[2] **Evrim Sürer Budak**[3] **Arsenal Sezgin Alikanoğlu**[2]

[1] Department of Nuclear Medicine, Faculty of Medicine, Afyonkarahisar Health Sciences University. Afyonkarahisar / Türkiye
[2] Department of Pathology, Antalya Training and Research Hospital. Antalya / Türkiye
[3] Department of Nuclear Medicine, Antalya Training and Research Hospital. Antalya / Türkiye

Abstract

In this study, it is aimed to determine the correlation between histopathologic-immunohistochemical factors, tumor subtypes and fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) parameters such standardized uptake value (SUVmax), metabolic tumor volume (MTV), total lesion glycolysis (TLG) in breast cancer (BC). Initial PET/CT examination of 110 histopathologically proven BC patients (age ranging 27-92, mean age 56.18 ± 14.59) were included in this retrospective study. The relationship between histopathological-immunohistochemical factors, tumor subtypes and PET/CT parameters were analyzed by regression analysis. The mean SUV max value of 110 breast tumors was 7.73 ± 5.62 (range 1.4 - 34.15). Histological subtypes were; invasive ductal carcinoma (n:94, 85.5%), invasive lobular carcinoma (n=6, 5.5%) and other types (n=10, 9.1%). The distribution of BC subtypes was as follows; Luminal A (Lum A) (n=38; 34.5%), Luminal B (Lum B) (n=56; 50.9%), HER2-positive (n=3; 2.7%) and Triple Negative (TN) (n=13; 11.8%). Univariate regression analysis revealed significantly higher SUV max values in ductal carcinomas than lobular carcinomas (p=0.03). SUVmax values of the Lum B, HER2 positive and TN groups were higher than Lum A group (p=0.03, p<0.001, p<0.001 respectively). Univariate regression analyses also showed that the MTV and TLG values of TN group were significantly higher than Lum A group (p=0.011, p=0.007, respectively). In multivariate regression analyses, no significant difference was observed in above mentioned groups. MTV, TLG and SUVmax values significantly correlated with histopathological-immunohistochemical factors and tumor subtypes in BC. So that, these parameters can be used to predict the tumors' behavior.

Keywords: Breast cancer, 18F-FDG PET/CT, standardized uptake value (SUVmax), metabolic tumor volume (MTV), total lesion glycolysis (TLG)

Citation: Öner AO, Yıldırım Ş, Sürer Budak, E, Alikanlıoğlu AS. The relationship between 18F-FDG PET/CT parameters and histopathological-immunohistochemical properties in breast cancer. Health Sci Q. 2023;3(4):259-68. https://doi.org/10.26900/hsq.2122

Corresponding Author:
Ali Ozan Öner
Email:draliozanoner@hotmail.com

Introduction

Breast cancer (BC) is one of the most common cancers in women and its incidence has increased in recent years [1]. Despite it's increasing incidence, early diagnosis by using new imaging techniques and the effective treatment modalities have reduced mortality rates in BC. An accurate initial staging is very important in the management of an effective personalized treatment and to predict the prognosis. Some of the prognostic factors are histological type, tumor size, presence of vascular, lymphatic and perineural invasion, proliferation rate and receptor status [2]. The relation of the BC subtypes such Luminal A (Lum A), Luminal B (Lum B), HER2 positive and triple negative (TN) with the prognosis is also known [3,4].

In BC, the use of fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) for initial staging becomes increasingly crucial [5,6]. It provides essential contributions to the clinical practice in therapy planning, assessing therapy response and recurrence determination [5,7]. There are many studies in the literature focused on the relationship between SUVmax and histopathological-immunohistochemical factors in BC [8-12]. The relationship between histopathological-immunohistochemical factors and PET/CT parameters such as metabolic tumor volume (MTV) and total lesion glycolysis (TLG) are also recently mentioned in the literature [13].

In this study, we aimed to determine the relationship between the histopathologic-immunohistochemical factors, tumor subtypes (lum A, lum B, HER2 positive, TN) and 18F-FDG PET/CT parameters (SUVmax, MTV, TLG) in BC patients.

Materials and Methods

Patients: A total of 110 biopsy proven BC patients who had undergone PET/CT examination for initial staging in the Antalya Training and Research Hospital Nuclear Medicine Clinic were included in this retrospective study. Sixty-three patients were operated after initial staging. Patients with additional malignancy and received treatment before PET/CT examination were excluded.

PET/CT Imaging: After 4 hours fasting, a dose of 0,1 mCi/kg F18-FDG was injected intravenously to the patients with blood glucose levels less than 180 mg/dL. All patients underwent whole-body PET/CT imaging with a Philips Gemini TF 16 PET/CT scanner (3 mm CT slice thickness, 110 mAs, 120 kV, 3 min PET per bed) 60 minutes after injection. PET, CT, and fusion PET/CT images were examined visually and semiquantitative measurements (SUVmax, MTV and TLG) were all performed by the same nuclear medicine physician. The SUVmax value was calculated automatically by drawing the three-dimensional region of interest (ROI) on the hypermetabolic breast tumour. MTV was obtained from attenuation-corrected FDG PET/CT images by drawing the boundaries of the whole mass. MTV was defined as the sum of the metabolic volumes of the primary tumor. The threshold value for the SUVmax was assumed to be 40% of SUVmax, and the tumor's boundaries were automatically drawn (Extended Brilliance Workspace, Philips). TLG was also calculated using attenuation-corrected FDG PET/CT images by the same way. The 40% of the primary tumor's SUVmax was considered as a threshold value and the contours of the mass were drawn automatically. The SUVmean value of the area within these contours was calculated. Then MTV and SUVmean values of this area were multiplied and TLG value was obtained.

Histopathologic and Immunohistochemistry Analyses: 110 patients had diagnosis by core biopsies; 63 of these underwent surgery after diagnosis. Final histopathological examination of opereated patients was based on these mastectomy specimens. Histological type, histological and nuclear grade, Ki-67 proliferation index, receptor status (ER, PR, HER2), subtypes (Lum A/B, HER2 positive and TN), presence of invasion (vascular, lymphatic and perineural) and axillary lymph node status were evaluated. Histologic grade (HG) was evaluated using *Elston–Ellis* modification of the *Scarff–Bloom–Richardson* grading system, based on tubular score (TS), nuclear pleomorphism score (PS) and mitotic score (MS). Expression of ER, PR, HER2 and Ki-67 proliferation index of tumor tissue was examined by standard avidin-biotin complex immunohistochemical staining

methods. Positive ER and PR staining is accepted when nuclear staining was demonstrated in more than 10% of tumor cells. Ki-67 expression is evaluated by calculating the percentage of immunoreactive tumor cells showing nuclear staining at X10 amplification. HER2 membrane immunostaining was scored from 0 to 3; Score 3+ was accepted as positive while Score 0 and 1+ was negative. Score 2+ cases were tested by Fluorescence in situ Hybridization (FISH) method for final determination of HER2 status.

Subtyping: BCs were divided into four subtypes according to 12th International Breast Conference recommendations:

Lum A: ER (+) and /or PR (+), HER2 negative, Kİ-67 <14%

Lum B: Lum B(-); ER (+) and /or PR (+), HER2 negative, Kİ-67 ≥14% or Lum B(+); ER (+) and / or PR (+), HER2 positive, Ki-67 expression independent

HER 2 Positive: ER (-), PR (-), HER2 (+)

Triple Negative (TN): ER (-), PR (-), HER2 (-)

Statistical Analysis

Statistical analysis was performed with the IBM Statistical Package for Social Sciences v20 (SPSS Inc., Chicago, IL, USA). *Kolmogorov-Smirnov* test was applied to check the normal distribution of the quantitative data. Parametric tests (Independent-samples t-test) were used to evaluate the data of normal distribution, and non-parametric tests (*Mann–Whiney U*-test) were used to evaluate the data of questionably normal distribution. *Pearson* chi-square test was applied to compare the distribution of categorical variables in both groups. The determinants were explored using multiple logistic regression analysis. All results are presented as mean±SD. Statistical significance was accepted as $p<0.05$.

The study was approved by the Antalya Training and Research Hospital Ethics Committee (2018-159).

Results

The mean age of the 110 female patients included in the study was 56.18 ± 14.59 (ranging 27-92) years. Patient characteristics are shown in Table 1.

Table 1. Histological and immunohistochemical characteristics of tumour.

NUMBER OF PATIENTS (%)	
	ER status
No	18 (16.4%)
Yes	92 (83.6%)
	PR status
No	32 (29.1%)
Yes	78 (70.9%)
	HER2 status
No	93 (84.5%)
Yes	17 (15.5%)
	KI-67
<%14	43 (39.1%)
≥%14	67 (60.9%)
	Histology
Ductal	94 (85.5%)
Lobular	6 (5.5%)
Other	10 (9.1%)
	Histologic grade
1	6 (5.5%)
2	34 (30.9%)
3	70 (63.6%)
	Nuclear grade
1	6 (5.5%)
2	74 (67.3%)
3	30 (27.3%)
	Mitosis
1	69 (62.7%)
2	39 (35.5%)
3	2 (1.8%)
	Score
1	22 (20%)
2	79 (71.8%)
3	9 (8.2%)
	Vascular invasion
Negative	43 (60.6%)
Positive	28 (39.4%)
	Lymphatic invasion
Negative	36 (50.7%)
Positive	35 (49.3%)
	Perineural invasion
Negative	48 (67.6%)
Positive	23 (32.4%)
	Axillary lymph node
Negative	35 (56.5%)
Positive	27 (43.5%)
	Subtype
Luminal A	38 (34.5%)
Luminal B	56 (50.9%)
HER2 positive	3 (2.7%)
Triple negative	13 (11.8%)

The mean SUVmax value of 110 breast tumors were 7.73±5.62 (range 1.4-34.15). The mean SUVmax value in invasive ductal carcinomas was 8.33±5.81 and in invasive lobular carcinomas was 3.49±1.52. Univariate regression analysis showed that the SUVmax values of ductal carcinoma were significantly higher than lobular carcinomas (p=0.03). Mean SUVmax values of LumA, Lum B, HER2 positive and TN subtypes were 5.28±3.24,

7.44±4.24, 18.38±9.43, and 13.71±8.44, respectively (Figure 1).

In univariate regression analysis, SUVmax values of the Lum B (p=0.03), HER2 positive and TN groups (p<0.001, for both) were significantly higher than Lum A group. However, significant results could not be obtained in multivariate analyses. In univariate regression analyses, ER and PR positivity had significantly correlated with lower SUVmax values than negative status (p<0.001). In multivariate analyses, no significant difference was observed between both ER positive/negative and PR positive/negative cases. SUVmax values of HER2 positive cases were significantly higher in univariate analyses than HER2 negative cases (p=0.013). However, any significant difference was not observed in multivariate analyses. In univariate regression analyses, SUVmax values were significantly lower in tumors with Ki-67 proliferation index <14% than those with ≥ 14% (p=0.007); significant values were not obtained in multivariate analyses. Also, in univariate analyses, significant increases were observed in SUVmax values as the mitosis, and score parameters were increased, but these significant increases were not present in multivariate analyses. The relation between SUVmax and aksillary lymph node status was also not significantly correlated. The detailed results of univariate and multivariate linear regression analysis showing the relationship between SUVmax values and histopathologic-immunohistochemical factors are shown in Table 2.

Mean MTV values of Lum A, Lum B, HER2 positive and TN subtypes were 6.93±4.84, 17.78±42.94, 72.49±93.14 and 69.35±200.22, respectively. When the relationship between MTV of tumors and histopathological-immunohistochemical data was examined (Table 3), univariate regression analyses showed that negative ER and PR status had significantly correlated with higher MTV values than positive ER and PR status (p=0.013, p=0,034, respectively). However, in multivariate regression analyses, no significant results were observed for both ER and PR status. In univariate regression analysis with subtypes; The MTV values of the TN group were significantly higher than those of the Lum A group (p=0.011). There was no other significant relationship between other subtypes.

Mean TLG values of Lum A, Lum B, HER2 positive and TN subtypes were 23.88±29.53, 92.3±232.44, 903.29±1278.43 and 991.1±3186.57, respectively. In univariate regression analysis between TLG and histopathologic-immunohistochemical characteristics of the tumor (Table 4); ER–negative and PR–negative cases were found to have significantly higher TLG values (p=0.005, p=0.036, respectively) than positive ones. Triple-

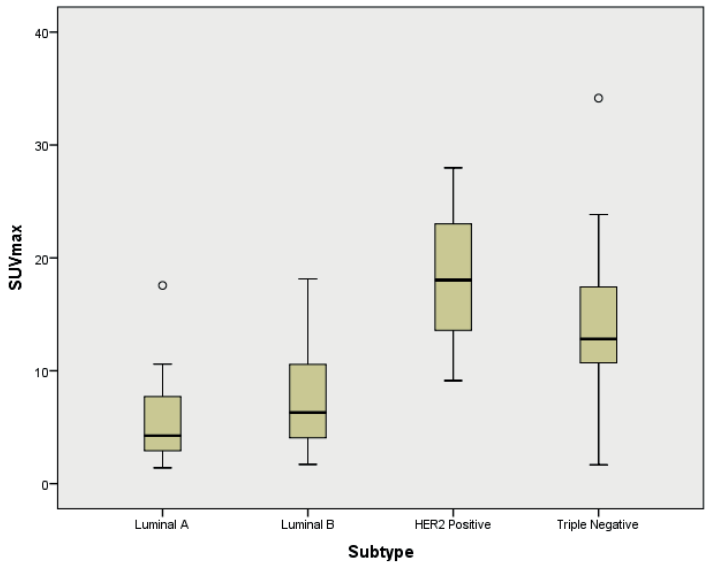

Figure 1. Mean primary tumor maximum standardized uptake value (PT SUVmax) according to tumor subtypes (Luminal A; Luminal B; HER2 positive; Triple negative).

negative tumors were found to have significantly higher TLG values than Lum A tumors (p=0.007). However, in multivariate regression analyses, no significant correlation was observed between TLG values and tumor histopathologic-immunohistochemical characteristics.

Discussion

In BC, therapy response and prognosis significantly depends on histopathological-immunohistochemical characteristics and subtypes. For this reason, in recent years, adjustment of treatment protocols by considering histopathological-immunohistochemical features and subtypes has been recommended [2].

18F-FDG PET/CT is a hybrid imaging technique which enables to observe metabolism and anatomical properties of tumor. In BC, it is

Table 2. Results of univariate and multivariate linear regression analysis for SUVmax.

	SUVmax	Univariate analysis		Multivariate regression analysis	
		Parameter estimate	*p* value	Parameter estimate	*p* value
Age		0.107	0.266		
Size		0.460	<0.001	0.269	0.023
ER status					
No	13.52±8.58				
Yes	6.6±4.03	-0.457	<0.001	-0.036	0.879
PR status					
No	10.96±7.69				
Yes	6.41±3.85	-0.37	<0.001	0.025	0.874
HER2 status					
No	7.17±5.15				
Yes	10.83±7.15	0.236	0.013	0.115	0.344
Kİ-67					
<%14	5.93±3.92				
≥%14	8.89±6.24	0.258	0.007	-0.379	0.223
Histology					
Ductal	8.33±5.81	1			
Lobular	3.49±1.52	-0.197	0.038	-0.198	0.061
Other	4.65±2.53	-0.189	0.046	-0.173	0.125
Histologic grade					
1	5.85±3.02	1			
2	5.96±3.75	0.009	0.966		
3	8.75±6.3	0.249	0.219		
Nuclear grade					
1	5.33±2.13	1			
2	7.81±6.14	0.208	0.302		
3	8.01±4.68	0.214	0.29		
Mitosis					
1	6.1±3.78	1			
2	10.3±7.12	0.359	<0.001	0.138	0.283
3	14.08±4.73	0.19	0.036	0.018	0.868
Score					
1	5.01±2.64	1			
2	8±6.04	0.24	0.023	0.007	0.96
3	12.04±3.88	0.344	0.001	-0.043	0.806
Vascular invasion					
Negative	7.11±5.6				
Positive	7.64±5.51	0.047	0.695		
Lymphatic invasion					
Negative	7.68±6.6				
Positive	7.28±4.59	-0.036	0.766		
Perineural invasion					
Negative	8.2±6.02				
Positive	5.5±3.84	-0.23	0.053		
Axillary lymph node					
Negative	7.16±5.76				
Positive	7.37±5.69	0.018	0.889		
Subtype					
Luminal A	5.28±3.24	1			
Luminal B	7.44±4.24	0.193	0.033	0.514	0.144
HER2 positive	18.38±9.43	0.381	<0.001	0.333	0.158
Triple negative	13.71±8.44	0.486	<0.001	0.673	0.054

used widely for staging and evaluating therapy response and also predicting prognosis [6,14].

In the literature, SUVmax was shown as one of the most commonly used PET/CT parameter correlating with histopathological features, receptor status, stage and prognosis in BC. As compatible with the literature, in our study invasive ductal carcinomas showed significantly higher primary tumor (PT) SUVmax values than invasive lobular carcinomas [10,12,13,15]. We observed the highest SUVmax values in HER2 positive group. While some of the studies were compatible with our results [16], most of them were conflicting with us. The highest SUVmax values were observed mostly in TN group in the literature [8,10,12,13,15,17].

Has Şimşek et al., analyzed BC subtypes as we grouped and SUVmax values in 436 patients

Table 3. Results of univariate and multivariate linear regression analysis for MTV.

	MTV	Univariate analysis		Multivariate regression analysis	
		Parameter estimate	*p* value	Parameter estimate	*p* value
Age		0.001	0.991		
Size		0.491	<0.001	0.415	0.001
ER status					
No	62.64±172.54				
Yes	13.59±33.93	-0.237	0.013	0.111	0.67
PR status					
No	45.87±130.28				
Yes	11.67±35	-0203	0.034	0.125	0.445
HER2 status					
No	20.43±81.73				
Yes	28.15±44.46	0.036	0.706		
Kİ-67					
<%14	8.92±7.92				
≥%14	29.77±97.94	0.133	0.167		
Histology					
Ductal	23.56±83.16	1			
Lobular	5.12±1.86	-0.055	0.574		
Other	13.29±11.35	-0.039	0.691		
Histologic grade					
1	12.87±22.01	1			
2	9.69±15.27	-0.019	0.926		
3	28.16±95.45	0.096	0.643		
Nuclear grade					
1	10.51±8.61	1			
2	26.02±93.09	0.095	0.638		
3	13±18.3	0.014	0.943		
Mitosis					
1	13.54±37.77	1			
2	35.79±118.9	0.139	0.152		
3	23.94±22.63	0.018	0.851		
Score					
1	8.88±12.21	1			
2	25.72±90.35	0.099	0.369		
3	16.76±16.17	0.028	0.798		
Vascular invasion					
Negative	15.71±46.99				
Positive	14.64±33.35	-0.013	0.917		
Lymphatic invasion					
Negative	21.44±57.98				
Positive	8.12±5.92	-0.161	0.181		
Perineural invasion					
Negative	18.75±50.34				
Positive	8.07±9.36	-0.12	0.318		
Axillary lymph node					
Negative	9.64±11.66				
Positive	14.69±33.88	0.106	0.414		
Subtype					
Luminal A	6.93±4.84	1			
Luminal B	17.78±42.94	0.071	0.495	0.096	0.461
HER2 positive	72.49±93.14	0.139	0.149	0.133	0.464
Triple negative	69.35±200.22	0.263	0.011	0.199	0.488

and reported that SUVmax values of ER and PR negative patients were significantly higher than those with ER and PR positive patients (p=0,001 for both group) [16]. In this study, the lowest SUVmax levels were observed in Lum A group followed by the Lum B, TN group, respectively, and the highest SUVmax values were observed in the HER2 positive group similar with our study. Koo et al., grouped 552 patients similar with our study as Lum A, Lum B, HER2 positive and TN and evaluated the relationship between PT SUVmax values and subtypes [10]. In this study, Lum A group formed the majority by number while it was lum B group in our study. ER and PR negativity was also similarly correlated with high PT SUVmax values in their study (p<0.001 for both group). The significant correlation between high SUVmax values

Table 4. Results of univariate and multivariate linear regression analysis for TLG.

	TLG	Univariate analysis		Multivariate regression analysis	
		Parameter estimate	*p* value	Parameter estimate	*p* value
Age		-0.008	0.932		
Size		0.434	<0.001	0.256	0.031
ER status					
No	867.51±2730.98				
Yes	65.82±184.69	-0.263	0.005	0.104	0.668
PR status					
No	549.33±2059.54				
Yes	52.46±179.29	-0.2	0.036	0.202	0.19
HER2 status					
No	185.27±1207.82				
Yes	261.2±574.24	0.024	0.801		
Kİ-67					
<%14	36.76±52.48				
≥%14	299.85±1444.12	0.114	0.236		
Histology					
Ductal	226.35±1222.57	1			
Lobular	9.82±5.19	-0.044	0.653		
Other	33.42±27.78	-0.049	0.612		
Histologic grade					
1	62.14±127.29	1			
2	46.58±122.17	-0.006	0.975		
3	281.62±1412.25	0.094	0.651		
Nuclear grade					
1	30.79±31.28	1			
2	257.96±1375.22	0.095	0.639		
3	79.89±150.15	0.019	0.923		
Mitosis					
1	61.21±194.2	1			
2	435.42±1873.98	0.159	0.101		
3	232.86±256.36	0.02	0.832		
Score					
1	32.6±67.34	1			
2	250.77±1332.33	0.087	0.428		
3	126.92±136.58	0.023	0.835		
Vascular invasion					
Negative	86.23±247.23				
Positive	119.77±443.36	0.049	0.684		
Lymphatic invasion					
Negative	154.11±465.05				
Positive	43.87±57.1	-0.165	0.168		
Perineural invasion					
Negative	131.26±403.8				
Positive	33.07±60.34	-0.138	0.252		
Axillary lymph node					
Negative	59.36±102.18				
Positive	120.11±451.67	0.099	0.443		
Subtype					
Luminal A	23.88±29.53	1			
Luminal B	92.3±232.44	0.03	0.768	0.127	0.297
HER2 positive	903.29±1278.43	0.127	0.185	0.314	0.069
Triple negative	991.1±3186.57	0.277	0.007	0.321	0.234

and ER and PR-negativity was commonly demonstrated in the literature [9,12,13,15,17]. In the study of Ekmekcioğlu et al., involving 140 BC patients, ER-negative patients were found to have significantly higher PT SUVmax values (p=0.004), but no significant differences were found between PR negative and positive patients (p=0.211) [11]. Despite the difference in BC patient numbers involved in the studies, ER and PR negativity are strongly correlated with PT SUVmax.

In the literature, results for the correlation between SUVmax and ER/PR status were substantially similar while it was conflicting for HER2 overexpression. In literature, some studies reported the highest SUVmax values in the HER2 positive group as in our study [10,13,16,18], while some had reported no correlation between them [11,12,17]. In Ugurluer et al., in the study, higher SUVmax values were detected in HER2 positive patients whereas the difference between the groups was not statistically significant (p=0.308) [15].

As compatible with our results, there is a positive association between PT SUVmax values and Ki-67 expression [10,11,16,19]. Ki-67 is a prognostic marker reflecting cell proliferation rate and tumor aggression. Ideal cutoff value for Ki-67 is still challenging. Different cut-off values are accepted in the literature. In this study we accepted 14% as a cutoff value as it was recommended in international Ki-67 in Breast Cancer Working Group [20].

In our study, as the mitosis score increased, a significant increase in PT SUVmax values were observed. This is an expected result and is similar to the findings of previous studies [16]. However, no significant differences were observed between PT SUVmax values and histologic grade, nuclear grade or invasion patterns.

There are recent studies investigating the correlations between tumor phenotypes, immunohistochemical profile and FDG PET/CT volumetric parameters like MTV and TLG. MTV and TLG have been reported to be capable of comprehensively reflecting glucose uptake within the whole tumor rather than a single-pixel value of 18F-FDG activity. Groheux et al., classified 171 stage 2 and 3 BC patients into three subgroups (TN, HER2 positive and ER-positive/HER2 negative) in their retrospective study [13]. There was no significant difference between the three groups regarding MTV values (p=0.089), but they reported significantly smaller MTVs in ER positive and in PR positive tumors than ER and PR negative tumors (p<0,03). TLG significantly differed among the three phenotype subgroups. Similarly, Chen et al., indicated that, TLG values were significantly different in group comparison (p=0.007), while MTV values were not (p=0.175) [21].

In our study, univariate regression analyses showed that those with negative ER and PR status had significantly higher MTV and TLG values than those with ER and PR positive status. The MTV and TLG values of TN patients were significantly higher than those of the Lum A group.

In our study, we investigated the potential efficacy of PET/CT parameters such as SUVmax, MTV and TLG in predicting the histopathological features and subtypes in BC patients. However, we have some limitations. We could not examine the association of PET parameters with survey because of inadequate data. Also, although our distribution of patients among subtypes is similar to the literature, there are very few patients in the HER2 positive group.

Conclusion

In this study, it was observed that SUVmax value was significantly correlated with histopathological-immunohistochemical factors and tumor subtypes in BC cases. In the literature, the relation between histopathological-immunohistochemical factors and MTV-TLG values are not commonly referred in BC patients. However, we've seen that these parameters might be higher in ER and PR-negative cases than in positive ones according to our results. We also observed that, higher MTV and TLG values are seen in TN patients compared to Lum A group. Further studies with larger patient groups are needed to provide more reliable statistical results.

Acknowledgment

This study was presented as an oral presentation at the 30th National Nuclear Medicine Congress (2018-Antalya/Türkiye).

Funding

There is no funding.

Conflict of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. doi: 10.3322/caac.21660.

2. Loibl S, Poortmans P, Morrow M, Denkert C, Curigliano G. Breast cancer. Lancet. 2021;397(10286):1750-69. doi: 10.1016/S0140-6736(20)32381-3.

3. Abubakar M, Figueroa J, Ali HR, Blows F, Lissowska J, Caldas C, et al. Combined quantitative measures of ER, PR, HER2, and KI67 provide more prognostic information than categorical combinations in luminal breast cancer. Mod Pathol. 2019;32(9):1244-56. doi: 10.1038/s41379-019-0270-4.

4. Ryu JM, Yu J, Kim S Il, Kim KS, Moon H-G, Choi JE, et al. Different prognosis of young breast cancer patients in their 20s and 30s depending on subtype: A nationwide study from the Korean Breast Cancer Society. Breast Cancer Res Treat. 2017;166(3):833-42. doi: 10.1007/s10549-017-4472-5.

5. Hadebe B, Harry L, Ebrahim T, Pillay V, Vorster M. The role of PET/CT in breast cancer. Diagnostics (Basel). 2023;13(4):597. doi: 10.3390/diagnostics13040597.

6. Cochet A, Dygai-Cochet I, Riedinger J-M, Humbert O, Berriolo-Riedinger A, Toubeau M, et al. 18F-FDG PET/CT provides powerful prognostic stratification in the primary staging of large breast cancer when compared with conventional explorations. Eur J Nucl Med Mol Imaging. 2014;41(3):428-37. doi: 10.1007/s00259-013-2595-4.

7. Hildebrandt MG, Naghavi-Behzad M, Vogsen M. A role of FDG-PET/CT for response evaluation in metastatic breast cancer? Semin Nucl Med. 2022;52(5):520-30. doi: 10.1053/j.semnuclmed.2022.03.004.

8. Muduly DK, Ephraim R, Sultania M, Ray S, Bhoriwal S, Pathak M, et al. Correlation of 18-fluorodeoxyglucose uptake values on PET-CT scan with histological prognostic markers in breast cancer. Asia Pac J Clin Oncol. 2023;19(2):106-10. doi: 10.1111/ajco.13799.

9. Zhang J, Liu Y, Fan H, Wang W, Shao W, Cao G, et al. Prediction of clinical molecular typing of breast invasive ductal carcinoma using 18F-FDG PET/CT dual-phase imaging. Acad Radiol. 2023;S1076-6332(22)00693-6. doi: 10.1016/j.acra.2022.12.036.

10. Koo HR, Park JS, Kang KW, Cho N, Chang JM, Bae MS, et al. 18F-FDG uptake in breast cancer correlates with immunohistochemically defined subtypes. Eur Radiol. 2014;24(3):610-8. doi: 10.1007/s00330-013-3037-1.

11. Ekmekcioglu O, Aliyev A, Yilmaz S, Arslan E, Kaya R, Kocael P, et al. Correlation of 18F-fluorodeoxyglucose uptake with histopathological prognostic factors in breast carcinoma. Nucl Med Commun. 2013;34(11):1055-67. doi: 10.1097/MNM.0b013e3283658369.

12. Heudel P, Cimarelli S, Montella A, Bouteille C, Mognetti T. Value of PET-FDG in primary breast cancer based on histopathological and immunohistochemical prognostic factors. Int J Clin Oncol. 2010;15(6):588-93. doi: 10.1007/s10147-010-0120-3.

13. Groheux D, Majdoub M, Tixier F, Le Rest CC, Martineau A, Merlet P, et al. Do clinical, histological or immunohistochemical primary tumour characteristics translate into different 18F-FDG PET/CT volumetric and heterogeneity features in stage II/III breast cancer? Eur J Nucl Med Mol Imaging. 2015;42(11):1682-91. doi: 10.1007/s00259-015-3110-x.

14. Hatt M, Groheux D, Martineau A, Espié M, Hindié E, Giacchetti S, et al. Comparison between 18F-FDG PET image-derived indices for early prediction of response to neoadjuvant chemotherapy in breast cancer. J Nucl Med. 201354(3):341-9. doi: 10.2967/jnumed.112.108837.

15. Ugurluer G, Yavuz S, Calikusu Z, Seyrek E, Kibar M, Serin M, et al. Correlation between 18F-FDG Positron-Emission Tomography 18F-FDG uptake

levels at diagnosis and histopathologic and immunohistochemical factors in patients with breast cancer. J Breast Heal. 2016;12(3):112-8. doi: 10.5152/tjbh.2016.3031.

16. Has Şimşek D, Şanli Y, Külle CB, Karanlik H, Kiliç B, Kuyumcu S, et al. Correlation of 18F-FDG PET/CT with pathological features and survival in primary breast cancer. Nucl Med Commun. 2017;38(8):694-700. doi: 10.1097/MNM.0000000000000694.

17. Kim BS, Sung SH. Usefulness of 18F-FDG uptake with clinicopathologic and immunohistochemical prognostic factors in breast cancer. Ann Nucl Med. 2012;26(2):175-83. doi: 10.1007/s12149-011-0556-1.

18. García Vicente AM, Soriano Castrejón Á, León Martín A, Chacón López-Muñiz I, Muñoz Madero V, Muñoz Sánchez MDM, et al. Molecular subtypes of breast cancer: Metabolic correlation with 18F-FDG PET/CT. Eur J Nucl Med Mol Imaging. 2013;40(9):1304-11. doi: 10.1007/s00259-013-2418-7.

19. Chojniak R, Marques EF, Souza JA De, Graziano L, Andrade WP, Bitencourt AG V, et al. Correlation between PET-CT results and histological and immunohistochemical findings in breast carcinomas. Radiol Bras. 2014;47(2):67-73. doi: 10.1590/S0100-39842014000200006.

20. Dowsett M, Nielsen TO, A'Hern R, Bartlett J, Coombes RC, Cuzick J, et al. Assessment of Ki67 in breast cancer: Recommendations from the International Ki67 in Breast Cancer working group. J Natl Cancer Inst. 2011;103(22):1656-64. doi: 10.1093/jnci/djr393.

21. Chen W, Zhu L, Yu X, Fu Q, Xu W, Wang P. Quantitative assessment of metabolic tumor burden in molecular subtypes of primary breast cancer with FDG PET/CT. Diagnostic Interv Radiol. 2018;24(6):336-41. doi: 10.5152/dir.2018.17367.