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Original Article

The importance of SUV_{max} in predicting prognosis of invasive breast carcinoma-no special types

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Abstract

Aim: We aimed to investigate the relationship between FDG uptake and clinicopathological characteristics of invasive breast carcinoma-no special type in the present study.

Materials and Methods: One hundred seventy invasive breast carcinoma-no special type cases who underwent PET-CT before surgery between 2011-2019 were included in the study. The clinicopathological features and SUV_{max} of the patients were compared.

Results: We observed a strong relationship between the size, grade, pathological stage groups and SUV_{max} of the tumors and revealed that the SUV_{max} increased as the size, grade, and pathological stage groups of the tumors increased ($p<0.001$). Carcinomas with high Ki67 proliferation index and ER and PR negative carcinomas exhibited higher SUV_{max} ($p<0.001$). Triple negative and HER2-enriched molecular subtypes had distinctly higher SUV_{max} than Luminal A and Luminal B ones ($p<0.001$). HER2-enriched tumors, the cases that were <40 years old and advanced stage designated higher SUV_{max} ($p<0.05$).

Conclusion: It is observed that invasive breast carcinoma-no special type with good prognostic factors have low SUV_{max}, while carcinomas with poor prognostic features have high SUV_{max}. It can be suggested that PET/CT can be use to predict the prognosis of invasive breast carcinoma-no special type.

Keywords: Breast; breast carcinoma; invasive ductal carcinoma; invasive breast carcinoma-no special type; PET-CT; FDG; SUV_{max}

INTRODUCTION

In women breast carcinoma is the most frequent cancer and is the second most common cause of death due to cancer, in addition it constitutes 30% of all new cancer diagnosis (1). Breast carcinomas are highly heterogeneous tumors and their prognosis varies according to histopathological type, stage, grade, hormone receptor status, CerbB2 status, and Ki67 proliferation index of the tumor. Luminal A, Luminal B, HER2-enriched and triple negative subtypes were determined for breast carcinomas according to the immunohistochemical properties, and these tumor subtypes are highly associated with prognosis. Although the prognosis of luminal A tumors is better, the prognosis of triple negative tumors is poor (2). Breast carcinomas are staged according to the diameter of tumor, presence of axillary lymph node and distant metastasis, and the stage of the tumor is closely related to the prognosis. In addition to these properties, the American Joint Committee on Cancer (AJCC) staged breast carcinomas, taking into account HER2, ER, PR status and the histological grade of the tumors, and some of the tumors were down staged according to these features (3). Determining prognostic factors and staging breast carcinomas is quite essential in management of the treatment.

18F-fluorodeoxygluxose positron emission tomography/computed tomography (FDG PET/CT) represents the glucose metabolism, and due to the increasing glycolysis in tumor cells, FDG uptake increase in malign tumors (4). Maximum standardized uptake value (SUV_{max}) represents the highest FDG uptake of the lesion. FDG uptake is used for the diagnosis and staging of the breast carcinomas and evaluating the presence of recurrence and treatment response and also can aid the foreseeing the prognosis. FDG uptake is related to pathological diagnosis and various prognostic parameters (5).

We aimed to investigate the relationship between FDG uptake and prognostic parameters of invasive breast carcinoma-no special type (IBC-NST) in our hospital in the present study.

MATERIALS and METHODS

A total of 170 female patients who underwent PET-CT before surgery, were treated by lumpectomy or mastectomy and were diagnosed as IBC-NST with tru-cut biopsy in

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the Konya Education and Research Hospital between September 2011 and February 2019 were included in the study. Cases with a diagnosis with special type of breast carcinomas, cases who received neoadjuvant chemotherapy or radiotherapy, who had multifocal/multicentric tumors, distant metastasis, cutaneous invasion, uncontrolled diabetes mellitus, or synchronous malignancy and patients who were performed excisional biopsy with tumor positive surgical margin were excluded. Clinicopathological features and SUV_{max} were obtained from the patient files. All of the cases had ER, PR, HER2 and Ki67 immunohistochemical evaluations. Subtypes of tumors were determined considering immunohistochemical staining characteristics. The cases were staged according to TNM and pathological stage groups were also determined in reference to AJCC eighth edition.

For statistical assessment; software SPSS (version 22.0, Chicago, IL, USA) was used. Non-parametric datas were presented as median (min–max) and the categorical variables were given as the percentage and number of cases. For analyzing the continuous variables the Shapiro-Wilk test was performed. The groups' SUV_{max} were qualified with Kruskal-Wallis test and the Mann-Whitney U test was used. In all statistical comparisons, p value was considered as significant if <0.05.

RESULTS

The age of the cases ranged between 29 and 84 years with median of 52 years, and 148 (87.1%) of the cases were ≥40 years old. The diameters of the tumors were between 1 cm and 7 cm and the median tumor diameter was 2.5 cm. The Ki67 proliferation indices and SUV_{max} of the tumors varied widely and ranged 2% to 85% (median 19.5%), and 1,65 to 40,31(median 7.87) respectively. The relationship between clinicopathological features and SUV_{max} of the cases were shown in Table 1.

Table 1. The relationship between clinicopathological features and SUV_{max} of the patients with invasive breast carcinoma-no special type

Features	n = 170 (%)	SUV_{max} median (min-max)	P value
Age			0.015
<40	22 (12.9)	11.89 (3.52-26.52)	
≥40	148 (87.1)	7.17 (1.65-40.31)	
Tumor size (pT)			<0.001
T1 (≤2)	66 (38.8)	6.00 (1.65-23.27)	
T2 (>2-≤5)	100 (58.8)	9.74 (2.37-40.31)	
T3 (>5)	4 (2.4	11.12 (5.08-25.70)	
Axillary lymph node			0.938
Negative	76 (44.7)	7.96 (1.65-40.31)	
Positive	94 (55.3)	7.87 (2.37-33.38)	
Axillary lymph node (pN)			0.785
N0 (0)	76 (44.7)	7.96 (1.65-40.31)	
N1 (1-3)	61 (35.9)	6.36 (2.37-30.47)	
N2 (4-9)	23 (13.5)	9.18 (2.65-32.23)	
N3 (>9)	10 (5.9)	10.74 (3.79-33.38)	
Histological grade			<0.001
1	22 (12.9)	5.53 (1.65-23.83)	
2	93 (54.7)	6.78 (2.37-27.33)	
3	55 (32.4)	13.02 (2.62-40.31)	
Stage			0.017
1	38 (22.4)	6.34 (1.65-18.93)	
2	101 (59.4)	8.59 (2.37-40.31)	
3	31 (18.2)	9.13 (2.65-33.38)	
Pathologic Stage Group			<0.001
1	126 (74.1)	6.55 (1.65-30.47)	
2	28 (16.5)	17.46 (2.37-40.31)	
3	16 (9.4)	13.28 (3.79-33.38)	
ER status			<0.001
Negative	29 (17.1)	17.07 (2.37-40.31)	
Positive	141 (82.9)	6.66 (1.65-33.38)	
PR status			<0.001
Negative	34 (20)	13.11 (3.01-40.31)	
Positive	136 (80)	6.62 (1.65-33.38)	
HER2 status			0.044
Negative	129 (75.9)	6.99 (1.65-40.31)	
Positive	41 (24.1)	11.50 (2.37-33.38)	
Ki67 status			<0.001
Low (<14)	53 (31.2)	5.67 (1.65-20.93)	
High (≥14)	117 (68.8)	9.57 (2.69-40.31)	
Subtype			<0.001
Luminal A	42 (24.7)	5.79 (1.65-20.93)	
Luminal B	103 (60.6)	7.75 (2.37-33.38)	
HER2-enriched	10 (5.9)	13.19 (4.84-26.52)	
Triple negative	15 (8.8)	18.93 (8.17-4031)	

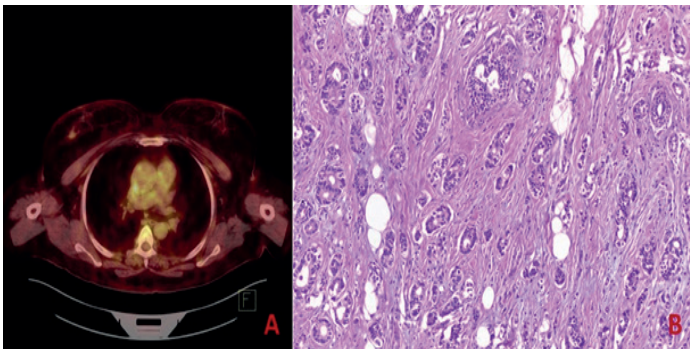

Figure 1. Invasive breast carcinoma-no special type with grade 1, Luminal A and low Ki67 proliferation index; A- FDG PET-CT image (SUVmax: 2.55) B- Histopathological appearance (HEX100)

We observed a strong relationship between SUV_{max} and the size, histological grade, pathological stage groups of the tumors and reveald that the SUV_{max} increased significantly as the size, histological grade, and the pathological stage groups of the tumors increased (p<0.001). Moreover we demonstrated that carcinomas with high Ki67 proliferation index and ER and PR negative carcinomas exhibited higher SUV_{max} than carcinomas with low Ki67 index and ER

and PR positive carcinomas respectively (p<0.001). The relationship between tumor subtypes that considering the immunohistochemical properties and SUV_{max} of the tumors was also significant, and HER2 positive tumors and triple negative tumors had distinctly higher SUV_{max} than Luminal A and Luminal B tumors (p<0.001) (Figure 1, Figure 2).

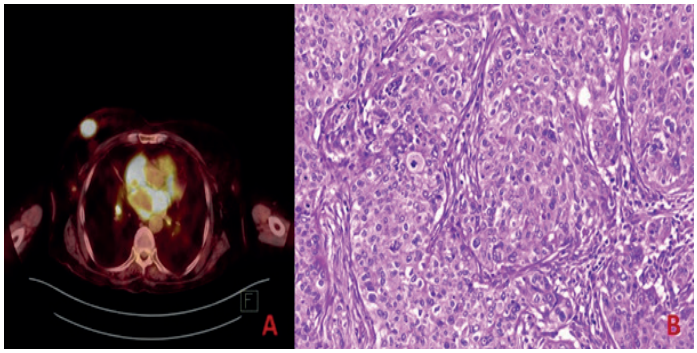

Figure 2. Invasive breast carcinoma-no special type with grade 3, triple negative and high Ki67 proliferation index; A- FDG PET-CT image (SUVmax: 27,69) B- Histopathological appearance (HEX200)

In addition cases that were <40 years old and HER2 positive tumors designated higher SUV_{max} and it is observed that as the stages of the tumors increased, the SUV_{max} of the tumors also increased (p<0.05). Although a slight increase in the the primary tumor's SUV_{max} was observed as the number of metastatic axillary lymph nodes increased, the difference was not significant (>0.05).

DISCUSSION

Breast cancers are very heterogeneous tumors biologically, clinically and pathologically, so the treatment responses of tumors also vary. It is important to determine the prognostic factors of breast carcinomas preoperatively since tumors can be down staged with neoadjuvant therapy and can be a chance to apply conservative surgery in these cases. Pathological features including histological type, tumor stage, grade, hormone receptors status, and HER2 status are well known prognostic factors in breast carcinomas. While prognosis is better in ER and PR positive tumors, HER2 positive tumors are more aggressive and prognosis is poor in advanced stage and high-grade tumors. Moreover, hormone receptor status and HER2 status are not only useful in predicting prognosis, but they are also essential for treatment decision in breast carcinomas. Tumor morphology and the presence of lymphovascular invasion also have a crucial part as prognostic factor (6). Ki67 proliferation index guides to foresee prognosis in breast carcinomas, and high Ki67 proliferation index is related with early recurrence and aggressive behavior. Therefore, Ki67 proliferation indices are beard in mind in patient's follow-up and treatment planning (7).

Stage at diagnosis was the strongest predictor of survival and traditional anatomical staging gives valuable information for prognosis and treatment management of breast carcinomas, which is performed according to the tumor size, presence of local and distant metastasis. Besides the anatomic stage groups determined by TNM, the AJCC recommends identifying clinical and pathological stage groups in breast carcinomas that is designated by ER, PR and HER2 status of tumors in addition to TNM. Pathological stage offers better information in determining prognosis than anatomical stage (8). Subtypes determined according to the immunohistochemical properties are also closely related to the prognosis. Luminal A tumors are the most common subtype and have the best prognosis, on the contrary triple negative tumors are the most aggressive ones (9).

In studies conducted to date, it has been shown that there is a relationship between SUV_{max} and many prognostic factors of breast carcinomas (10). Abubakar et al. indicated that SUV_{max} is higher in cases <40 years old (5). A correlation between the SUV_{max} and the size and the histological grade of the IBC-NST has been designated, and has been reported that the SUV_{max} rise with increasing tumor size and histological grade (11). In our study, in accordance with the literature, we found the SUV_{max} higher in cases <40 years old and observed that the SUV_{max} increased as the tumor size and histological grade increased.

Although breast carcinomas which have metastatic lymph node in the axilla displayed higher SUV_{max} in some previous studies, it was also reported that there was no relationship between SUV_{max} and presence of metastatic lymph node (12,13). We didn't detect any differences between the SUV_{max} of the cases with and without metastatic axillary lymph nodes in our study. As the count of metastatic lymph nodes increased, the SUV_{max} of the breast carcinoma was also increased, but the difference was not significant. On the other hand, stages performed considering the tumor size and the count of metastatic axillary lymph nodes were ascertained correlated with SUV_{max}, and we observed that advanced stage tumors have high SUV_{max}. Such as the anatomical stages, pathological stage groups determined according to the AJCC's recommendation were also closely associated with SUV_{max} and this relationship was stronger than the previous one.

While low SUV_{max} was encountered in ER and PR positive breast carcinomas, high SUV_{max} was reported in HER2 positive carcinomas and carcinomas with high Ki67 proliferation index (14). In parallel with these findings, a difference was observed between SUV_{max} and the subtypes determined according to immunohistochemical ER, PR, HER2 status and Ki67 proliferation indices, and triple negative tumors that is the subtype with the worst prognosis were introduced the highest SUV_{max} (5). Our findings promoted the literature, and we observed that IBC-NSTs have statistically strong relationship between SUV_{max} and hormone receptor status, Ki67 proliferation indices, and subtypes of tumors.

CONCLUSION

In summary; it is observed that IBC-NSTs with good prognostic factors have low $SUV_{max,}$ while tumors known

to be associated with poor prognosis have high SUV_{max}. Based on this; it can be asserted that the SUV_{max} are related to the prognosis of IBC-NSTs and it can be suggested that FDG PET/CT can be used to predict the prognosis of IBC-NSTs.

Conflict of interest : The authors declare that they have no competing interest.

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Ethical approval: For this study, ethical approval was obtained from the Ethics Committee of KTO Karatay University, Faculty of Medicine (2019/0019).

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