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Comparison of the efficiency of nomograms used to predict preoperative sentinel lymph node positivity in breast cancer with clinical findings, PET/CT images and laboratory parameters

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ABSTRACT

Aim: To compare the efficacy of nomograms used to predict preoperative sentinel lymph node involvement in patients diagnosed with breast cancer and clinical findings, PET/CT imaging and laboratory parameters.
Methods: In this retrospective study, patients who were operated for invasive breast carcinoma with sentinel lymph node biopsy in our Generel Surgery Department between 2015 and 2020, were identified from our database. Laboratory parameters (PLR, NLR, LMR and MPR) were calculated from the complete blood count taken within 24 hours before surgery. Memorial Sloan Kettering Cancer Center (MSKCC) method was used from nomograms. Patients were compared according to sentinel lymph node positivity. All obtained data were compared with statistical tests.
Results: A total of 48 patients could be included in the study. A statistically significant correlation was found between physical examination, USG and PET/CT findings in terms of axilla positivity and pathology results (p<0.001, p=0.005 and p=0.002). The SUVmax value of the axilla was found to be statistically significantly higher in patients with positive SLNB group than in SLNB negative group (2.90±3.46 vs. 0.66±1.86, p=0.004). Although the rates of PLR, NLR, LMR and MPR among the laboratory parameters were higher in the SLNB positive group, they were not statistically significant (p=0.683, p=0.6, p=0.948 and p=0.354).
MSKCC nomogram values were higher in SNLB positive group, however it was not statistically significant (p=0.243).
Conclusion: In our study, clinical examination, laboratory testings, PET/CT imaging results and nomograms; on their own, have limited prediction about sentinel lymph node involvement. Therefore, we think it is necessary to design new algorithms that are more effective to predict axillary involvement and this will give better results in this regard.

Key words: Breast cancer, laboratory parameters, nomogram, PET/CT, sentinel lymph node, biopsy.

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Introduction

Breast cancer is the most commonly diagnosed cancer in women and its incidence is increasing day by day. This increase has led scientists to do more research on this subject, and has led to the disease being more understandable, important steps to be taken in identifying risk factors and new developments in diagnosis and treatment modalities. Breast cancers are heterogeneous tumor groups with different characteristics according to their morphology, clinical findings and response to treatment. Breast cancer often shows the characteristics of a systemic disease by spreading lymphaticly and sometimes hematogenously from the beginning of the disease.

18-fluoro-2-deoxy-D-glucose (18F-FDG) Positron Emission Tomography/Computed Tomography (PET/CT), which is used to obtain information about the physiology and biochemical character of the tumor and to determine the behavioral pattern of the tumor, has been started to be used for evaluation of breast cancer and axillary metastasis [1-3]. Recently, with the clarification of the role of the inflammation in cancer prognosis, some laboratory parameters (elevation of C-reactive protein (CRP), increase in platelet and neutrophil numbers) have been focused on and their relationship with cancer prognosis has begun to be investigated [4,5]. Similarly, nomograms were created and to be used to predict sentinel lymph node (SLN) involvement before the surgery. Nomograms prepared by Memorial Sloan Kettering Cancer Center (MSKCC) and MD Anderson Cancer Center (MDACC) are some of these.

The aim of our study is to compare the MSKCC nomogram and clinical findings, PET/CT images and laboratory parameters used to predict preoperative SLN involvement in breast cancer patients.

Materials and methods

The patients, who had undergone breast carcinoma surgery at the Bolu Abant Izzet Baysal Training and Research Hospital between 2015-2020 were retrospectively scanned from the electronic database. The inclusion criteria of the patients were as follows: Absence of the metastatic disease at the time of diagnosis, access to the USG, PET/CT images and reports, not receiving noeadjuvant therapy before sentinel lymph node biopsy (SNLB), no history of any surgical operation to that breast, not have inflammatory carcinoma. A total of 48 patients included in the study. The study was approved by the Clinical Researches Ethics Committee of the Bolu Abant Izzet Baysal University (Decision number: 277/2020).

The patients were divided into two groups as SLNB positive and SLNB negative. Demographic data, physical examination findings, ultrasonography (USG), PET/CT data and laboratory data of the patients were arranged for the groups.

Laboratory parameters were calculated from the complete blood count taken within 24 hours before surgery. From laboratory parameters; leukocyte (WBC), platelet (PLT), red cell distribution (RDW), lymphocyte (LYM), monocyte (MONO), neutrophil (NEU), mean platelet volume (MPV), albumin, serum C reactive protein (CRP) and total bilirubin was included in the study. NLR value (NEU/LYM ratio), PLR value (PLT/LYM ratio), LMR value (LYM/MONO value) and MPR value (MONO/PLT ratio) were calculated.

Patients were divided into two another groups as axillary positive and negative; according to physical examination findings,

USG and PET/CT imaging results. Tumor SUVmax and axillary SUVmax values were used in PET/CT. MSKCC nomogram value was calculated.

All data obtained from lymph node positive and negative patients were compared with statistical tests. Descriptive statistics; for numerical variables, mean, standard deviation, median, minimum and maximum were given. The compliance of the variables to normal distribution was evaluated with Shapiro-Wilk tests and histogram graphs. T-test was used for normally distributed variables to compare numerical data in two independent groups. Variables that were not normally distributed were compared with Mann-Whitney U tests. For categorical variables, Pearson's chi-square test or Fisher's exact test was used, depending on the distribution of the data. The performance of SUVmax values in distinguishing the group with positive lymph nodes and the group with negative lymph nodes (Receiver Operating Characteristic) was evaluated by ROC curve analysis. Logistic regression analysis was performed to show whether the variables examined in the study were independent factors in predicting lymph node positivity, and the odds ratio (OR) for each factor was calculated with 95% confidence intervals. Significance was determined at p <0.05 and analyzes were performed using Statistical Package for Social Sciences 25.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Results

48 patients were included in the study. SLNB results were positive in 21 patients (43.75%) and negative in 27 (56.25%).

Sentinel lymph nodes were negative in 5 of 22 patients whose axilla was evaluated as positive on physical examination (PE). SLNB results were found to be positive in 4 of 26 patients whose axillae were evaluated as negative on PE. While the axilla was evaluated as positive in 19 patients on USG, the SLNB result was found to be negative in 6 of these patients. SLNB result was positive in 8 of 29 patients whose axilla was evaluated as negative on USG. The SLNB result was found to be negative in 4 of the 16 patients with axilla involvement on PET/CT, and the SLNB result was positive in 9 of the 32 patients with no involvement. A statistically significant relationship was found between PE, USG and PET/CT findings and pathology results in predicting axilla positivity (p<0.001, p=0.005 and p=0.002) (Table 1).

The SUVmax value of the tumor did not show any significant difference between SLNB negative and positive groups (7.09±4.19 vs. 7.11±4.83, p=0.901). The SUVmax value of the axilla was higher in SLNB positive group, and this was statistically significant (2.90±3.46 vs. 0.66±1.86, p=0.004) (Table 2).

The performance of tumor SUVmax and axilla SUVmax values in distinguishing the SLNB positive group from the SLNB negative group was evaluated by ROC curve analysis, and the SUVmax axilla value was found to be statistically significant (p = 0.004) (Figure 1).

In the ROC analysis, the area under the ROC curve (AUC) for the SUVmax axilla value was found to be 0.707 (95% Confidence Interval: 0.552-0.862). When the patients' SUVmax axilla values were examined, the cut-off value to predict positive lymph nodes was determined as 1.6 (sensitivity 57.1%, specificity 88.9%) (Figure 1).

When the hemogram parameters of the patients were examined, no significant difference was found between the SLNB negative or positive groups (p>0.05).

Table 1. Distribution of patients' axillary lymph node involvement according to PE, USG and SLNB results.

Total	(n=48)	SLNB Negative (n=27)	SLNB Positive (n=21)	p^a
Axillary PE				*<0.001*
Negative	(n=26)	22 (%81.5)	4 (%19.0)	
Positive	(n=22)	5 (%18.5)	17 (%81.0)	
Axillary USG				*0.005*
Negative	(n=29)	21 (%77.8)	8 (%38.1)	
Positive	(n=19)	6 (%22.2)	13 (%61.9)	
Axillary PET/BT				*0.002*
Negatif	(n=32)	23 (%85.2)	9 (%42.9)	
Pozitif	(n=16)	4 (%14.8)	12 (%57.1)	

Table 2. Distribution of patients according to SUVmax values.

Total	(n=48)	SLNB Negative (n=27)	SLNB Positive (n=21)	p^a
SUVmax value of tumor		7.09±4.19	7.11±4.83	*0.901*
		6.1 (2.1-16.1)	0.0 (0.0-8.3)	
SUVmax value of axillae		0.66±1.86	2.90±3.46	*0.004*
		6.1(1.36-18.3)	2.2 (0.0-12.3)	

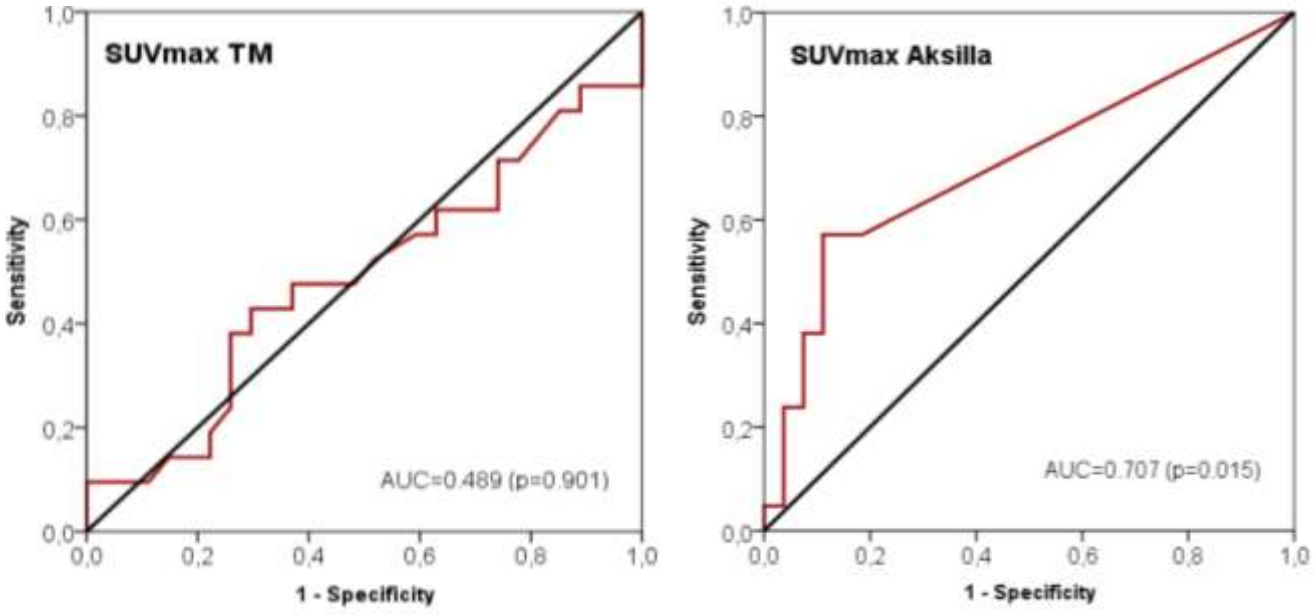

Figure 1. Prediction of lymph node positivity by ROC curve analysis for SUVmax tumor and SUVmax axilla.

MSKCC nomogram value did not show a significant difference between positive and negative groups with SLNB result (51.8±22.9 vs 43.9±23.0, *p*=0.243).

Logistic regression analysis was performed to evaluate parameters that can be used to predict sentinel lymph node positivity. In the regression analysis, the dependent variable was lymph node positivity, and the independent variables were age, SUVmax TM, SUVmax axilla, histopathological tumor size, Estrogen receptor positivity, Progesterone receptor positivity, HER2/neu positivity, Ki67 index, and presence of Lymphovascular Invasion, PLR, NLR and LMR values. . It was observed that the increase in SUVmax Axilla value positively affected lymph node positivity (OR: 1.570, 95% CI: 1.020- 2.416, p = 0.040). Other parameters were not found to be statistically significant (p>0.05).

Discussion

Breast cancer is the most common type of cancer in women in our country, as well as all over the world. In modern breast cancer treatment, a personalized treatment strategy is determined, and the initial staging of the tumor and the predictability of the prognosis have an important role in the treatment modality to be chosen.

Among axillary imaging methods; USGis the most frequently used method because it is easily accessible and allows morphological evaluation and simultaneous biopsy. Axillary evaluation by physical examination is often considered insufficient and it is stated that it must be supported by USG [6].

The most important difference between PET/CT and other imaging methods in the evaluation of cancer is that PET/CT also evaluates the functional and metabolic properties of the tumor [7]. The sensitivity of USG in determining the sentinel lymph node varies between 48.8-87.1% [8]. In our study, a significant relationship was found between axillary involvement in physical examination (81.5%), USG (61.9%) and PET/CT (85.2%) and a positive SLNB result. Due to increased 18F-FDG uptake in metastatic lymph nodes on PET/CT; there are many studies evaluating the role of PET/CT in axillary staging before surgery in breast cancer patients, and PET/CT sensitivity in detecting axillary lymph node metastasis is reported as 84-100% and specificity as 85-100% in the literature [9]. Alavi et al. found that the SUVmax value of the tumor was higher in patients with axillary lymph node metastases (4.1±3.5) than in those without axillary metastasis (2.8±2.3) [10]. In our study, no significant difference was detected in terms of the SUVmax value of the primary tumor between the group with histopathologically axillary sentinel lymph node metastases and those without. However, a statistically significant relationship was found between axillary SUVmax value and SLNB positivity.

The sentinel lymph node is the first lymph node to receive drainage from the primary tumor site. Sentinel lymph node biopsy is a method that aims to show the first axillary lymph node that drains the primary tumor and most likely contains tumor cells [11]. Although SLNB is a very sensitive method, the surgical procedure takes time, which causes surgeons to resort to different methods to evaluate the condition of the axilla without performing SLNB. At this point, PET/CT is used as the frequently used method today and its specificity in guiding axillary dissection is reported to be between 93-100% [12]. In our study, the sensitivity of PET/CT in showing axillary positivity was found to be 57.1% and its specificity was 88.9%.

In recent years, statistical prediction models have been developed for most cancer types [13]. Memorial Sloan Kettering Cancer Center (MSKCC) nomogram is one of them [14]. Among the 48 patients included in the study, the MSKCC nomogram value in patients with positive SLNB results was higher than in patients with negative SLNB results, but this value was not found to be statistically significant.

There are many studies investigating that treatment and prognosis results of cancer patients do not depend only on tumor characteristics, but also that systemic inflammatory responses can predict prognosis and survival in different types of cancer [15-18]. It is emphasized that especially white blood cells such as neutrophils, lymphocytes, platelets and monocytes and their combinations with each other may have this effect [19]. Since there is an inflammatory response in cancer patients and lymphocytes (LYM) and platelets play an active role in this inflammation, it is thought that the platelet/lymphocyte ratio (PLR) can be used as a prognostic marker.

Platelet-to-lymphocyte ratio (PLR), which has been suggested as a prognostic marker in various types of cancer, including stomach, ovarian, colorectal, pancreatic cancers, and cholangiocarcinoma; Lymphocyte-monocyte ratio (LMR), which is recommended as a prognostic marker in head and neck cancers, bladder cancer and soft tissue sarcomas, is also expressed as other important inflammatory indices [20-23]. Although studies on breast cancer have focused mostly on NLR, there is less data on the roles of PLR and LMR in breast cancer prognosis [24]. In our study, although PLR, NLR, LMR and MPR values were higher in patients with positive SLNB results than in SLNB-negative patients, this difference was not statistically significant.

In conclusions, early detection of axillary lymph node involvement in breast cancer through physical examination and laboratory findings has a significant impact on the prognosis of the disease and treatment options. It was also seen in our study that physical examination findings, laboratory parameters, PET/CT imaging and nomograms alone have limited predictions about axillary lymph node involvement. We think that a new algorithm that includes all these parameters and combines their results will provide better results in predicting axillary lymph node involvement.

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Open Access Statement

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