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Predictive significance of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients undergoing stereotactic breast marking

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Abstract

Aim: In recent years, parallel to the progress in breast screening programs and radiological examinations, many breast abnormalities have been detected in radiological images of the breast that cannot be distinguished from malignancy and therefore require histopathological evaluation. With the advances in interventional radiology and stereotactic marking methods, histopathological evaluation has become common. It is now widely accepted that inflammation plays an effective role in cancer development and spread. This study aimed to demonstrate the predictive value of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) values obtained from a cheap and simple peripheral venous blood analysis that is easily accessible in every clinic.

Material and Methods: The retrospective database of 76 female patients who underwent excisional biopsy with mammography using the stereotactic technique in the Clinic of Surgical Oncology of the Ankara University Faculty of Medicine was examined. All blood test results and histopathology reports of the patients were examined retrospectively. The demographic and clinicopathological characteristics of the patients were found. NLR and PLR values were calculated from the number of peripheral blood cells. The data were presented as mean±standard deviation (SD) and minimum-maximum values and were statistically analyzed.

Results: Significant differentiation was observed in the statistical analysis of patients' NLR values between the patient group diagnosed with benign findings and the group of patients with invasive tumor diagnosis ($p=0.01$, <0.05). Patients with malignant tumors had high NLR values. Patients with axillary lymph node involvement also had high PLR values compared to patients in this group without involvement ($p=0.028$, <0.05).

Discussion: NLR values were high in cases of invasive malignant breast masses. PLR values were found to be high in the group with invaded lymph nodes among these patients. Further randomized prospective studies are needed for the improvement of clinical practice.

Keywords

Breast Mass, Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, Stereotactic Biopsy

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Introduction

Benign breast diseases represent a broad spectrum. Sometimes they appear with abnormalities only in imaging methods without any clinical symptoms. Most clinical breast changes in women are benign, and only 3% to 6% of cases are related to breast cancer [1]. Therefore, management of benign breast changes requires clinical, radiological, and histological diagnostic studies to exclude malignancy if necessary. Some changes increase the risk of cancer in the affected breast, while some increase the risk of breast cancer in both breasts. Breast cancer poses an increasing threat to women in proportion to their advancing age, but mortality rates have decreased due to improvements in early diagnosis and treatment modalities. Most governments have made breast cancer screenings a part of their health policy. Nearly 25-35% of breast cancers are diagnosed without palpation due to the widespread application of breast screening programs and improvements in diagnostic imaging [2, 3]. Screening by mammography increases breast cancer incidence, shifts the mean of stage distribution to earlier stages, and is associated with better survival in developed countries [4]. However, numerous breast abnormalities that cannot be distinguished from malignancy and therefore require a histological evaluation are also detected during screening. Approximately 20% of suspicious lesions are proven to be malignant after histological evaluation [5, 6].

Diagnostic methods include breast examination, imaging, and biopsy methods. One of the early diagnostic modalities of biopsy methods is excisional biopsy by stereotactic marking. When a suspicious breast finding is detected, the separation of benign and malignant tissue can only be determined by biopsy. During stereotactic breast marking, mammography, ultrasound, and sometimes magnetic resonance imaging are used to guide the placement of the biopsy needle into the breast. This method has been considered the gold standard for unpalpable lesions for the last 30 years [7]. Inflammatory markers (procalcitonin, C-reactive protein, white blood cell count, etc.) have been investigated for many solid tumors, especially gastrointestinal system malignancies [8], and these markers are accepted to have predictive value in the early diagnosis of complications in cancer patients [9]. This method has both diagnostic and therapeutic significance in 21% of patients. It is now widely recognized that chronic inflammation is closely related to the cancer development process and hematological parameters in simple, noninvasive routine blood tests are considered as inflammation markers [10]. These parameters can be obtained simply and inexpensively in all hospitals. They are requested for all patients as part of routine blood tests.

In this study, we aimed to reveal the predictive value of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) values among these markers in patients who underwent excisional biopsy of the breast by marking with the stereotactic method.

Material and Methods

In our study, the retrospective database of 76 consecutive female breast patients who were marked with mammography by the stereotactic method and for whom excisional biopsy was performed in Ankara University's Surgical Oncology Clinic between January 2017 and December 2021 was examined. Predictive data were preoperational. Patients who used steroids that could affect the peripheral blood picture, had hematological disorders, were previously diagnosed with malignancy, or had acute or chronic inflammation during the procedure were not included in the study. Clinical properties were collected including age, diagnosis, clinical TNM stage, blood test results, pathological type, and results. Cases diagnosed as malignant were staged according to the American Cancer Joint Committee's TNM staging system (AJCC 7th edition, 2010). The counts of neutrophils, thrombocytes, and lymphocytes was obtained from medical records a week before treatment. NLR was calculated by dividing the absolute count of neutrophils by the absolute count of lymphocytes. In the same manner, PLR was defined by dividing the absolute count of platelets by the absolute count of lymphocytes.

Patient selection

The study included female patients with nonpalpable breast masses with mammographic findings who were examined in our clinic or referred from external centers between January 2017 and December 2021. Mammographic findings were classified according to the Breast Imaging Reporting and Data System (BIRADS). BIRADS 3 and 4 lesions were marked with mammography.

Wire localization method

This procedure was supposed to be performed on the same day as the surgery. After local anesthesia was administered, a marking needle with a thin wire was placed in the suspicious area under the guidance of mammography imaging. The needle was then withdrawn and the wire was left inside. Part of the wire was in the breast and part was outside. The part that was left out was taped onto the breast and a plain radiograph was taken to show the location of the wire.

The procedure was performed in the radiology department, and the patient went from there to the operating room. The tip of the wire was hook-shaped, so it was clinging to the tissue and did not slip. However, it was necessary to take care not to pull the wire accidentally and not to move the arm too much. The surgeon first found the wire during surgery and then removed the tissue around it within safe limits. All samples were sent back to the radiology unit, and radiography was performed to verify the margins. The samples were then sent to the pathology laboratory for histopathological examination in storage containers containing formaldehyde.

The mean age of the patients included in the study was 51.1±8.4 years. All of the patients were female. While 45.5% of patients (n=30) had disease in the right breast, 54.5% (n=36) had disease in the left breast. Furthermore, 72% of cases (n=55) were diagnosed as benign and 28% (n=21) were diagnosed as malignant. Among the malignant cases, 57% (n=12) of the patients had in situ tumors and 43% (n=9) had invasive ductal carcinoma. Four of the patients with invasive ductal carcinoma had axillary lymph node involvement and the others had clean axilla. The mean NLR value was 2.23±1.80 (1.05-8.11) and the mean PLR value was 136.16±59.46 (47.30-356.50). The mean neutrophil count was 4.46±1.45 (1.96-7.40), mean lymphocyte count was 2.20±0.61 (0.69-4.34), and mean platelet count was 267.70±66.75 (92-483) (Tables 1 and 2).

The Ankara University Faculty of Medicine's Hospital Ethics Committee approved this study (Decision Number: İ10-628-20).

Statistical analysis

All data were presented as mean±standard deviation (SD) and minimum-maximum values, and parametric test assumptions were reviewed before differential analysis was performed. Normality was checked by the Shapiro-Wilk test, skewness, and kurtosis. Since the assumption of normality was not provided, difference analysis was performed by Mann-Whitney U test. Statistical analyses were conducted within the confidence range of 95% and values of $p<0.05$ were considered statistically significant.

Results

The demographic characteristics and blood test results of the patients included in this study are presented in Table 1 and histopathological characteristics of excised breast tissues are shown in Table 2.

In the statistical analysis performed, the PLR values of the patients did not differ statistically significantly according to the pathological diagnosis ($p>0.05$). However, a statistically significant difference was found in NLR rates between patients with a benign diagnosis and patients with an invasive tumor ($p=0.01$, <0.05). NLR ratios of patients diagnosed with invasive tumors were significantly higher than those with a benign diagnosis. PLR values of patients with axillary lymph node involvement were statistically higher in patients with a malignant diagnosis than patients with non-pathological axilla ($p=0.028$, <0.05).

Table 1. Characteristics of patients and blood test results

Characteristics	Median	Min-max values	Standard deviation
Age	51.1	20-76	8.4
NLR value	2.23	1.05-8.11	1.80
PLR value	136.16	47.30-365.50	59.46
Neutrophil count	4.46	1.96-7.40	1.45
Platelet count	267.70	92-483	66.75
Lymphocyte count	2.20	0.69-4	0.61

Table 2. Histopathological characteristics of the patients

Pathology (n=76)	Number (n)	Percentage (%)
Benign	55	72
Malign	21	28
In situ carcinoma	12	57
Invasive carcinoma	9	43
Lymphatic involvement (+)	4	44
Lymphatic involvement (-)	5	56

Discussion

In this study, we aimed to reveal the predictive importance of NLR and PLR values in patients who underwent mammography-guided marking and then an excisional breast biopsy. Our study showed that there was a significant difference in NLR values between the patient group with benign diagnoses and the patient group with invasive carcinoma. That is, the NLR values of patients diagnosed with invasive carcinoma were significantly higher than those of patients with a benign diagnosis. This differentiation was not observed in PLR values, however. In subgroup analysis, the PLR values of the patients with lymphatic metastasis in the patient group with invasive carcinoma were again found to be higher than those of patients without metastasis.

Breast cancers are often detected before they are palpated and without invasive pathological features by screening mammograms. This has significantly increased the number of breast cancers diagnosed. It also provides improvement in survival by creating a decrease in the size and stage of breast cancers during the first application. Nonpalpable breast cancers may present radiographically as masses, calcifications, masses with calcification, or changes in breast density. This radiographic appearance also depends on the age of the patient, the density of the breast, and the biology of the tumor [11]. Correct localization of these radiological changes before surgery is a great necessity. There are various methods in which wire-guided marking in association with radiology is considered as the gold standard [7].

In the early days, surgical excisional biopsy was the only option and could only be performed for masses large enough to be localized by palpation during surgery. From the mid to late 1980s, a new and rapid series of practical advances occurred in minimally invasive procedures. Initially, three hands were required for ultrasound-guided biopsy, but Lindgreen, a radiologist who was disturbed by the difficulty of this method, developed a one-handed biopsy system that included springs and buttons. Later, mammography and magnetic resonance were integrated into this stereotactic biopsy system and modified. Thus, the system was developed to perform both marking and biopsy [12]. Today, the increasing use of mammography and the initiation of breast screening programs have clinically led to an increase in occult breast cancer, enabling the diagnosis of one-third of all breast cancers without palpation. Cancers diagnosed in this way also have a different natural history and biology compared to others [13].

Many recent studies have revealed the relationship between cancer development and inflammation and demonstrated that neutrophils, lymphocytes, and platelets, which are components of peripheral blood-based inflammation, manage this process with the cytokines and chemokines they secrete [14, 15]. In this process, although the cytokine microenvironment generated by neutrophils and thrombocytes is mostly associated with tumor growth and metastasis, it has been observed that lymphocytes represent the host immune response against cancer with the cytotoxic activities of cytokines and T cells [16, 17]. Scoring systems for breast cancer have been developed using NLR and PLR values derived from these inflammation components [18]. Many researchers have studied the prognostic and predictive significance of NLR and PLR values in many solid tumors and breast cancer patients [19-21]. As a result, the numerators of NLR and PLR values (neutrophil and thrombocyte counts) are poor, while the denominators (lymphocyte count) are good result markers.

Indeed, NLR values were found to be higher in the patient group diagnosed with invasive tumors than the patient group

with a benign diagnosis in our study. The PLR values of the subgroups with axillary lymph node metastasis were also high in patients with an invasive cancer diagnosis. In a controlled retrospective study by Okuturlar et al., leukocyte, lymphocyte, and NLR values were found to be high in the breast cancer patient group [21], while in the study of Sun et al., both NLR and PLR values were found to be high in the patient group [10]. In a study conducted in our clinic in 2013, a high NLR was found in breast cancer patients with lymph node involvement, albeit it without statistical significance [22].

In the study of Koh et al., including 2059 breast cancer patients, high NLR values were significantly correlated with tumor size, lymph node involvement, and metastasis [18]. In the study of Yersal et al., no such relationship was found for the NLR value, but they found the PLR value to be higher in patients with lymph node metastasis [23].

Conclusion

Studies have shown that the NLR value is a sensitive prognostic marker and that inflammation components and the scoring systems derived from them are important factors in tumor growth and progression, but further prospective studies are still needed to reflect these findings in clinical practice.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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