# Euro Surgery 2020: Neutrophil / Lymphocyte Ratio (NLR) – Trombocyte / Lymphocyte Ratio (TLR): A Predictor of Axillary Lymph Node Metastasis in Breast Cancer Patients?- Tugba Han Öner- Baskent University School of Medicine

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**Introduction:** Sentinel lymph node biopsy is the standard application for assessing axillary disease in breast cancer patients. The Z0011 study by the American College of Surgeons Oncology Group (ACOSOG) emphasizes that axillary dissection (AD) is not required in selected patients with positive sentinel lymph nodes (SLN) [1]. It is known that axillary lymph node status is an important prognostic indicator in patients with invasive breast cancer [2,3]. Sentinel lymph node biopsy (SLNB) has been reported to cause fewer complications than axillary lymph node dissection (ALND), although extensive studies have shown wound infection, seroma, hematoma, paresthesia, and allergic reactions to isosulfan blue dye [4,5]. As components of the systemic inflammatory response, lymphocytes, neutrophils, and platelets are increasingly accepted as playing an important role in carcinogenesis and tumor progression [6]. Neutrophil / lymphocyte ratio (NLR), trombocyte / lymphocyte ratio (TLR) and Glasgow Prognostic Score are prognostic markers in cancer [7]. High NLR (> 3.3) is associated with larger tumors and later stages [8]. Similarly, high TLR has been reported to adversely affect survival in gastrointestinal cancers [9]. NLR and TLR reflect systemic inflammation and have independent prognostic value for various cancer patients [6,10]. However, the role of these biomarkers in breast cancer prognosis is less well known. Researchers have questioned whether NLR and TLR help to predict the axillary situation. This study therefore evaluated the relationships between preoperative NLR, TLR, clinicopathological factors, and axillary lymph node metastasis in stage I-III breast cancer.

**Patients and Methods:** The study recruited 158 Stage I-III breast cancer patients operated on at Baskent University Zubeyde Hanim Research Center between 2011 and 2018. Sentinel lymph node biopsy and axillary lymph node clearance in the presence of sentinel lymph node metastasis was performed on all the patients. Their medical records were examined and their medical history, age, radiological and pathological results, and laboratory data were collected. Patients who had received chemotherapy or received immunosuppressive drugs, such as glucocorticoids, cyclosporine, tacrolimus, or interferon, were excluded. The pathological data were analyzed and size of tumor, histological grade, axillary lymph node status, hormone receptor status, Cerb B2 status, presence of lymphovascular invasion (LVI) and Patients and Methods perineural invasion (PNI), radiological results, and laboratory data were evaluated. Estrogen receptor (ER) and progesterone receptor (PR) status were studied immunohistochemically (IHC). Venous blood samples were taken just before surgery. The ratio of neutrophil and trombocyte count to lymphocyte count, and NLR cut-off values were calculated for both 3.5 and 1.

**Statistical analysis:** Data were analyzed using SPPS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Mean ± standard deviation, percentage and frequency values of the variables were used. Variables were evaluated after checking for normality and homogeneity of variances (Shapiro Wilk and Levene Test). The analysis showed that the prerequisites for independent 2-group t test (Student's t test) where not met, so Mann Whitney-U test was used to compare the two groups. Categorical data were analyzed

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by Fisher's Exact Test and Chi-Square Test. In cases where the expected frequencies are less than 20%, the Monte Carlo Simulation Method was used to analyze these frequencies, ROC for distinguishing + from – lymph node metastases, and to assess cut-off point. Sensitivity and specificity calculations, positive predictive value, negative predictive value, positive and negative Likelihood Ratio (accuracy ratio), and exact accuracy were calculated. For the significance level of the tests, $p < 0.05$ and $p < 0.01$ were accepted.

**Results:** The mean age of our patients was 59.41 ± 14.34. Only 1 was male. 32% had stage I, 50.9% stage II, and 16.9% stage III disease. 62.7% had invasive ductal carcinoma, 8.7% invasive lobular carcinoma, and 28.6% other types of carcinoma. 2.2% patients had histological grade 1, 59.3% histological grade 2, and 38.5% histological grade 3. Lymphovascular invasion was detected in 31.6% patients and perineural invasion in 19.1%. 32.9% patients were C-erb B2 negative, 22.1% patients were 1 +, 15.7% patients 2 +, and 29.3% patients 3 +. In the physical examination, only 29.5% patients had palpable axillary lymph nodes while 23% patients had suspected axillary lymph nodes radiologically. 38% patients underwent modified radical mastectomy, 36.7% patients had breast-conserving surgery + sentinel lymph node biopsy, 20.3% patients had breast-conserving surgery + axillary dissection, and 5.1% patients had simple mastectomy + sentinel lymph node biopsy. There were 65 (41.9%) patients with lymph node metastases (Table 1).

The patients' mean neutrophil, lymphocyte, and platelet counts were 4549.13 ± 1991.2, 2484.66 ± 1105.47, and 276575.95 ± 68361.1 respectively. The mean tumor radiological size was 19.44 ± 11.34mm, mean number of lymph node metastases 2.19 ± 5.6, mean tumor size 20.3 ± 14.8 mm and mean number of resected lymph nodes 11.73 ± 8.9. The mean TLR was 123.81 ± 54.29 while the mean NLR was 1.98 ± 0.83 (Table 2). Min Max ± Std. Deviation Age 27 92 59.41 ± 14.349 Neutrophil /µl 1470 21002 4549.13 ± 1991.242 Lymphocyte / µl 741 12785 2484.66 ± 1105.47 Platelet / µl 30000 470000 276575.95 ± 68361.096 Radiological Tumor Size mm 0 60.0 19.439 ± 11.3431 Tumor Size mm 4 150.0 20.297 ± 14.8128 Lymph Node Resected 1 40 11.73 ± 8.863 Metastatic Lymph Node Count 0 34 2.19 ± 5.609 ER 0 100 65.32 ± 37.588 PR 0 100 47.58 ± 38.878 TLR 8.02 551.96 123.81 ± 54.29 NLR 0.72 5.16 1.98 ± 0.83 Table 2: Patient characteristics, clinical, radiological, pathological, and and laboratory findings. We found statistically significant differences between patients with and without lymph node metastasis in neutrophil, platelet count, and (radiological and pathological) tumor size. Neutrophil and trombocyte values were significantly higher in patients with lymph node metastasis. NLR and TLR values were higher in patients with axillary lymph node metastasis, although this was not statistically significant. Axillary lymph node metastasis was not associated with age, lymphocyte, monocyte, ER, or PR. As expected, tumor size was statistically significantly lower in patients without lymph node metastases (Table 3). There were statistically significant relationships between axillary lymph node metastasis and palpability of breast mass and the axillary lymph node, lymphovascular invasion, and radiological BIRADS score of the mass. However, there were no statistically significant relationships between tumor histology, grade, presence of perineural invasion, C erb B2 status, and lymph node metastasis. Axillary lymph node metastasis was statistically significantly more frequent in the presence of LVI. As expected, axillary lymph node metastasis was statistically significantly more frequent in the presence of palpable mass and palpable axillary lymph nodes in the physical examination, with lymphadenopathy detected by the radiological examination, and with high BIRADS scores (Table 4).

metastasis, neutrophil, platelet counts, LVI status, radiological and pathological mass size, and presence of radiological axillary lymphadenopathy are statistically significant independent variables. They can therefore provide information to help surgeons decide on the treatment of breast cancer patients with certain NLR values ($NLR < 1$ and $NLR \geq 3.5$).

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