Original Article

International Journal of Integrated Health Sciences (IIJHS)
ISSN Print: 2302-1381; ISSN Online: 2338-4506

# Association Between Neutrophil-to-Lymphocyte Ratio and Recurrence in Triple Negative Breast Cancer Patients

**Christian Sihite, Raden Yohana, Kiki Lukman, Kiki Ahmad Rizki, Euis Maryani, Putie Hapsari**

**Departement of Surgery, Faculty of Medicine Universitas Padjadjaran-Dr. Hasan Sadikin General Hospital, Bandung, Indonesia**

**Article History**

Received: January 18, 2026
Accepted: April 29, 2026
Published: June 30, 2026

**DOI:** 10.15850/ijihs.v14n1.4743
**IJIHS. 2026;14(1):51–57**

**Correspondence:**
Christian Sihite,
Departement of Surgery, Faculty of Medicine Universitas Padjadjaran-Dr. Hasan Sadikin General Hospital, Bandung, Indonesia
Email: dr.christiansihite@gmail.com

## Abstract

**Background**: Triple-negative breast cancer (TNBC) is the most aggressive form of cancer, characterized by a high recurrence rate and a poor prognosis. The lack of widely accessible predictive biomarkers, such as PD-L1, poses a challenge in predicting recurrence. This study aimed to describe the Neutrophil-Lymphocyte Ratio (NLR), an indicator of systemic inflammation, as a potential prognostic biomarker for recurrent TNBC because it is simple, inexpensive, and can be performed in different healthcare facility settings.

**Objective**: To study the NLR pattern in TNBC stage 2 and identify the association between NLR and recurrence.

Methods: This cohort retrospective study obtained data from the medical records of TNBC patients treated at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. Neutrophil-Lymphocyte Ratio (NLR) values and recurrence status were analyzed in 56 consecutive cases.

**Results**: There was a significant correlation between NLR values and recurrence events in patients with TNBC. Patients with recurrence had higher NLR values (3.83 ± 2.39) compared to those without recurrence (1.81 ± 0.57). The highest NRL value in the recurrence group reached 11.14. This difference was statistically significant ($p < 0.001$).

**Conclusion**: NLR has the potential to serve as a simple and effective predictive biomarker for identifying the risk of recurrence in TNBC patients. The use of NLR may provide an initial alternative in determining prognosis and guiding patient follow-up strategies, especially in healthcare facilities with limited access to biomolecular tests such as PD-L1.

**Keywords**: Biomarker, inflammation, neutrophil-lymphocyte ratio, recurrence breast cancer, triple negative breast cancer

## Introduction

TNBC is defined as cancer that lacks progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), or estrogen receptor (ER).[1] The highest risk of recurrence in TNBC patients was the first 3 years after the disease diagnosis and moreover than 35% of deaths by breast cancer are caused by TNBC.[2] Furthermore, one in five TNBC patients will die of metastatic disease within five years. Five-year survival rates for local, regional, and metastatic TNBC are 91%, 65%, and 11%, respectively.[3]

TNBC recurrence is often thought to be influenced by inflammatory factors and the immune system. Previous studies in breast cancer cells and animal models have confirmed that inflammatory factors play a key role in breast cancer cell proliferation, invasion, and metastasis.[4–6] Systemic inflammatory factors have been shown to be closely related to the tumor microenvironment.[7] Systemic inflammatory factors increase the invasion and

proliferation of cancer cells, thus promoting tumor growth and progression.[8]

The neutrophil-to-lymphocyte ratio (NLR), simple ratio between the neutrophil and lymphocyte counts measured in peripheral blood, is a biomarker which conjugates two faces of the immune system: the innate immune response, mainly due to neutrophils, and adaptive immunity, supported by lymphocytes. NLR measurement is simple, inexpensive, and widely accessible, making it a promising prognostic biomarker in clinical practice.[9]

Previous studies have demonstrated that elevated pre-treatment NLR is associated with poor prognosis in various malignancies, including TNBC.[8,10] However, data regarding the association between NLR and recurrence in TNBC patients remain limited, particularly in developing countries. Therefore, this study aimed to evaluate the association between pre-chemotherapy NLR values and recurrence in patients with stage II TNBC treated at a tertiary referral hospital. Few studies have examined this association in the Indonesian TNBC population, where access to molecular biomarkers is often limited and a low-cost marker derived from a routine blood count may therefore be particularly valuable.

## Methods

This retrospective comparative study comprised 44 surgically treated, post-chemotherapy female patients with stage II TNBC who were admitted to the Department of Surgical Oncology between 2020 and 2025 at Dr. Hasan Sadikin General Hospital, Bandung.

Clinical data were obtained from the medical records. The study comprised 22 patients with recurrence and 22 without recurrence. Age, histopathological type and grade, chemotherapy regimen and response, pre-chemotherapy NLR, clinical stage, tumor (T) category, and nodal (N) status were extracted. Records with incomplete data were excluded. In all patients, NLR was measured before any therapy. All patients underwent follow-up imaging with ultrasound, CT, or MRI to detect recurrence status during post-treatment surveillance. Recurrence was defined as imaging-confirmed or biopsy-proven reappearance of disease after completion of primary treatment, and was classified as local (ipsilateral breast or chest wall), regional (ipsilateral axillary, internal mammary, or supraclavicular nodes), or distant (any other site). Patients were followed from completion of primary treatment until the first recurrence event or the last available follow-up within the 2020 to 2025 study period. Ethical clearance for this study was obtained from Ethics committee of DR. Hasan Sadikin General Hospital, Bandung, under ethical approval number DP.04.03/D.XIV.4.4/2032/2025.

Statistical analysis was performed using IBM SPSS Statistics. Continuous variables were summarized as mean with standard deviation and as median with range, and categorical variables as counts and percentages. The distribution of continuous variables was assessed with the Shapiro-Wilk test. NLR was not normally distributed and was therefore compared between groups with the Mann-Whitney U test, whereas age was compared with the independent-samples t test. Categorical variables were compared with the Pearson chi-square test, or the Fisher exact test when expected cell counts were small. The association between NLR and recurrence was further examined using binary logistic regression, with results reported as odds ratios and 95% confidence intervals, both unadjusted and adjusted for age and nodal status. The discriminative ability of NLR was assessed using the area under the receiver operating characteristic curve, with the optimal cut-off identified by the Youden index. A two-sided p value below 0.05 was considered statistically significant.

## Result

A total of 44 patients met the inclusion criteria and were analyzed in two groups of equal size: 22 patients with documented recurrence and 22 without recurrence. All patients were female. The baseline characteristics of the two groups are summarized in Table 1.

The two groups were comparable in age (p=0.276), tumor (T) category, nodal (N) status, and clinical stage (all $p > 0.05$). Histopathological grade differed between groups, with grade III tumors more frequent among patients with recurrence (18 of 22, 81.8%) than among those without recurrence (10 of 22, 45.5%; $p = 0.027$ for grade II versus III). A complete response to chemotherapy was much less frequent in the recurrence group (2 of 22) than in the non-recurrence group (16 of 22); because response was assessed during follow-up, this association is best interpreted as a correlate of recurrence rather than a predictor. Among the 22 patients with recurrence, recurrence was most often distant (11, 50.0%) or regional (6, 27.3%), and

**Table 1 Baseline characteristics of the study population (n=44).**

| Variable | Recurrence (n=22) | Non-recurrence (n=22) | Total (n=44) | p-value |
|---|---|---|---|---|
| Age (years) | | | | |
| Mean ± SD | 52.09 ± 9.54 | 49.05 ± 8.75 | 50.57 ± 9.18 | 0.276a |
| Median (range) | 51.5 (37-68) | 50 (32-69) | 51 (32-69) | |
| Histopathology | | | | |
| No special type (NST) | 17 (77.3) | 19 (86.4) | 36 (81.8) | 1.000b |
| Invasive ductal carcinoma | 1 (4.5) | 0 (0.0) | 1 (2.3) | |
| Invasive lobular carcinoma | 3 (13.6) | 2 (9.1) | 5 (11.4) | |
| Mucinous carcinoma | 0 (0.0) | 1 (4.5) | 1 (2.3) | |
| Invasive solid papillary carcinoma | 1 (4.5) | 0 (0.0) | 1 (2.3) | |
| Tumor (T) | | | | |
| T2 | 10 (45.5) | 12 (54.5) | 22 (50.0) | 0.763b |
| T3 | 12 (54.5) | 10 (45.5) | 22 (50.0) | |
| Node (N) | | | | |
| N0 | 16 (72.7) | 19 (86.4) | 35 (79.5) | 0.457b |
| N1 | 6 (27.3) | 3 (13.6) | 9 (20.5) | |
| Clinical stage | | | | |
| IIa | 4 (18.2) | 9 (40.9) | 13 (29.5) | 0.185b |
| IIb | 18 (81.8) | 13 (59.1) | 31 (70.5) | |
| Grade | | | | |
| I | 0 (0.0) | 1 (4.5) | 1 (2.3) | 0.027c |
| II | 4 (18.2) | 11 (50.0) | 15 (34.1) | |
| III | 18 (81.8) | 10 (45.5) | 28 (63.6) | |
| First-line chemotherapy | | | | |
| AC (doxorubicin-cyclophosphamide) | 3 (13.6) | 1 (4.5) | 4 (9.1) | d |
| Docetaxel-carboplatin | 8 (36.4) | 8 (36.4) | 16 (36.4) | |
| Paclitaxel-carboplatin | 7 (31.8) | 4 (18.2) | 11 (25.0) | |
| Doxorubicin-carboplatin | 0 (0.0) | 1 (4.5) | 1 (2.3) | |
| FAC | 0 (0.0) | 5 (22.7) | 5 (11.4) | |
| Paclitaxel (other) | 1 (4.5) | 0 (0.0) | 1 (2.3) | |
| Not documented | 3 (13.6) | 3 (13.6) | 6 (13.6) | |
| Chemotherapy response | | | | |
| Complete | 2 (9.1) | 16 (72.7) | 18 (40.9) | <0.001c |
| Partial | 13 (59.1) | 4 (18.2) | 17 (38.6) | |
| Stable | 1 (4.5) | 0 (0.0) | 1 (2.3) | |
| Progressive | 2 (9.1) | 0 (0.0) | 2 (4.5) | |
| Not documented | 4 (18.2) | 2 (9.1) | 6 (13.6) | |

Note: Data are presented as n (%) unless otherwise indicated. Percentages represent column percentages. p-values were calculated using the independent-samples t test or Fisher's exact test, as appropriate. NST = no special type (invasive ductal carcinoma). Chemotherapy regimen and treatment response data were unavailable for six patients

**Table 2 Comparison of Pre-Chemotherapy Nlr Between Patients With And Without Recurrence**

| NLR | Recurrence (n=22) | Non-recurrence (n=22) | Total (n=44) |
|---|---|---|---|
| Mean ± SD | 3.83 ± 2.40 | 1.86 ± 0.64 | 2.85 ± 2.00 |
| Median | 3.11 | 1.90 | 2.17 |
| Range (min-max) | 1.26-11.14 | 0.71-3.22 | 0.71-11.14 |

Comparison between groups by Mann-Whitney U test, $p < 0.001$. NLR, neutrophil-to-lymphocyte ratio.

**Table 3 Binary Logistic Regression For Recurrence**

| Variable | Unadjusted OR (95% CI) | p | Adjusted OR (95% CI)[a] | p |
|---|---|---|---|---|
| NLR (per 1-unit increase) | 4.14 (1.57-10.97) | 0.004 | 7.28 (1.98-26.78) | 0.003 |
| Age (per 1-year increase) | 1.04 (0.97-1.11) | 0.271 | 1.11 (1.00-1.24) | 0.050 |
| Nodal status (N1 vs N0) | 2.38 (0.51-11.05) | 0.270 | 3.76 (0.56-25.50) | 0.175 |

adjusted model includes NLR, age, and nodal status (n = 44; 22 events). Owing to the small number of events, the adjusted estimates are imprecise. OR, odds ratio; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio

most events occurred between one and five years after diagnosis (17, 77.3%).

Pre-chemotherapy NLR was significantly higher in patients with recurrence than in those without recurrence (Table 2). The median NLR was 3.11 in the recurrence group and 1.90 in the non-recurrence group ($p < 0.001$, Mann-Whitney U test).

In binary logistic regression, each one-unit increase in pre-chemotherapy NLR was associated with higher odds of recurrence (unadjusted odds ratio [OR] 4.14, 95% CI 1.57 to 10.97; $p = 0.004$). After adjustment for age and nodal status, the association persisted (adjusted OR 7.28, 95% CI 1.98 to 26.78; $p = 0.003$). With only 22 recurrence events, however, the adjusted model is based on few events per variable, so its estimates are imprecise and should be regarded as exploratory, as reflected in the wide confidence intervals (Table 3).

The area under the receiver operating

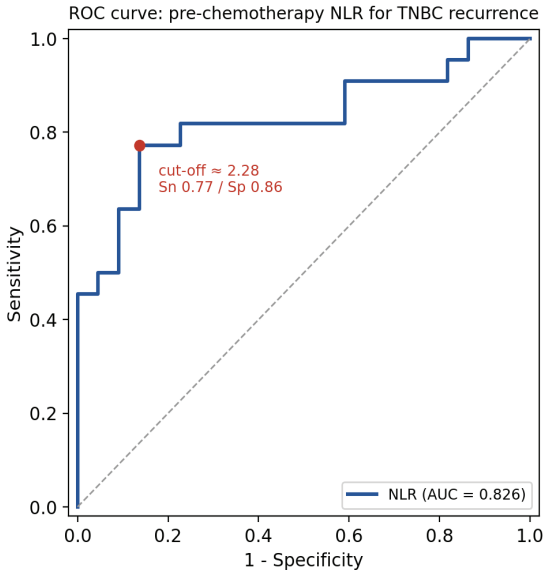


**Fig 1. Receiver Operating Characteristic Curve of Pre-Chemotherapy NLR For Predicting Recurrence (AUC 0.83)**

characteristic curve for pre-chemotherapy NLR was 0.83 (95% CI 0.70 to 0.95; Figure 1), indicating acceptable discrimination between patients with and without recurrence. At an exploratory cut-off of 2.28 identified using the Youden index, sensitivity was 77% and specificity was 86%. This cut-off is data-derived and would require validation in an independent cohort before any clinical application.

## Discussion

TNBC is defined as cancer lacking progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), or estrogen receptor (ER). Clinical characteristics of TNBC include a higher chance of recurrence, shorter overall survival (OS), and disease-free survival (DFS) compared to other breast cancer subtypes, as well as a more aggressive behavior.[1,3] Due to the lack of biomarkers in early-stage TNBC (stages I to III), patients experience disease recurrence in 50% of cases, and 37% of patients die within 5 years of surgery.[1,3]

Lymphocytes are one of the white blood cells (leukocytes) in the human immune system. Lymphocytes include natural killer cells (which function in innate immunity mediated by cytotoxic mechanisms). Lymphocytes are composed of T cells (for cell-mediated cytotoxic adaptive immunity) and B cells (for antibody-mediated adaptive immunity and form humoral immunity). Lymphocytes are the main cell type found in lymph nodes. Lymphocytes constitute between 25% of white blood cells.[10,11]

In contrast, neutrophils can also act as tumor-promoting leukocytes, capable of stimulating and suppressing antitumor immune responses in tumorigenesis; participating in the metastatic cascade; being effectors of angiogenesis; promoting the spread of tumor cells and endothelial cells into the circulation, thereby contributing to shifting the inflammatory response towards a tumor-promoting one.[12,13] Some immunocytes, such as neutrophils, can secrete vascular endothelial growth factor (VEGF) which promotes tumor progression; therefore, an increase in neutrophil numbers can stimulate tumor angiogenesis and contribute to disease progression, thus leading to a negative correlation between neutrophil density and patient survival.[13]

This study found that a higher pre-chemotherapy NLR was associated with TNBC recurrence. In unadjusted logistic regression, each one-unit increase in NLR was associated with approximately four-fold higher odds of recurrence (OR 4.14, 95% CI 1.57 to 10.97); after adjustment for age and nodal status the association persisted, although the small number of events means the adjusted estimate is imprecise and should be interpreted with caution (OR 7.28, 95% CI 1.98 to 26.78). NLR also showed acceptable discrimination for recurrence (area under the ROC curve 0.83, 95% CI 0.70 to 0.95). Most recurrences occurred between one and five years after diagnosis and were most often distant. NLR is a simple marker that has previously been implicated as a potential prognostic and predictive biomarker after neoadjuvant chemotherapy for early breast cancer.[14]

NLR reflects the intensity of the immune inflammatory response and stress response to cancer. It is a sensitive marker of cancer-related systemic inflammation, along with other inflammatory markers such as CRP, albumin, platelets, and fibrinogen.[15] The NLR reflects the balance of systemic inflammation between neutrophils (pro-tumor through the release of cytokines, NETs, and suppression of adaptive immunity) and lymphocytes (anti-tumor, primarily T cells).[16,17] TNBC is known to be more immunogenic and aggressive; A high NLR indicates a predominance of pro-tumor inflammation and/or decreased immune competence, thus supporting the finding that the risk of relapse increases with a higher NLR.[16,17] A higher NLR is consistent with a predominance of pro-tumor inflammation and reduced immune competence, in keeping with the higher risk of recurrence observed at higher NLR values.

Given its simplicity and cost-effectiveness, NLR may serve as a valuable prognostic biomarker to guide risk stratification and surveillance strategies, particularly in healthcare settings with limited access to advanced molecular testing such as PD-L1 expression analysis. More studies are needed to assess the potential role of NLR in guiding treatment decisions, patient selection and clinical trial design. Routine examination of full blood count in preoperative workup positions NLR as a cost-effective adjunct in risk stratification.[14,18]

This study has several limitations. It was a single-centre, retrospective study with a small sample, and the two groups were defined by recurrence status rather than followed forward over time, so the design is comparative (case-control in structure); absolute recurrence risk therefore cannot be estimated, and the

adjusted regression estimates are based on few events and are unstable. Several prognostic factors were unevenly distributed and may confound the association between NLR and recurrence, including histopathological grade, nodal status, tumor burden, and differences in chemotherapy regimen and response; residual confounding by unmeasured factors is also likely. Follow-up duration was not uniformly documented for patients without recurrence, which may misclassify recurrence status. Finally, absolute neutrophil and lymphocyte counts were not separately available, so the reported NLR values could not be independently recomputed. These findings should therefore be regarded as hypothesis-generating and require confirmation in larger, prospective, multi-centre studies.

In this retrospective comparative study, a higher pre-chemotherapy NLR was associated with recurrence in patients with stage II TNBC. NLR is inexpensive and routinely available and may help support risk stratification, but these findings are exploratory and require prospective validation before any clinical use.

## References


1. Yin L, Duan JJ, Bian XW, Yu SC. Triple-negative breast cancer molecular subtyping and treatment progress. Breast Cancer Res. 2020;22(1):61. doi: 10.1186/s13058-020-01296-5.
2. Cai SL, Liu JJ, Liu YX, Yu SH, Liu X, Lin XQ, *et al*. Characteristics of recurrence, predictors for relapse and prognosis of rapid relapse triple-negative breast cancer. Front Oncol. 2023;13:1119611. doi: 10.3389/fonc.2023.1119611.
3. Gupta GK, Collier AL, Lee D, Hoefer RA, Zheleva V, Siewertsz van Reesema LL, *et al*. Perspectives on triple-negative breast cancer: current treatment strategies, unmet needs, and potential targets for future therapies. Cancers (Basel). 2020;12(9):2392. doi: 10.3390/cancers12092392.
4. Ciurescu S, Buciu V, Şerban D, Borozan F, Tomescu L, Cobec IM, *et al*. Role of cytokines in breast cancer: a systematic review and meta-analysis. Biomedicines. 2025;13(9):2203. doi: 10.3390/biomedicines13092203.
5. Rosado-Sanz M, Martínez-Alarcón N, Abellán-Soriano A, Golfe R, Trinidad EM, Font de Mora J. Cytokine networks in triple-negative breast cancer: mechanisms, therapeutic targets, and emerging strategies. Biomedicines. 2025;13(8):1945. doi: 10.3390/biomedicines13081945.
6. Faria SS, Costantini S, de Lima VCC, de Andrade VP, Rialland M, Cedric R, *et al*. NLRP3 inflammasome-mediated cytokine production and pyroptosis cell death in breast cancer. J Biomed Sci. 2021;28:26. doi: 10.1186/s12929-021-00724-8.
7. Greten FR, Grivennikov SI. Inflammation and cancer: triggers, mechanisms, and consequences. Immunity. 2019;51(1):27–41. doi: 10.1016/j.immuni.2019.06.025.
8. Hanahan D. Hallmarks of cancer: new dimensions. Cancer Discov. 2022;12(1):31–46. doi: 10.1158/2159-8290.CD-21-1059.
9. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. Int J Mol Sci. 2022;23(7):3636. doi: 10.3390/ijms23073636.
10. Abbas AK, Lichtman AH, Pillai S. Basic immunology: functions and disorders of the immune system. 6th ed. Philadelphia: Elsevier; 2020.
11. Tigner A, Ibrahim SA, Murray IV. Histology, white blood cell. [Updated 2026 Feb 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan– [cited 2026 Aug 7]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563148/
12. Yang S, Sun B, Li J, Li N, Zhang A, Zhang X, *et al*. Neutrophil extracellular traps promote angiogenesis in gastric cancer. Cell Commun Signal. 2023;21:176. doi: 10.1186/s12964-023-01196-z.
13. Huang X, Nepovimova E, Adam V, Sivak L, Heger Z, Valko M, *et al*. Neutrophils in cancer immunotherapy: friends or foes?. Mol Cancer. 2024;23:107. doi: 10.1186/s12943-024-02004-z.
14. Polho GB, Murazawa LK, Oliveira VV, Pinheiro VR, Labanda DDCP, Shinkado YR, *et al*. Neutrophil-to-lymphocyte ratio predicts long-term survival in early triple negative breast

cancer treated with neoadjuvant chemotherapy. Ecancermedicalscience. 2025;19:2034. doi: 10.3332/ecancer.2025.2034.
15. Birsin Z, Nazlı İ, Alkan O, Odabaşı Bükün H, Günaltılı M, Çerme E, *et al*. Inflammatory and nutritional markers predicting pathological complete response to neoadjuvant therapy in HER2-positive breast cancer: a multicenter real-world study. J Clin Med. 2025;14(20):7271. doi: 10.3390/jcm14207271.
16. Grassadonia A, Graziano V, Iezzi L, Vici P, Barba M, Pizzuti L, *et al*. Prognostic relevance of neutrophil to lymphocyte ratio (NLR) in luminal breast cancer: a retrospective analysis in the neoadjuvant setting. Cells. 2021;10(7):1685. doi: 10.3390/cells10071685.
17. Pieniążek M, Polakiewicz-Gilowska A, Las-Jankowska M, Wronowicz J, Jarząb M, Łacko A, *et al*. Baseline hemoglobin and neutrophil-to-lymphocyte ratio as prognostic biomarkers in patients with metastatic triple negative breast cancer treated with sacituzumab govitecan in second line and beyond: a real-world analysis. Breast Cancer Res Treat. 2025;214(3):397–407. doi: 10.1007/s10549-025-07825-0.
18. Jaffer AA, Cullinane C, Davey MG, Jalali A, Buckley J, Baban C, *et al*. Evaluating the neutrophil-lymphocyte ratio as a predictor of long-term oncological and survival outcomes in patients treated surgically for breast cancer. Clin Breast Cancer. 2026;26(2):136–45.e2. doi: 10.1016/j.clbc.2025.08.015.