Predicting prognosis of patients with triple-negative breast cancer undergoing neoadjuvant chemotherapy based on inflammatory status at different time points: A propensity score matching analysis

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Abstract. Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer with limited targeted treatment options, making the identification of reliable prognostic markers crucial for improving patient outcomes. The present study aimed to assess the predictive ability of pre-chemotherapy and pre-surgery inflammatory status on the prognosis of patients with TNBC undergoing neoadjuvant therapy. A total of 422 patients with TNBC who received neoadjuvant chemotherapy at the Inner Mongolia People's Hospital between January 2017 and December 2022 were selected for analysis. Fasting venous blood samples were collected 1 day prior to chemotherapy and 1 day prior to surgery to assess and calculate inflammatory markers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI). The optimal cut-off values of the inflammatory markers were determined using receiver operating characteristic curves. Survival analysis was used to evaluate the differences in survival and significant prognostic factors. Propensity score matching (PSM) analysis was performed to further asses the prognostic value of the relevant factors. Survival analysis indicated that patients with high pre-chemotherapy and pre-surgery NLR, PLR, SII and SIRI scores exhibited shorter overall survival (OS) rates compared with those with low scores (all P<0.05). Multivariate analysis revealed that tumor-node-metastasis stage, pathological complete response and pre-surgery SII were independent prognostic factors for OS. Following PSM, the area under the curve for SII was 0.642 and patients with high SII scores exhibited shorter OS rates than those with low scores (χ^2=8.452; P=0.004). Therefore, these results indicated that both pre-chemotherapy and pre-surgery inflammatory statuses are associated with the OS of patients with TNBC undergoing neoadjuvant chemotherapy, notably pre-surgery SII.

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Introduction

Breast cancer is the most frequently diagnosed cancer in women and the second leading cause of cancer-related death among women worldwide. According to global cancer statistics, breast cancer was the most frequently cancer worldwide in 2020, representing 11.7% of all cases (2,261,419 cases) and 6.9% of cancer-related deaths (684,996 deaths) (1). Despite continuous advancements in treatment methods and medications, the incidence of new cases continues to rise and breast cancer remains a major threat to the health of women (2). Triple-negative breast cancer (TNBC) is a particularly aggressive subtype characterized by the lack of expression of estrogen receptors (ER), progesterone receptors and human epidermal growth factor receptor 2 (HER2) (3). Although TNBC accounts for a relatively low proportion of all new cases (only 10-20%), its aggressive nature and resistance to several treatments render its management a major challenge (4).

In recent years, notable progress has been made in neoadjuvant chemotherapy for patients with TNBC (5). Several patients experience significant tumor shrinkage following neoadjuvant chemotherapy, which increases the likelihood of surgical resection (6). However, due to the high malignancy of TNBC, certain patients may still experience recurrence and metastasis, even following comprehensive neoadjuvant treatment and surgery (7). Therefore, the identification of factors that can predict clinical outcomes and prompt timely intervention for high-risk patients is crucial for improving TNBC treatment.

The inflammatory status is a key factor influencing the prognosis of patients with solid tumors. A 2024 analysis by Zhang *et al* (8) on 259,435 women reported that inflammatory status may be an important factor in the development of breast cancer. In addition, several studies have reported the notable potential of inflammatory markers in identifying high-risk patients with breast cancer, including those with TNBC. Grassadonia *et al* (9) analyzed the neutrophil-to-lymphocyte ratio (NLR) in patients with breast cancer undergoing neoadjuvant chemotherapy. After collecting and analyzing data from 168 patients, the authors concluded that NLR is a predictive factor for breast cancer recurrence. A meta-analysis by Cupp *et al* (10), which integrated all studies on NLR up to May 29, 2020, reported that NLR is a notable prognostic factor for multiple high-risk cancers. The application of inflammatory markers in patients with breast cancer who receive neoadjuvant chemotherapy has also gained attention (11). However, it is important to emphasize that the goal of neoadjuvant chemotherapy is to achieve surgical resection and the pre-operative inflammatory status is equally worth noting. Therefore, the present study aimed to assess the role of multiple inflammatory markers prior to surgery in predicting clinical outcomes for patients with TNBC.

Materials and methods

Patients. The present study included 422 female patients with breast cancer who received treatment at Inner Mongolia People's Hospital (Hohhot, China) between January 2017 and December 2022. The inclusion criteria were as follows: i) Diagnosis of TNBC via histopathological examination; ii) ≥3 cycles of neoadjuvant chemotherapy; iii) surgery following neoadjuvant chemotherapy; iv) age of >18 years; and v) complete clinical data and follow-up records. Patients with acute or chronic inflammatory diseases and those lost to follow-up were excluded from the present study. Written informed consent was obtained from all participants. Furthermore, the present study adhered to the principles of the Declaration of Helsinki and its amendments and was approved by the Ethics Committee of the Inner Mongolia People's Hospital (Hohhot, China; approval no. 202404704L).

Data collection and follow-up. Basic patient information was collected through the hospital medical record system. Moreover, blood samples were obtained from the elbow veins of the patients prior to the first chemotherapy session and the day prior to surgery, with 5 ml fasting venous blood collected at each time point. The samples were tested within 10 min. A total of 2 ml blood was transferred into an EDTA anticoagulant tube and thoroughly mixed, followed by automatic analysis of routine hematological parameters using a BC-6000 Automatic Hematology Analyzer (Shenzhen Mindray Bio-Medical Electronics Co., Ltd.). In addition, 3 ml blood was transferred to a dry tube and allowed to stand at room temperature to obtain the supernatant, which was subsequently centrifuged at 3,260 x g for 5 min at room temperature (20-25˚C) using a Sorvall™ ST 8 Small Benchtop Centrifuge (Thermo Fisher Scientific, Inc.) to separate the serum. Serum biochemical parameters were automatically measured using the cobas® c 311 analyzer (Roche Diagnostics GmbH).

The primary endpoint of the present study was the overall survival (OS), defined as the period from the start of treatment to death from any cause or the time of the last follow-up. OS was determined via routine telephone follow-up, with a follow-up period of 80 months.

Inflammatory markers. In the present study, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI) were calculated for each patient prior to chemotherapy and the day prior to surgery. The calculation formulae are presented in Table I.

Furthermore, the optimal cutoff values for the inflammatory markers were determined using the maximum Youden index calculated from receiver operating characteristic (ROC) curves and the patients were divided into two groups. The optimal cutoff values for NLR, PLR, SII and SIRI prior to chemotherapy were 1.74, 150.50, 403.15 and 0.60, respectively. The optimal cutoff values for NLR, PLR, SII and SIRI prior to surgery were 1.78, 149.99, 397.21 and 1.43, respectively.

Statistical analysis. Continuous variables were expressed as mean ± standard deviation and analyzed using an independent sample t-test. Categorical variables were presented as n (%) and analyzed using the chi-square (χ^2) test or Fisher's exact test. Survival differences between different patient groups were compared using Kaplan-Meier survival curves and log-rank tests. Univariate and multivariate Cox proportional hazard regression analyses were performed to assess the factors influencing prognosis and Least Absolute Shrinkage and Selection Operator (LASSO) regression was used to detect potential multicollinearity. The associated risks are presented as the hazard ratio (HR) with 95% confidence intervals. Propensity score matching (PSM) was further applied to analyze the prognostic value of the related indicators. All statistical analyses were performed using SPSS 25 (IBM Corp.), GraphPad 8.0 (Dotmatics) and R 4.3.1 (www.r-project.org). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 422 patients were included in the present study, with a mean age of 50.07±9.64 years. Among all patients, 35 (8.3%) had a family history of breast cancer, suggesting a potential genetic predisposition, and 220 (52.1%) were postmenopausal, which could influence the prognosis and treatment response. The TNM staging system, developed by the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC), is a globally recognized classification method that assesses tumor size (T), regional lymph node involvement (N) and distant metastasis (M) to determine the extent of cancer progression (12). A total of 212 (50.2%) patients exhibited tumor-node-metastasis (TNM) stage II, indicating a more localized stage of cancer, while 210 (49.8%) patients were at TNM stage III, reflecting a more advanced stage. Postoperative pathological examination revealed that 131 (31.0%) patients achieved a pathological complete response (pCR), highlighting a favorable response to the treatment in

Table I. Calculation formulae for inflammatory markers.

Marker	Formula
NLR	Neutrophils (10^9/l)/lymphocytes (10^9/l)
PLR	Platelets (10^9/l)/lymphocytes (10^9/l)
SII	Platelets (10^9/l) x neutrophils (10^9/l)/ lymphocytes (10^9/l)
SIRI	Neutrophils (10^9/l) x neutrophils (10^9/l)/ lymphocytes (10^9/l)

NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammatory response index.

this proportion of patients. The detailed patient information is presented in Table II.

Survival analysis of inflammatory markers. Following grouping of the patients based on the optimal cutoff values, the survival curves for the inflammatory indices prior to chemotherapy and prior to surgery were plotted. The results indicated that higher levels of pre-chemotherapy NLR (χ^2=2.617; P=0.022), PLR (χ^2=3.556; P=0.009), SII (χ^2=2.114; P=0.042) and SIRI (χ^2=1.933; P=0.047) were significantly associated with a lower OS (Fig. 1). In addition, higher levels of pre-surgery NLR (χ^2=3.417; P=0.017), PLR (χ^2=2.353; P=0.018), SII (χ^2=5.887; P<0.001) and SIRI (χ^2=4.406; P=0.017) were significantly associated with a lower OS (Fig. 2).

Cox survival analysis. To further assess the factors influencing prognosis, univariate Cox regression analysis was performed on the main patient clinical information and inflammatory indices. The results indicated that TNM stage, pCR and all pre-chemotherapy and pre-surgery inflammatory indices were significantly associated with the patient OS (all P<0.05; Table III).

Due to the inevitable significant multicollinearity among the same inflammatory indices, LASSO regression analysis was performed on the significant indicators from univariate analysis prior to performing multivariate analysis (Fig. 3A). The LASSO model achieved the optimal λ value of 0.04 following 287 iterations (Fig. 3B). Ultimately, pre-chemotherapy SII, pre-chemotherapy SIRI, pre-surgery NLR and pre-surgery PLR were demonstrated to exhibit multicollinearity and were excluded from the Cox multivariate model. The results of the multivariate analysis revealed that TNM stage (HR=3.569; P=0.001), pCR (HR=2.619; P=0.012) and pre-surgery SII (HR=0.453; P=0.006) were independent prognostic factors in the present study (Table IV).

PSM analysis. As pre-operative SII was identified as an independent prognostic factor, PSM analysis was performed. Prior to PSM, SII was significantly associated with age (P=0.001), blood type (P=0.032), TNM stage (P=0.018) and P53 status (P=0.031) (Table V), which partially reflected its prognostic value. Following matching for age, blood type, TNM stage and P53 status, a total of 138 patients were included in the analysis, consisting of 69 patients with low SII and 69 patients with high SII scores. Following PSM, no significant differences were observed in the clinical and pathological data between the two groups (all P>0.05; Table V).

Table II. Characteristics of patients with triple-negative breast cancer in the present study.

Characteristic	Patients with TNBC (n=422)
Age, years	50.07±9.64
BMI, kg/m^2	24.94±4.28
Family history	
Yes	35 (8.3)
No	387 (91.7)
Menstrual status	
Postmenopausal	220 (52.1)
Premenopausal	202 (47.9)
Blood type	
A	132 (31.3)
B	134 (31.8)
AB	42 (10.0)
O	114 (27.0)
Axillary lymph node	
Positive	260 (61.6)
Negative	162 (38.4)
TNM stage	
II	212 (50.2)
III	210 (49.8)
Ki67	
<30%	128 (30.3)
≥30%	294 (69.7)
P53	
Positive	213 (50.5)
Negative	209 (49.5)
pCR	
Yes	131 (31.0)
No	291 (69.0)

Data are presented as mean ± standard deviation or n (%). TNBC, triple negative breast cancer; BMI, body mass index; TNM, tumor-node-metastasis; pCR, pathological complete response.

Survival analysis of SII following PSM. Following PSM, the ROC curve for SII indicated an area under the curve of 0.642, suggesting a relatively high prognostic value (Fig. 4A). Survival analysis revealed significant survival differences between patients with low and high SII scores following matching, with patients with low SII scores demonstrating an improved prognosis compared with patients with high SII scores (χ^2=8.452; P=0.004; Fig. 4B).

Discussion

In recent years, there has been growing interest in the study of inflammatory markers as potential prognostic indicators for

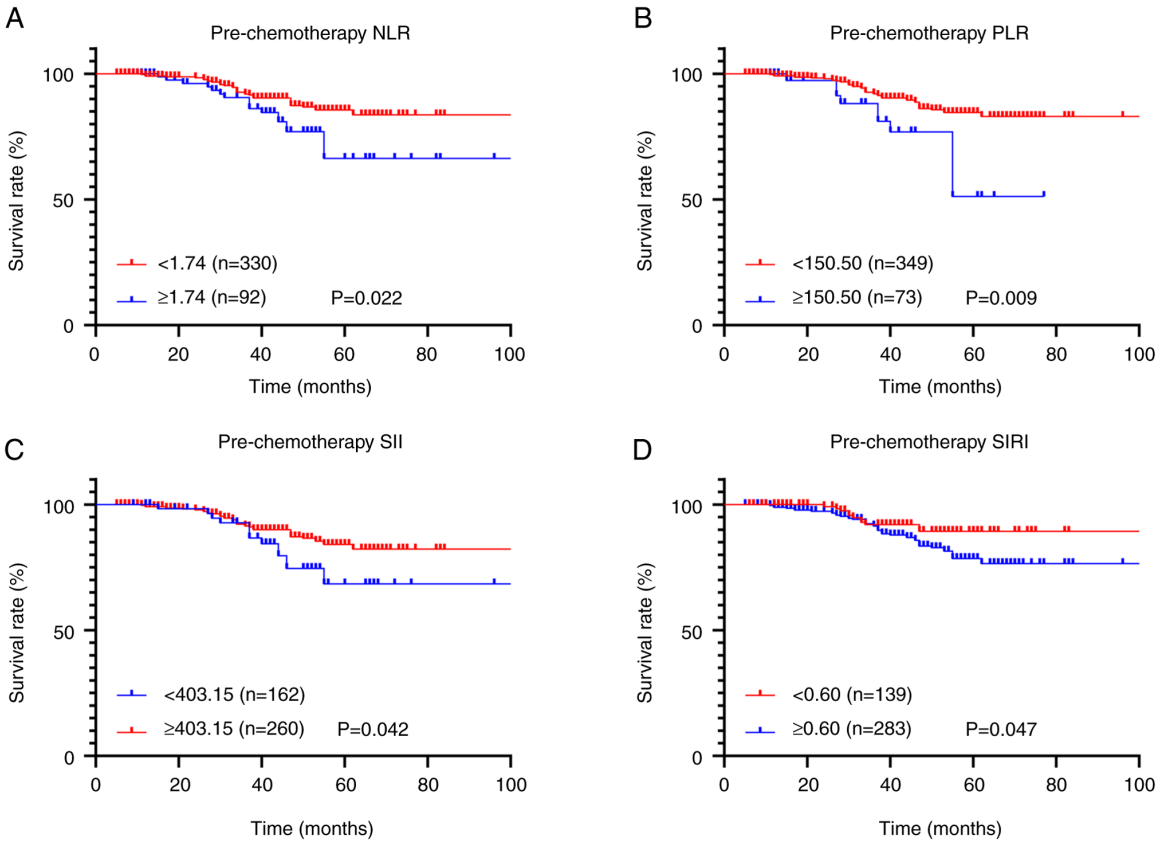

Figure 1. Survival curves for pre-chemotherapy inflammatory markers. Survival curves for pre-chemotherapy (A) NLR, (B) PLR, (C) SII and (D) SIRI. NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammatory response index.

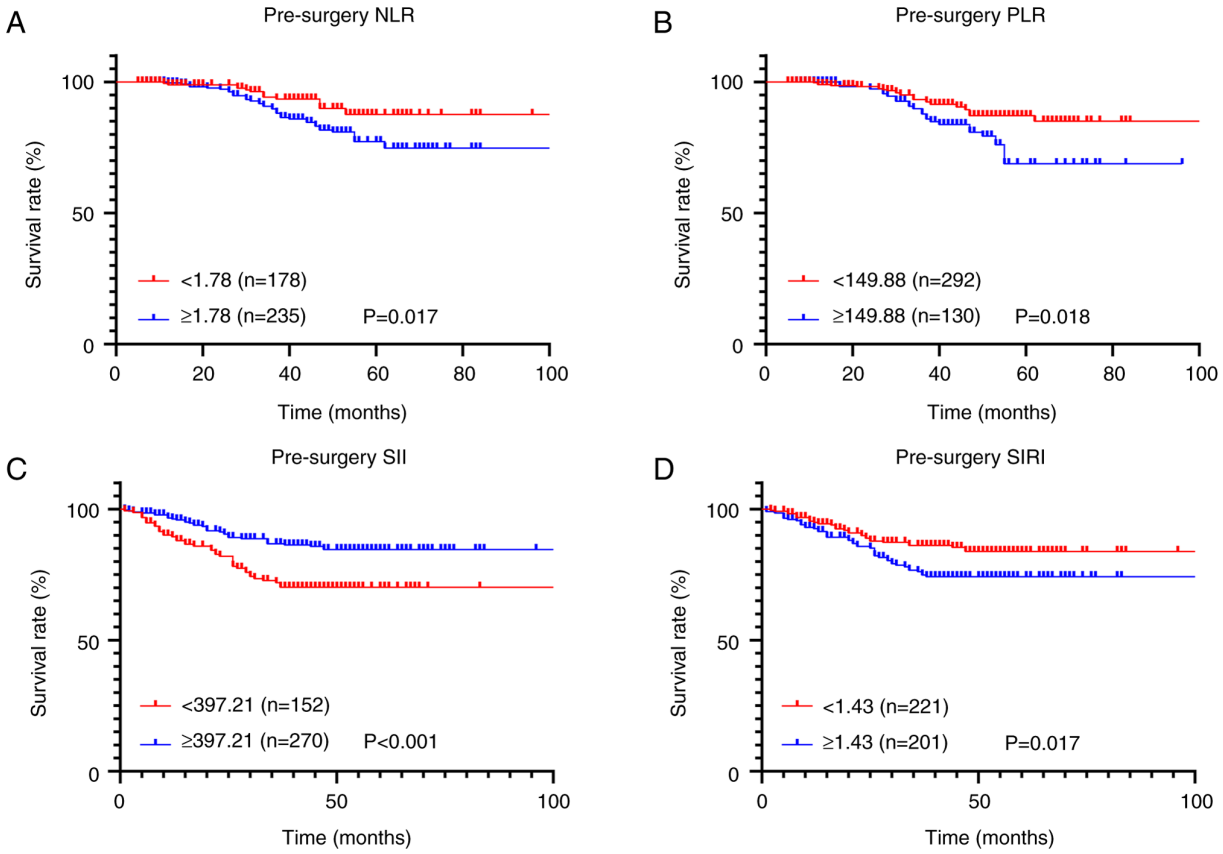

Figure 2. Survival curves for pre-surgery inflammatory markers. Survival curves for pre-surgery (A) NLR, (B) PLR, (C) SII and (D) SIRI. NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammatory response index.

Table III. Univariate Cox regression survival analysis.

Characteristic	HR	95% CI	P-value
Age	0.997	0.995-1.053	0.112
BMI	1.039	0.991-1.089	0.116
Family history	1.766	0.800-3.897	0.159
Menstrual status	1.416	0.831-2.414	0.201
Blood type	0.877	0.701-1.097	0.252
Ki67	0.824	0.483-1.405	0.477
P53	0.978	0.580-1.647	0.932
TNM stage	2.820	1.598-4.976	<0.001
pCR	2.511	1.189-5.302	0.016
NLR			
Pre-chemotherapy	2.083	1.201-3.614	0.009
Pre-surgery	2.072	1.162-3.693	0.013
PLR			
Pre-chemotherapy	2.864	1.481-5.538	0.002
Pre-surgery	2.074	1.231-3.493	0.006
SII			
Pre-chemotherapy	0.535	0.293-0.979	0.042
Pre-surgery	0.338	0.119-0.573	<0.001
SIRI			
Pre-chemotherapy	1.928	1.174-3.722	0.036
Pre-surgery	2.499	1.430-4.370	0.001

HR, hazard ratio; CI, confidence interval; BMI, body mass index; TNM, tumor-node-metastasis; pCR, pathological complete response; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammatory response index.

Table IV. Multivariate Cox regression survival analysis.

Characteristic	HR	95% CI	P-value
TNM stage	3.569	1.435-4.599	0.001
pCR	2.619	1.237-5.546	0.012
Pre-chemotherapy NLR	1.427	0.765-2.663	0.264
Pre-chemotherapy PLR	1.955	0.926-4.128	0.079
Pre-surgery SII	0.453	0.257-0.798	0.006
Pre-surgery SIRI	1.174	0.576-2.391	0.658

HR, hazard ratio; CI, confidence interval; TNM, tumor-node-metastasis; pCR, pathological complete response; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammatory response index.

cancer, notably in TNBC (13). Although neoadjuvant therapy has become a key strategy for reducing tumor burden prior to surgical intervention, several patients with TNBC still face the risk of recurrence and metastasis (14). Therefore, it is crucial to identify factors that can effectively predict patient prognosis and enable timely intervention. Previous studies have mainly focused on the inflammatory status prior to treatment; however, the present study assessed multiple inflammatory markers, as well as the pre-surgery inflammatory status of patients with TNBC following neoadjuvant therapy (14-16). Therefore, the present study not only deepens the understanding of the impact of inflammatory markers throughout the entire TNBC treatment process, but also provides a potential new strategy for identifying high-risk patients.

Inflammatory markers are easily accessible indicators for patients with cancer, notably those with solid tumors, and they can reflect relatively and accurately the inflammatory status of a patient (17-20). The prognostic value of the inflammatory markers in breast cancer has also gathered widespread attention. In 2020, a study was performed that integrated data from 2,724 patients with gynecologic and breast cancer across 11 databases. The study assessed the prognostic role of SII and reported that its high expression was associated with poor outcomes. Furthermore, in subgroup analysis, SII demonstrated stronger prognostic predictive ability in patients with ovarian cancer and TNBC compared with those of other inflammatory markers (21). Another study reached similar conclusions: By integrating the data from 8,563 patients with breast cancer, the study further confirmed the notable association between high NLR and poor prognosis in patients with breast cancer, notably in ER-negative and HER2-negative patients (22). This conclusion was further corroborated in studies specifically targeting TNBC. One study collected data from 605 patients with TNBC between 1985 and 2012 and developed a clinical prediction model that could predict long-term outcomes. Ultimately, the prediction model, which included NLR, demonstrated high accuracy in both internal and external validation (23). In 2019, Liu *et al* (24) performed a retrospective analysis of SII, reporting its association with the prognosis of patients with breast cancer. By collecting and analyzing data from 160 patients with TNBC, the study reported that patients with high SII exhibited markedly lower survival rates compared with those with low SII, and SII was demonstrated to be an independent prognostic factor for OS. Moreover, a study on SII in patients with TNBC yielded similar results (25).

Neoadjuvant chemotherapy is an effective treatment option for patients with TNBC and the prognostic value of inflammatory markers in patients receiving neoadjuvant chemotherapy has been widely studied. Chen *et al* (26) evaluated the application of SIRI in patients with breast cancer undergoing neoadjuvant chemotherapy. The study retrospectively collected data from 262 patients and reported that SIRI exhibited notable prognostic value in all subgroup analyses. Similarly, Jiang *et al* (27) and Dong *et al* (28) reached similar conclusions in the respective studies which focused on TNBC.

In the present study, a comprehensive analysis of the prognostic ability of inflammatory markers prior to chemotherapy and prior to surgery was performed in patients. The survival analysis results indicated that pre-chemotherapy and pre-surgery NLR, PLR, SII and SIRI were all significantly associated with the OS of patients. In addition, univariate analysis further confirmed their strong relationship with OS. Following exclusion of pre-chemotherapy SII, pre-chemotherapy SIRI, pre-surgery NLR and pre-surgery PLR via LASSO regression analysis, TNM stage, pCR and pre-surgery

Table V. Propensity score matching analysis of the systemic immune-inflammation index.

	Before PSM			After PSM		
Characteristic	Low SII (n=152)	High SII (n=270)	P-value	Low SII (n=69)	High SII (n=69)	P-value
Age, years	47.75±9.76	54.89±9.92	0.001	50.67±10.20	50.80±10.19	0.940
BMI, kg/m^2	25.61±3.67	24.87±3.44	0.308	25.47±3.41	24.63±2.74	0.383
Family history			0.170			0.784
Yes	122 (87.8)	257 (92.1)		61 (88.4)	62 (89.9)	
No	30 (12.2)	13 (7.9)		8 (11.6)	7 (10.1)	
Menstrual status			0.292			0.863
Postmenopausal	66 (42.3)	129 (47.9)		29 (42.0)	30 (43.5)	
Premenopausal	86 (57.7)	141 (52.1)		40 (58.0)	39 (56.5)	
Blood type			0.032			0.526
A	56 (39.8)	103 (38.1)		28 (40.6)	27 (39.1)	
B	34 (22.0)	92 (34.1)		18 (26.1)	23 (33.3)	
AB	22 (12.2)	11 (4.1)		7 (10.1)	3 (4.3)	
O	40 (26.0)	64 (23.7)		16 (23.2)	16 (23.2)	
Axillary lymph node			0.265			0.385
Positive	84 (56.9)	172 (62.8)		39 (56.5)	44 (63.8)	
Negative	68 (43.1)	98 (37.2)		30 (43.5)	25 (36.2)	
TNM stage			0.018			0.173
II	86 (58.5)	123 (45.9)		40 (58.0)	32 (46.4)	
III	66 (41.5)	147 (54.1)		29 (42.0)	37 (53.6)	
Ki67			0.488			0.703
<30%	49 (28.5)	63 (25.2)		18 (26.1)	20 (29.0)	
≥30%	103 (71.5)	207 (74.8)		51 (73.9)	49 (71.0)	
P53			0.031			0.088
Positive	64 (40.7)	136 (50.3)		28 (40.6)	38 (55.1)	
Negative	88 (59.3)	134 (49.7)		41 (59.4)	31 (44.9)	
pCR			0.321			0.721
Yes	94 (65.0)	193 (70.0)		44 (63.8)	46 (66.7)	
No	58 (35.0)	77 (30.0)		25 (36.2)	23 (33.3)	

Data are presented as mean ± standard deviation or n (%). PSM, propensity score matching; SII, systemic immune-inflammation index; BMI, body mass index; TNM, tumor-node-metastasis; pCR, pathological complete response.

SII were demonstrated to be independent prognostic factors for OS in patients with TNBC. This result further highlights the significant prognostic value of the inflammatory status prior to surgery. Notably, SII following PSM still indicated a strong prognostic value.

Although the present study did not assess the specific mechanisms by which inflammatory markers affect prognosis, there are several potential explanations for the results. High levels of inflammatory markers indicate that a patient is in an active inflammatory state, which may lead to a series of physiological changes (29). Chronic inflammation has several detrimental effects on the immune system, potentially leading to immune cell suppression or dysfunction, thereby weakening the ability of the immune system to attack tumors (30). Concomitantly, chronic inflammation also promotes the generation of suppressive immune cells (such as regulatory T cells), inhibiting the activity of other immune cells and further decreasing the ability of the immune system to suppress tumors (31). Moreover, in a chronic inflammatory state, several cytokines, including interleukin-1 (IL)-1, IL-10, IL-6, IL-8, TNF-α and TGF-β, are secreted (32,33). These cytokines can directly stimulate tumor cell proliferation and enhance tumor invasion and metastasis by inhibiting the activity of immune cells and promoting angiogenesis (34). Notably, the inflammatory state may affect the response of a patient to neoadjuvant therapy. High levels of systemic inflammation may lead to increased resistance of the tumor to neoadjuvant chemotherapy drugs, thereby reducing their effectiveness (35).

The present study demonstrated that pre-surgery SII exhibited significant prognostic value. Surgery serves a crucial role in the treatment of patients with TNBC, and the inflammatory status markedly influences surgical outcomes (36). Elevated levels of inflammation not only reduce the tolerance of a patient to surgery, but they also

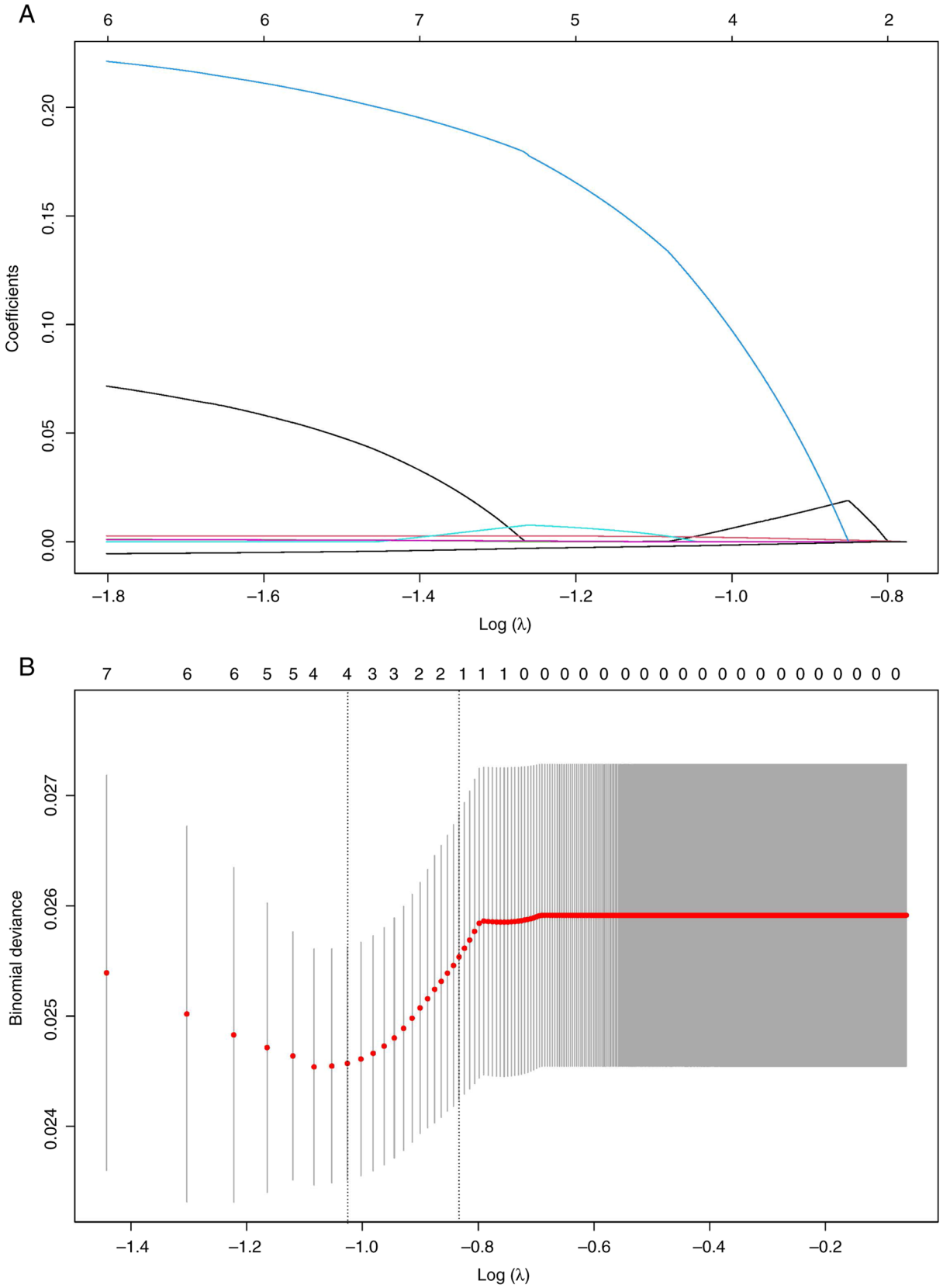

Figure 3. LASSO regression analysis. (A) LASSO regression analysis of significant variables from univariate analysis. (B) Determination of the optimal λ value following 287 iterations. LASSO, Least Absolute Shrinkage and Selection Operator.

exert adverse effects on postoperative recovery and increase the risk of postoperative infections. By contrast, neoadjuvant chemotherapy is a long-term treatment that has a profound impact on the nutritional status, inflammatory state and immune system of the patient (37). Therefore, compared with pre-neoadjuvant chemotherapy, pre-surgery inflammatory

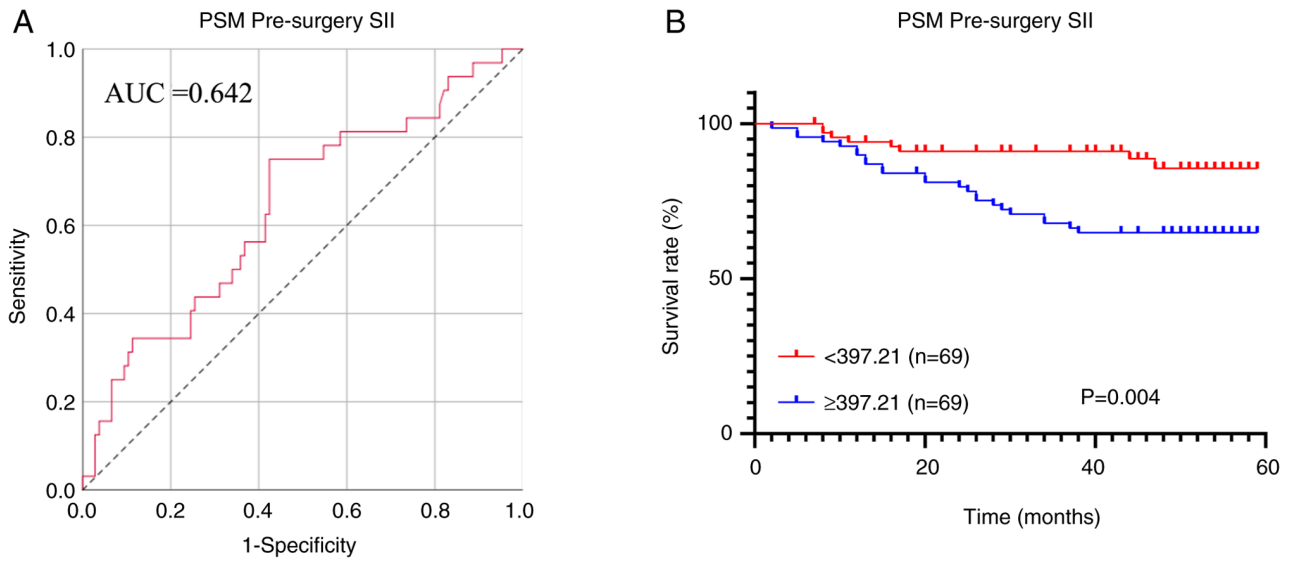

Figure 4. Survival analysis of SII following PSM. (A) Receiver operating characteristic curve of SII following PSM, indicating an AUC of 0.642, suggesting a significant prognostic value. (B) Survival curves of patients with low and high SII following PSM. Patients with low SII exhibited significantly improved overall survival compared with those with high SII (χ^2=8.452; P=0.004). SII, systemic immune-inflammation index; PSM, propensity score matching; AUC, area under the curve.

markers can more accurately reflect the impact of inflammation on prognosis.

SII consists of platelets, neutrophils and lymphocytes, all of which serve important roles in breast cancer prognosis (38). Platelets and neutrophils are key participants in the inflammatory response of the body (39). Their elevated levels not only reflect a higher tumor burden, but they also promote tumor progression via several mechanisms of action, leading to poor treatment outcomes (40). By contrast, lymphocytes are a crucial component of antitumor immunity and serve an irreplaceable role in recognizing and destroying tumor cells (41). A decrease in lymphocyte count inevitably weakens the ability of the immune system to resist tumors (42). These factors are likely the reasons why pre-surgery SII has high predictive value.

Previous studies on neoadjuvant therapy for TNBC have often focused on the pre-treatment period, overlooking the crucial role of surgery throughout the entire treatment process (43-45). The present study, for the first time, to the best of our knowledge, assessed the inflammatory status of patients from the completion of neoadjuvant therapy to the time of surgery, revealing a significant association with prognosis. In addition, the use of neoadjuvant drugs can, to a certain extent, influence the immune, inflammatory and nutritional status of a patient, making the assessment of inflammation during this period more accurately reflective of the condition of the patient. Therefore, the present study holds clear practical significance and has the potential to advance clinical practice for TNBC management. Firstly, by highlighting that both pre-chemotherapy and pre-surgery inflammatory markers-particularly pre-surgery SII - are strongly associated with overall survival, the present work underlines the importance of monitoring inflammatory status throughout the entire treatment process. Such monitoring could refine patient risk stratification, aiding clinicians to identify those patients at higher risk of recurrence or metastasis and adjust therapeutic approaches accordingly. Secondly, the simplicity and accessibility of measuring these markers suggest that they can be easily integrated into routine clinical workflows, thereby providing a cost-effective tool for guiding personalized treatment decisions. Lastly, the findings offer a foundation for future translational research on the immunological and inflammatory mechanisms underlying TNBC progression. By enhancing the understanding of these mechanisms, further studies may lead to novel therapeutic strategies and ultimately improve patient outcomes, underscoring the relevance of the present study to both current medical practice and future research directions.

However, the present study exhibits several limitations that need to be considered. Firstly, the retrospective design may introduce potential information bias into the results. Secondly, the study was performed at a single medical center, limiting the generalizability of the findings. In addition, the present study did not account for the treatment heterogeneity among patients with TNBC, which may affect the reliability of the results. Furthermore, there is a lack of mechanistic research on the relationship between inflammatory markers and patient outcomes. Lastly, although the prognostic value of SII was highlighted, its practical applicability and integration into treatment decisions in clinical practice require further investigation. Moreover, inflammatory markers may be influenced by the underlying conditions of the patients, their infection status or treatment protocols, such as types of medications, which were not fully accounted for in the present study and could impact the interpretation of their prognostic value. These limitations highlight the necessity for future research to address these challenges, and future studies should perform multi-center studies involving larger and more diverse patient populations. By utilizing larger sample sizes and more detailed statistical analyses, findings of the present study can be further validated and deeper insights into the relationship between inflammatory

markers and the prognosis of TNBC patients can be gained. Expanding the sample size and incorporating several demographic groups and treatment regimens will help enhance the generalizability of the results, further validating the practical applicability of inflammatory markers in clinical decision-making.

In conclusion, both pre-chemotherapy and pre-surgery inflammatory status are associated with OS in patients with TNBC receiving neoadjuvant chemotherapy, particularly pre-surgery SII.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

QG and BW contributed to the conception and design of the study, participated in data analysis and interpretation, and were responsible for drafting the original manuscript as well as revising it critically for important intellectual content. XG was responsible for extracting relevant clinical data from the hospital's electronic medical record system, performing initial data organization, cleaning, variable standardization, and database construction. In addition, XG conducted part of the telephone follow-ups with patients, including data verification and supplementation, to ensure the completeness and accuracy of the dataset. PZ contributed to the methodology design and provided supervision throughout the study. SL was involved in the study's conceptualization, provided resources, secured funding, and oversaw project administration. QG and SL confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of the Inner Mongolia People's Hospital (approval no. 202404704L). Written informed consent was obtained from the participants for the use of their samples.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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