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Changes in Inflammatory Markers before and after Neoadjuvant Chemotherapy and Their Association with Pathological Complete Response in Breast Cancer

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ABSTRACT

Aim: This study aimed to investigate the association between pre- and post-neoadjuvant chemotherapy (NAC) inflammatory indices and pathological complete response (pCR) in breast cancer patients.

Methods: In this retrospective study, we reviewed the medical records of 412 patients with breast cancer who received NAC between January 2013 and January 2023. We recorded the following indices: pan-immune systemic inflammatory index (PIV), systemic immune-inflammation index (SII), prognostic nutritional index; neutrophil-to-lymphocyte, platelet-to-lymphocyte, and lymphocyte-to-monocyte ratios; hemoglobin and counts of white blood cells, neutrophils, platelets, monocytes, and lymphocytes; and pre-NAC-to-post-NAC ratios of these parameters. Pre-NAC and post-NAC values and their ratios were analyzed. Receiver operating characteristic analysis was used to explore optimal cut-off values. Univariate and multivariate logistic regression analyses were performed to identify factors associated with pCR.

Results: 119 (29%) patients achieved pCR. Cut-off values were explored for the pre-NAC/post-NAC ratios of PIV, SII, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, neutrophil, and hemoglobin. Multivariate analysis showed that HER2 positivity, hormone receptor negativity, earlier T stages, and elevated pre-NAC/post-NAC platelet-to-lymphocyte ratios and hemoglobin levels were independently associated with pCR.

Conclusion: The pre-NAC-to-post-NAC ratios of inflammatory markers were statistically associated with pCR following NAC in breast cancer patients. In addition to established clinicopathological factors such as HER2 positivity, hormone receptor negativity, and earlier T-stage, higher pre-NAC and post-NAC platelet-to-lymphocyte and hemoglobin ratios were associated with pCR. However, the discriminative performance of these markers was limited, as reflected by relatively low area under the curve values. Therefore, these findings represent statistical associations rather than predictive capability, and these markers should not be interpreted as standalone predictive biomarkers. Instead, they may serve only as complementary parameters alongside established clinicopathological factors.

Keywords: Breast cancer, inflammatory indices, neoadjuvant chemotherapy, pathological complete response

Introduction

Neoadjuvant therapies are a key component of breast cancer treatment protocols, owing to their ability to downstage the disease and minimize the extent of interventions in the breast and axilla. The pathological evaluation of the treatment response can inform the design of the regimen. In this sense, pathological complete response (pCR) is recognized as a pivotal prognostic indicator [1,2]; it refers to the absence of residual tumors in the breast and axilla in the resection material following neoadjuvant chemotherapy (NAC) [3]. Patients with HER2-positive and triple-negative

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breast cancers are widely regarded as ideal candidates for neoadjuvant treatments and exhibit notably high rates of pCR following NAC [4]. It should also be noted that it is imperative to select the most suitable patients for NAC, as those who can achieve pCR often demonstrate improved overall survival and disease-free survival compared to their counterparts [1,5].

The host systemic inflammatory response is key in tumor formation, progression, metastasis, and chemotherapy resistance [6,7]. A variety of serum markers influence this response, and the prognostic and predictive value of the response has been extensively examined in a plethora of studies [8,9]. The inflammatory markers include peripheral blood components such as neutrophils, lymphocytes, and platelets, as well as acute-phase proteins (e.g., albumin). In addition, the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), lymphocyte-monocyte ratio (LMR), systemic immune-inflammation index (SII), pan-immune systemic inflammatory index (PIV), prognostic nutritional index (PNI), and systemic inflammation response index (SIRI) hold prognostic significance [10-15]. Although the literature hosts research exploring the response to neoadjuvant treatment in breast cancer [16-18], only a few studies evaluated the changes in these inflammatory factors in the treatment response [19, 20].

Ultimately, the present study aimed to explore the association between routinely available peripheral blood-derived inflammatory indices and pCR in breast cancer patients receiving NAC. To this end, we evaluated both baseline values and changes from pre- to post-chemotherapy in these inflammatory markers. In this context, the study contributes to the limited body of literature examining the dynamic changes of inflammatory parameters in relation to treatment response.

Methods

In this study, we analyzed data from a cohort of 412 breast cancer patients who underwent surgical procedures following NAC between January 2013 and January 2023 at a tertiary oncology center. Nevertheless, we excluded incomplete records and patients who were unable to complete neoadjuvant therapy, had metastatic disease, or had surgical, traumatic, infectious, or immune-system disorders (e.g., autoimmune diseases and human immunodeficiency virus), because their parameters would have been affected before NAC. The data collection and methods used in this study adhered to the ethical guidelines established by both the institutional and national research committees. Furthermore, they complied with the principles outlined in the 1964 Helsinki Declaration and its subsequent revisions or equivalent ethical standards. The Research Ethics Committee of University of Health Sciences Türkiye, Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, granted ethical approval to our study (approval number: 2024-07/104, date: 25.08.2022). The data collection program for this study was approved by ethics committee with a waiver for individual informed consent for this retrospective study.

We defined pCR as the absence of residual disease in the breast or axilla on pathological examination of specimens obtained during surgery. According to the residual cancer burden (RCB) index, RCB-0 patients were classified as pCR, whereas other patients were classified as non-pCR. We then generated a comprehensive dataset, including patient age, T-stage, pre-NAC nodal status, histopathology, grade, hormone receptor status, HER2 status, molecular subtype, and Ki-67 level. The pathological staging of patients was established according to the American Joint Committee on Cancer tumor, node, metastasis Staging Manual (8th edition) [21].

We retrospectively extracted the following parameters from pre-NAC and preoperative blood samples in the hospital database: neutrophil count, platelet count, lymphocyte count, hemoglobin, and albumin. We calculated the following pre- and post-NAC parameters for the NAC response:

PIV = (neutrophil × platelet × monocyte)/lymphocyte

SII = (platelet×neutrophil)/lymphocyte

PNI = [10×serum albumin (g/dL)]+[0.005× lymphocyte count(/mm^3)]

NLR = neutrophil/lymphocyte

PLR = platelet/lymphocyte

LMR = lymphocyte/monocyte

Statistical Analysis

We performed a comparative analysis to reveal alterations in these parameters before and after NAC. The optimal cut-off values for inflammatory markers were calculated through receiver operating characteristic (ROC) curve analysis. Accordingly, we designated the value at the point with the highest Youden index as the optimal cut-off value and performed categorization based on this cut-off value. While examining the relationships between pCR and clinicopathological variables using a chi-square test, we performed logistic regression analysis to identify factors affecting pCR. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and Jamovi; a p value<0.05 was considered statistically significant. Model discrimination was evaluated using the area under the ROC curve (AUC). Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. Multicollinearity among predictors was evaluated using variance inflation factors (VIF). VIF values below 5 were considered to indicate the absence of significant multicollinearity.

Results

Comparison of Patients' Clinicopathological Features

Of 412 patients, 119 (29%) demonstrated pCR (pCR group), while 293 (71%) did not (non-pCR group). We found that 233 (39%) of the patients were older than 50 years. The patients were further categorized based on their follow-up status: 50 (12%) were T1, 270 (66%) were T2, and 92 (22%) were T3. 24 (48%) of T1 patients, 76 (28%) of T2 patients, and 19 (21%) of

T3 patients achieved pCR (p=0.002). Pre-NAC node positivity was noted in 205 patients (50%) and 379 patients (92%) had no special type histopathology. While 252 (61%) were Grade III, 160 (39%) were Grades I and II. Additionally, 113 (27%) were hormone-negative. 55 (49%) of hormone-negative and 64 (21%) of hormone-positive cases achieved pCR (p=0.001). Of the patients, 251 (61%) were HER2-negative; pCR was achieved by 42 (17%) of HER2-negative and 77 (48%) of HER2-positive patients (p=0.001, Table 1).

Findings of ROC Analysis on Inflammatory Markers

In the ROC analysis, we could not determine significant cut-off values for pre-NAC blood parameters: hemoglobin; white blood cell (WBC), neutrophil, platelet, monocyte, and lymphocyte counts; PIV; SII; PNI; neutrophil/lymphocyte; platelet/lymphocyte; and lymphocyte/monocyte. It was also the case for post-NAC blood parameters: hemoglobin, WBC, neutrophil, platelet, monocyte, and lymphocyte counts; and PNI, neutrophil/lymphocyte, platelet/lymphocyte, and lymphocyte/monocyte. However, we calculated the optimal cut-offs to be 281 for post-NAC PIV (sensitivity =47%, specificity =32%, p=0.024, AUC=0.429) and 685.37 for SII (sensitivity =55%, specificity =45%, p=0.021, AUC=0.428).

We also determined pre- and post-NAC values of PIV, SII, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, neutrophil count, hemoglobin level, platelet count, and PNI and evaluated changes in these parameters. Accordingly, we calculated optimal cut-off values for the following pre-NAC/post-NAC ratios: PIV=0.8564 (sensitivity =54%, specificity =46%, p=0.01, AUC=0.575); SII=0.8853 (sensitivity =54%, specificity =46%, p=0.01, AUC=0.581); neutrophil/lymphocyte =0.8766 (sensitivity =54%, specificity =46%, p=0.03, AUC=0.568); platelet/lymphocyte =0.7560 (sensitivity =57%, specificity =43%, p=0.03, AUC=0.568); neutrophil =1.2173 (sensitivity =56%, specificity =44%, AUC=0.563); and hemoglobin =1.1245 (sensitivity =57%, specificity =43%, AUC=0.575) (Table 2). The ROC curves of the variables for which the optimal cut-off was determined are shown in Figures 1-6.

Univariate and Multivariate Analyses

The parameters were then categorized into two groups (i.e., < cut-off and ≥ cut-off). In univariate analysis, the pre-NAC/post-NAC ratios of PIV (p=0.025), SII (p=0.011), platelet/lymphocyte (p=0.011), neutrophil (p=0.018), and hemoglobin (p=0.011) were associated with pCR to neoadjuvant treatment (Table 3). The logistic regression analysis showed that the pre-NAC/post-NAC ratios of platelet/lymphocyte and hemoglobin, together with hormone receptor status, HER2 status, and T-stage, were independent factors associated with pCR following neoadjuvant treatment. The multivariable model demonstrated good discrimination with an AUC of 0.798. Model calibration was acceptable according to the Hosmer-Lemeshow goodness-of-fit test (χ^2=8.99, df=8, p=0.343). Multicollinearity analysis showed no significant correlation among predictors (all VIF values <2). Furthermore, elevated pre-NAC platelet/lymphocyte ratio and hemoglobin, along with HER2 positivity, hormone negativity, and earlier T stages, were associated with pCR to neoadjuvant therapy (Table 4). These findings indicate statistical associations between certain inflammatory marker ratios and pCR; however, the observed relationships should not be interpreted as evidence that these markers function as independent predictive biomarkers.

Discussion

In this study, we retrospectively reviewed the medical records of 412 breast cancer patients receiving NAC and evaluated the association between inflammatory markers and pCR, including PIV, SII, and PNI; neutrophil-to-lymphocyte, platelet-to-lymphocyte, and lymphocyte-to-monocyte ratios; hemoglobin, WBC, neutrophil, platelet, monocyte, and lymphocyte counts; and pre-NAC/post-NAC ratios of these parameters. The pCR to neoadjuvant treatment was more prevalent among patients whose pre-NAC/post-NAC platelet-to-lymphocyte and

Table 1. Patients' clinicopathological features

Clinicopathological Variables	pCR (%) n=119	Non-pCR (%) n=293	p value
Age (years) <50 ≥50	 52 (44) 67 (56)	 127 (43) 166 (57)	0.517
T-stage T1 T2 T3	 24 (20) 76 (64) 19 (16)	 26 (9) 194 (66) 73 (25)	0.002*
Pre-NAC nodal status Negative Positive	 57 (48) 62 (52)	 148 (51) 145 (49)	0.710
Histopathology NST Lobular Others	 114 (96) 4 (3) 1 (1)	 265 (91) 18 (6) 10 (3)	0.122
Grade Grade III Grades I and II	 83 (70) 36 (30)	 169 (58) 124 (42)	0.003*
HR status Negative Positive	 55 (46) 64 (54)	 58 (20) 235 (80)	<0.001*
Ki-67 ≤14 >14 Missing	 10 (8) 103 (87) 6 (5)	 30 (10) 246 (84) 17 (6)	0.713
HER2 status Negative Positive	 42 (35) 77 (65)	 209 (71) 84 (29)	<0.001*
Molecular sub-type HR(+) HER2(+) HR(+) HER2(-) HR(-) HER2(+) Triple Negative	 44 (37) 20 (17) 33 (28) 22 (18)	 65 (22) 173 (59) 20 (7) 34 (12)	<0.001*

*: Statistically significant (p<0.05)
pCR: Pathologic complete response, NAC: Neoadjuvant chemotherapy, HR: Hormone receptor, HER2: Human epidermal growth factor receptor 2, Ki-67: Ki-67 proliferation index, NST: No special type

hemoglobin ratios exceeded the cut-off values. Moreover, the multivariate analysis revealed that HER2 positivity, hormone negativity, and earlier T-stages were associated with increased pCR to neoadjuvant treatment. However, the discriminative ability of these markers was limited.The ROC analyses demonstrated relatively low AUC values (<0.60), indicating a modest ability to distinguish between patients who achieved pCR and those who did not. Therefore, these findings should be interpreted as exploratory associations rather than evidence of clinically useful predictive biomarkers.

Inflammation plays a key role in cancer pathogenesis. The alterations in inflammatory cells have therefore been scrutinized for many years, as they serve as a reflection of the tumor's inflammatory response [7]. Moreover, the routine evaluation of pre-treatment blood parameters has been investigated for potential associations with treatment response. As is widely acknowledged, NAC, high grade, hormone negativity, and HER2/neu amplification are the factors that predict pCR in breast cancer [22]. Similarly, we found that hormone receptor status, T-stage, and HER2 amplification status were significant predictors of pCR in both univariate and multivariate analyses.

Numerous studies have explored the relationship between blood parameters and pCR in breast cancer patients receiving NAC. In their study, Yang et al. [10] found significant associations between low neutrophil/lymphocyte (<2.46), platelet/lymphocyte (<118.78), and SII (<403.20) with pCR in breast cancer. While Ma et al. [23] showed lymphocyte/monocyte (>6.2) to be associated with pCR to NAC, Goto et

Table 2. Findings of ROC analysis

	Value	AUC (95%)	Cut-off	p value	Sensitivity %	Specificity %
RATES pre-NAC/post-NAC	PIV (pre-NAC/post-NAC) ratio	0.575	0.8564	0.01*	54	46
	SII (pre-NAC/post-NAC) ratio	0.581	0.8853	0.01*	54	46
	Neutrophil/lymphocyte (pre-NAC/post-NAC) ratio	0.568	0.8766	0.03*	54	46
	Platelet/lymphocyte (pre-NAC/post-NAC) ratio	0.568	0.7560	0.03*	57	43
	Pre-NAC/post-NAC neutrophil ratio	0.563	1.2173	0.04*	56	44
	Pre-NAC/post-NAC hemoglobin ratio	0.575	1.1245	0.01*	57	43
	Pre-NAC/post-NAC platelet ratio	0.560	-	0.055	-	-
	Pre-NAC/post-NAC PNI ratio	0.472	-	0.365	-	-
PRE-NAC	Pre-NAC PIV	0.514	-	0.666	-	-
	Pre-NAC SII	0.516	-	0.617	-	-
	Pre-NAC PNI	0.500		0.997		
	Pre-NAC neutrophil/lymphocyte	0.508	-	0.797	-	-
	Pre-NAC PLT/lymphocyte	0.526	-	0.405	-	-
	Pre-NAC lymphocyte/monocyte	0.501	-	0.968	-	-
	Pre-NAC hemoglobin	0.494	-	0.843	-	-
	Pre-NAC WBC	0.493	-	0.840	-	-
	Pre-NAC neutrophil	0.499	-	0.986	-	-
	Pre-NAC PLT	0.541	-	0.204	-	-
	Pre-NAC monocyte	0.494	-	0.856	-	-
	Pre-NAC lymphocyte	0.480	-	0.542	-	-
POST-NAC	Post-NAC PIV	0.429	281	0.024*	47	32
	Post-NAC SII	0.428	685.37	0.021*	55	45
	Post-NAC PNI	0.516		0.618		
	Post-NAC neutrophil	0.436	-	0.042*	-	-
	Post-NAC PLT/lymphocyte	0.463	-	0.234	-	-
	Post-NAC lymphocyte/monocyte	0.538	-	0.232	-	-
	Post-NAC hemoglobin	0.459	-	0.917	-	-
	Post-NAC WBC	0.470	-	0.343	-	-
	Post-NAC neutrophil/lymphocyte	0.443	-	0.71	-	-
	Post-NAC PLT	0.468	-	0.312	-	-
	Post-NAC monocyte	0.470	-	0.338	-	-
	Post-NAC lymphocyte	0.516	-	0.606	-	-

*: Statistically significant (p<0.05)
ROC: Receiver operating characteristic, AUC: Area under the curve, NAC: Neoadjuvant chemotherapy, PIV: Pan-immune-inflammation value, SII: Systemic immune-inflammation index, PNI: Prognostic nutritional index, PLT: Platelet, WBC: White blood cell

al. [24] could not find a significant correlation between them. Similarly, Ma et al. [25] found a significant correlation between high pre-NAC platelet counts and treatment response; however, this was not the case in the study by Corbeau et al. [26]. Şahin et al. [27] identified a significant relation between pCR in patients with low PIV. Marín et al. [28] and Losada et al. [29] discovered no significant link between neutrophil/monocyte and pCR. Therefore, among the abovementioned variables, we could not identify useful parameters with optimal cut-off values for predicting pCR. Although most individual inflammatory parameters were not significantly associated with pCR, ratios reflecting changes between pre- and post-NAC values were significantly associated with treatment response. This observation may suggest that dynamic changes in inflammatory markers reflect treatment-related biological responses more than single baseline measurements. However, given the limited discriminative performance observed in the current study, these findings

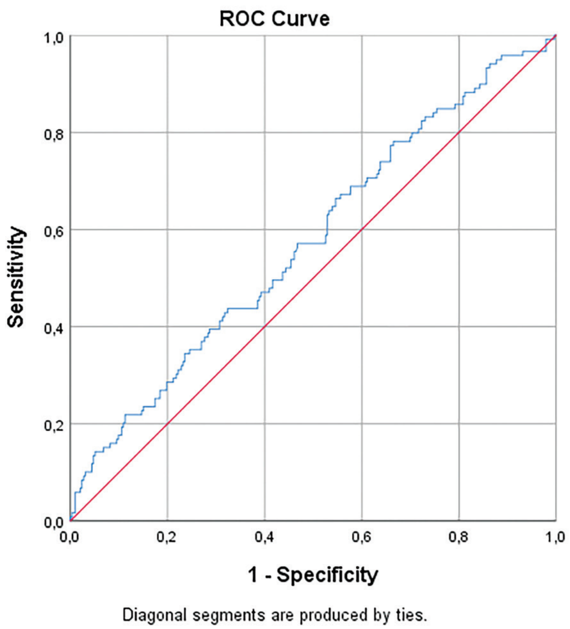

Figure 1. PIV (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic, PIV: Pan-immune systemic inflammatory index

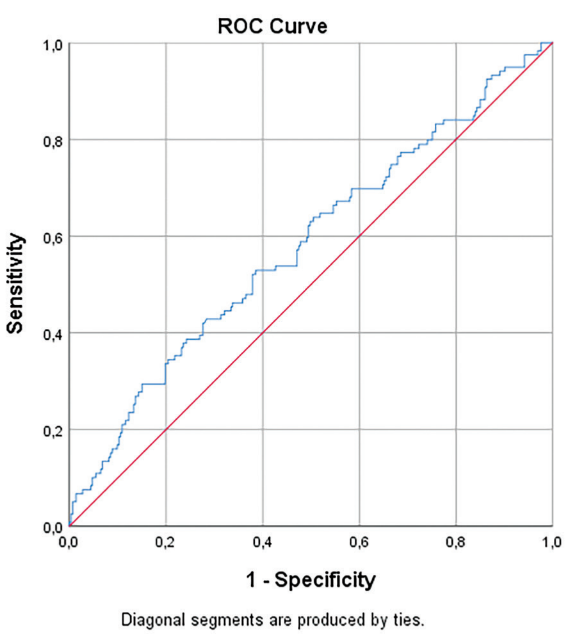

Figure 2. SII (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic, SII: Systemic immune-inflammation index

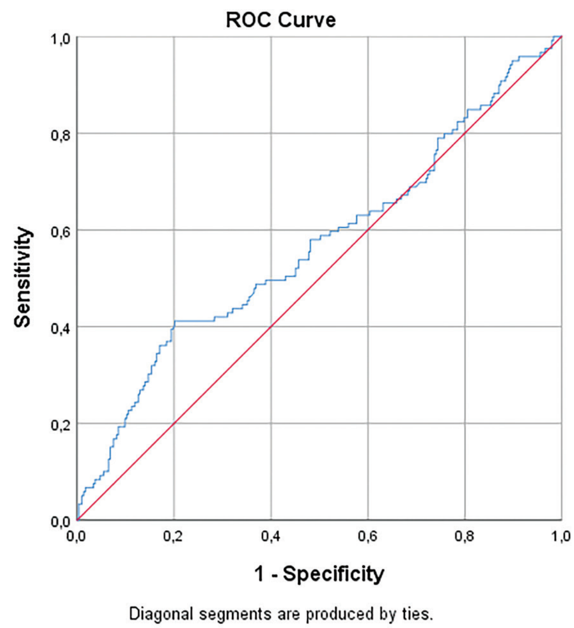

Figure 3. Neutrophil/lenfosit (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic

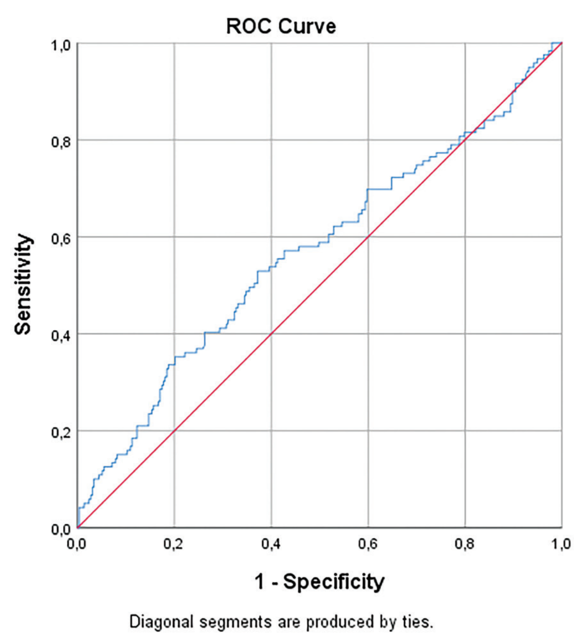

Figure 4. PLT/lenfosit (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic, PLT: Platelet should be interpreted cautiously and confirmed in larger prospective cohorts.

In this study, we observed that pre-NAC/post-NAC ratios of PIV (p=0.01), SII (p=0.01), neutrophil/lymphocyte (p=0.03), platelet/lymphocyte (p=0.03), neutrophil (p=0.04), and hemoglobin (p=0.01) were significantly associated with pCR following NAC based on derived cut-off values.

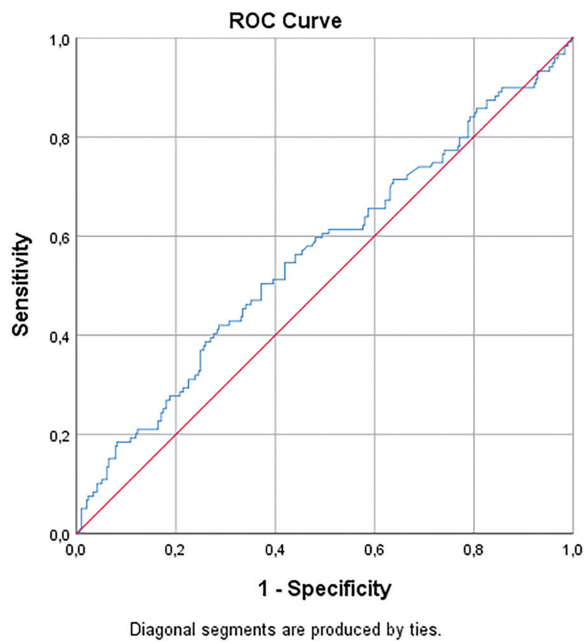

Figure 5. Neutrophil (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic

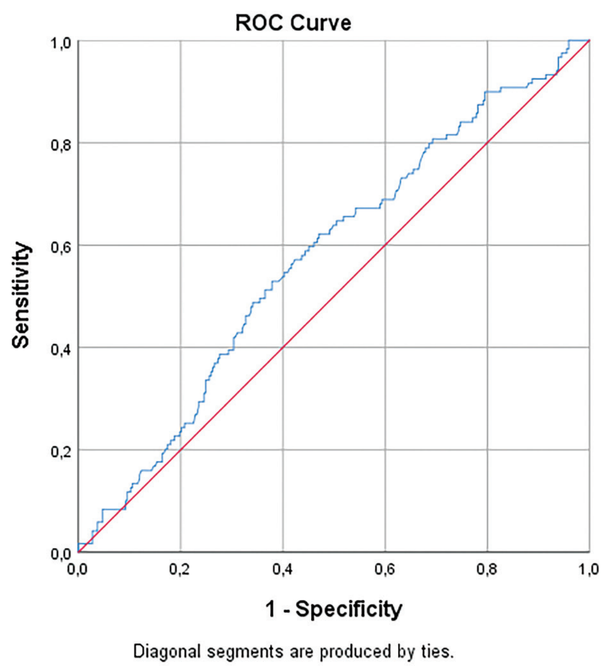

Figure 6. Hemoglobin (Pre-NAC-post-NAC) ratio

Pre-NAC: Pre- and post-neoadjuvant chemotherapy, ROC: Receiver operating characteristic

The significance of this study may lie in its pioneering attempt to elucidate the impact of changes in inflammatory markers on pCR to NAC, as a review of the extant literature reveals a paucity of studies addressing this subject. In their study, Dan et al. [20] reported an association between pre- and post-treatment alterations in NLR and pCR following NAC in breast cancer patient. In another study, Omarini et al. [19] focused on the association between the decline in hemoglobin and pCR to NAC and found a >2 g/dL decrease in hemoglobin level to be linked with a diminished pCR (15% vs. 43%, p=0.047). In contrast, we could not identify a significant association between NLR and pCR; however, we found that high pre-NAC/post-NAC hemoglobin ratios were statistically associated with pCR in our cohort.

This study has notable strengths. The analysis was conducted in a relatively large cohort of patients treated in routine clinical practice over a 10-year period, and it systematically assessed multiple inflammatory indices derived from standard blood tests. Importantly, we focused on changes from pre- to post-treatment, which may better reflect treatment-related biological dynamics than baseline values alone. Importantly, the results of this study demonstrate statistical associations rather than causal or predictive relationships. Therefore, inflammatory marker dynamics should not be considered standalone predictive biomarkers. Instead, they may be incorporated as complementary variables in future multivariable prediction models alongside established clinicopathological factors.

Study Limitations

This study has several limitations. First, its retrospective, single-center design may introduce selection bias and limit the generalizability of the findings. Second, although several inflammatory marker ratios showed statistically significant associations with pCR, their discriminative performance was limited. The ROC analyses yielded relatively low AUC values, indicating that these markers have only a modest ability to discriminate between patients achieving pCR and those who do not. Third, cut-off values were derived from the same dataset, and the study lacked an external validation cohort, which raises the possibility of overfitting and limits the applicability of these thresholds to other populations. Therefore, the possibility of model overfitting cannot be excluded, and the derived thresholds should be interpreted with caution, as their generalizability to other patient populations remains uncertain. Fourth, the timing of post-NAC blood sampling and potential unmeasured confounders (e.g., intercurrent infections, concomitant medications, nutritional status, and treatment-related toxicities) may have influenced inflammatory markers. The sample size within molecular subgroups was relatively limited, which may have reduced the power of subgroup analyses. Prospective multicenter studies with standardized sampling time points and external validation are warranted to confirm these findings and clarify the incremental value of inflammatory marker dynamics beyond established clinicopathological predictors. The multivariable model also demonstrated acceptable calibration according to

Table 3. Pairwise comparisons of inflammatory markers

	pCR (%) n=119	Non-pCR (%) n=293	p-value
PIV ratio (pre-NAC/post-NAC)			
<0.8564	52 (44)	161 (55)	0.025*
≥0.8564	67 (56)	132 (45)	
SII ratio (pre-NAC/post-NAC)			
<0.8853	49 (41)	159 (54)	0.011*
≥0.8853	70 (59)	134 (46)	
Neutrophil/lymphocyte ratio (pre-NAC/post-NAC)			
<0.8766	55 (46)	157 (54)	0.193
≥0.8766	64 (54)	136 (46)	
Platelet/lymphocyte ratio (pre-NAC/post-NAC)			
<0.7560	52 (44)	166 (57)	0.011*
≥0.7560	67 (56)	127 (43)	
Neutrophil ratio (pre-NAC/post-NAC)			
<1.2173	52 (44)	163 (56)	0.018*
≥1.2173	67 (56)	130 (44)	
Hemoglobin ratio			
<1.1245	46 (39)	165 (56)	0.011*
≥1.1245	73 (61)	128 (44)	
Post-NAC PIV			
<281	63 (53)	139 (47)	0.329
≥281	56 (47)	154 (53)	
Post-NAC SII			
<685.37	65 (55)	130 (44)	0.065
≥685.37	54 (45)	163 (56)	

*: Statistically significant (p<0.05)
pCR: Pathologic complete response, NAC: Neoadjuvant chemotherapy, PIV: Pan-immune-inflammation value, SII: Systemic immune-inflammation index

Table 4. Model coefficients - pCR

						95% Confidence interval	
Predictor	**Estimate**	**SE**	**Z**	**p**	**Odds ratio**	**Lower**	**Upper**
Intercept	-0.904	0.546	-1.656	0.09	0.405	0.139	1.180
T Stage							
T3-T1	1.027	0.448	2.2906	0.022	2.792	1.160	6.722
T2-T1	0.794	0.372	2.1337	0.033	2.212	1.067	4.587
Grade							
Grade II - Grade III	0.456	0.286	1.5958	0.111	1.578	0.901	2.764
PIV pre-NAC/post-NAC)							
Ref.<Cut-off value	0.121	0.357	0.3397	0.734	1.129	0.561	2.274
SII pre-NAC/post-NAC)							
Ref.<cut-off value	0.373	0.439	0.8508	0.395	1.453	0.615	3.434
Neutrophil/lymphocyte ratio							
Ref.<cut-off value	-0.377	0.384	-0.9829	0.326	0.686	0.323	1.455
Platelet/lymphocyte ratio							
Ref.<cut-off value	0.714	0.331	2.1585	0.031	2.042	1.068	3.905
Neutrophil ratio (pre-NAC/post-NAC)							
Ref.<cut-off value	-0.525	0.326	-1.6098	0.107	0.592	0.312	1.121
Hemoglobin ratio (pre-NAC/post-NAC)							
Ref.<cut-off value	0.544	0.268	2.0283	0.043	1.722	1.018	2.912
HR status							
Negative-positive (ref)	-1.064	0.271	-3.9223	<.001	0.345	0.203	0.587
HER2 status							
Negative-positive (ref)	1.475	0.263	5.6093	<.001	4.370	2.610	7.315

the Hosmer-Lemeshow test; however, external validation was not performed, and the results should therefore be interpreted cautiously.

Conclusions

Changes in inflammatory marker ratios before and after NAC were significantly associated with pCR among breast cancer patients. However, these results demonstrate only associations and do not support the use of these markers as standalone predictive biomarkers. This limitation is further supported by the relatively low AUC values observed in ROC analyses and the absence of an independent validation cohort. Therefore, inflammatory markers should be interpreted as complementary indicators alongside established clinicopathological factors. Higher pre-NAC/post-NAC platelet-to-lymphocyte and hemoglobin ratios, HER2 positivity, hormone receptor negativity, and earlier T-stage were independently associated with pCR. However, given their limited discriminative performance, these inflammatory markers should not be considered standalone predictive tools but rather complementary to established clinicopathological factors; further prospective validation is required.

Ethics

Ethics Committee Approval: The Research Ethics Committee of University of Health Sciences Türkiye, Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, granted ethical approval to our study (approval number: 2024-07/104, date: 25.08.2022).

Informed Consent: The data collection program for this study was approved by ethics committee with a waiver for individual informed consent for this retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.F.S., A.K., C.Ö., Concept: M.F.S., A.K., C.Ö., Design: M.F.S., A.K., C.Ö., Data Collection or Processing: M.F.S., E.G., C.Y.B., F.A., A.K., C.Ö., Analysis or Interpretation: M.F.S., A.K., C.Ö., Literature Search: M.F.S., E.G., C.Y.B., A.K., C.Ö., Writing: M.F.S., A.K., C.Ö.

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