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ARE INFLAMMATORY AND NUTRITIONAL MARKERS A PROGNOSTIC FACTOR IN GASTRIC CANCER PATIENTS?

(Article Officially Endorsed by Science Citation Index)

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ABSTRACT

Background/Aim: *Inflammatory and nutritional markers are associated with the detection of prognosis in malignancy. This study aims to investigate the changes in inflammatory biomarkers during neoadjuvant therapy and after surgery to predict the prognosis in patients with gastric cancer.*

Materials and Methods: *Blood samples were collected before and after surgery from n=138 patients with gastric cancer after receiving neoadjuvant chemotherapy (NACT) to determine the prognostic importance of inflammatory and nutritional markers.*

Results: *Postoperative albumin and platelet-lymphocyte ratio (PLR) values were decreased significantly compared to the preoperative period ($p < 0.05$). Similarly, the postoperative neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP), CRP-albumin ratio (CAR), and systemic immune inflammation index (SII) values increased significantly compared to the preoperative period ($p < 0.05$). However, no significant change was observed in postoperative CRP levels compared to preoperative values ($p > 0.05$). The preoperative and postoperative CRP and the CAR, and postoperative NLR, PLR, and SII values exhibited significant effects on the length of survival in the univariate analysis ($p < 0.05$). In multivariate analysis, preoperative CRP and postoperative NLR and PLR values emerged as significant and independent predictors of survival ($p < 0.05$). On the Kaplan-Meier analysis results, the shortest survival time, 4.73 months, was observed in the group with SII values greater than 2500.*

Conclusions: *Systemic inflammatory markers preoperative CRP and postoperative NLR and PLR may be reliable parameters for independent prediction of survival in patients receiving curative treatment for gastric cancer.*

Registry Number: *Registration No. 2717 on 20th July 2023, Health Sciences University, Adana City Training, and Research Hospital, Turkey.*

Keywords: *Gastric tumors, general survival, hematologic biomarkers, prognostic factor.*

INTRODUCTION

Gastric cancer (GC) is widely known as a severe global health concern due to its increasing prevalence, it is the fifth leading cause of morbidity, and a fourth of mortality (1, 2). Patients other than GC, with the same stages of tumor, node, and metastasis (TNM), or receiving similar treatments may show different results (1, 3-6). The prognosis in patients with GC is evaluated based on the clinical stage, tumor diameter, and therapeutic methods. Effective clinical prognostic indicators are

therefore very important in preliminary treatment and follow-up (2). Systemic inflammatory responses assess to identify the location and progression of the cancer and play a pivotal role in all stages of the tumor including its invasion, development, and metastasis (7).

Recent studies have proposed that these markers are independent and known prognostic indicators in various cancers including GC (1). The inflammation due to tumors has a great impact on DNA damage, mutation, abnormal proliferation, and angiogenesis (8-10). The host's immunoinflammatory response determines the tumor microenvironment (4). Albumin and inflammatory markers play critical roles in various biological processes, the body can reduce albumin production to increase inflammatory markers and decrease albumin levels (11). Conditions such as mild to severe infections, chronic diseases, and aging can increase inflammatory markers by decreasing physical activity, increased stress, and inadequate nutrition (12). The role of systemic inflammation is pivotal in tumor progression because neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP), CRP-albumin ratio (CAR), and systemic immune inflammation index (SII) have attracted significant attention as prognostic markers in cancers including GC. platelet-to-lymphocyte ratio (PLR) is a biomarker for the balance between the inflammatory and the immune response (13) in severe/chronic diseases. Patients with high NLR exhibited lower survival rates. High PLR may be an important prognostic biomarker for poor overall survival (OS). The SII has generally not reported or documented survival rates and has usually addressed only the relationship between the cut-off point and tumor differentiation or stage or the risk of mortality. Age has been identified specifically as a key factor affecting levels of inflammatory markers (14).

The current literature has focused on the pre-and post-neoadjuvant chemotherapy (NACT) periods, while the present research spans the post-NACT and post-gastrectomy periods. Therefore, the current study evaluated a set of complete analyses of the inflammatory and nutritional markers used during pre-and post-NACT and then pre-and post-gastrectomy periods to investigate the mutual relationship between these markers and survival.

MATERIALS and METHODS

Patients: One hundred and thirty-eight (n=138) patients diagnosed with primary GC and undergoing total or subtotal gastrectomy after NACT at the Adana City Training and Research Hospital, Türkiye, from January 2014 to January 2023 were included in the current retrospective study. The data for the current study were recovered from the hospital's electronic records.

Patients with histologically confirmed GC, stage pT2A-3C, undergoing total or subtotal R0 gastrectomy, without missing medical or follow-up data, and with survival times greater than 3 months were included. Patients receiving radiotherapy before surgery, with previously diagnosed malignant diseases, distant metastasis, or cancers other than GC during diagnosis, with organ failure, autoimmune, inflammatory, or hematological diseases, receiving a blood transfusion or with active infection the previous month before blood collection, and those with recurrence were excluded. The effect on age, sex, tumor location, operative procedure, pathological stage, positive lymph nodes, lymphovascular invasion, peri neural invasion, tumor diameter, and pre-and postoperative inflammatory and nutritional markers was reviewed. The pathological stages after the operation of the participants were categorized according to the American Joint Committee on Cancer, the eighth edition's guideline. All patients underwent regional lymph node dissection and total or subtotal gastrectomy after NACT. Causes of death, such as recurrence, laboratory data, ultrasound, computed tomography, and laparotomies, were determined from the medical records or directly asked by patients' families. The median period for follow-up analysis was (mean) 20.2 months.

The procedure for the current study was conducted according to the ethical committee, under registration No. 2717 on 20th July 2023, Health Sciences University, Adana City Training, and Research Hospital, Turkey. The volunteer participants were informed of the study protocol and willingly filled out and signed the consent before enrollment in the current study.

Data Collection and Analysis: Blood samples were centrifuged to collect serum to determine the inflammatory and nutritional markers neutrophil, lymphocyte, platelet, leukocyte, CRP, and albumin. Blood samples for peripheral analysis were collected approximately five weeks after the last chemotherapy session in the preoperative period, 1-4 days before surgery, and 30-35 days after surgery, and the test results were subjected to analysis. Two groups were constituted, one consisting of stages 1 and 2 and the other of stage 3 only.

The hospital hematological index was neutrophil 10^3/µl (1.9–8.2), lymphocyte 10^3/µl (1.1–3.1), platelet 10^3/µl (179–548), CRP mg/l (0–5), and albumin g/l (35–55).

The NLR (neutrophils to lymphocytes ratio), and the PLR (platelets to lymphocytes ratio) were calculated by peripheral blood analysis. The CAR was determined by the proportion of CRP in serum CRP to albumin serum. Finally, the SII was defined as absolute platelet levels x absolute neutrophil levels/lymphocyte levels (1).

Univariate and subsequently multivariate Cox regression analyses were done to determine the effect of age, sex, preoperative and postoperative laboratory markers, and pathological characteristics as predictive biomarkers. The cut-off points for the CRP, NLR, PLR, CAR, and SII by using the Youden index were 10 mg/l, 6 mg/l, 250 mg/l, 0.4 mg/l, and 250 mg/l, respectively. In addition, the parameters of the two groups were classified as high and low, based on the cutoff values. Optimal cut-off values were determined to assess the effect of preoperative and postoperative prognostic indicators on overall survival (OS; the time frame, from the day of surgery till to death), Kaplan-Meier survival curves were used to highlight survival probabilities at biomarker thresholds to facilitate evaluation of their prognostic importance before and after surgery. At the same time, both preoperative and postoperative settings were considered for assessment purposes to provide a strong framework within which such predictions could be made with confidence. In doing so, not limited to identifying only what each one does, but also makes them better tools for prognosis in clinical practice.

Statistical Analysis: The data was statistically analyzed by using SPSS (version 28.0) to analyze the effects, and the effect's significant values were expressed ($p<0.05$, $p<0.01$) and non-significant ($p>0.05$). The distribution of variables was assessed with the use of the Kolmogorov-Smirnov test. Wilcoxon's test was used for repeated measurement analysis and COX regression and Kaplan-Meier (log-rank) for the survival (OS) analysis.

RESULTS

Clinicopathological Characteristics: A total of (n=138) individuals were evaluated in which Women represented 26.1% (n=36) of the patient group and men 73.9% (n=102). The mean age was 61.97 (27-87) years. The GC in the upper third was 39.9%, the middle third 23.9%, and the lower third in 36.2% of the cases. Subtotal gastrectomy was performed on 35.5% of the patients and total gastrectomy on the remaining was 64.5%. Differentiation was weak in 35.5% of the patients, moderate in 49.3%, and outstanding in 15.2%. The most common tumor stage was 2A, seen in 50.0% of the patients. On pathological examination, the positive lymph node rate was 72.5%, the lymphovascular invasion rate was 67.4%, and the perineural invasion rate was 52.2%. The mean tumor diameter was 4.55 (1-12.5) cm, and the mean survival time was 20.25 (3.13-105) months. Demographic characteristics are shown in Table I.

Changes in inflammation and nutritional indicators in the pre-and postoperative periods were analyzed in albumin, CRP, NLR, PLR, CAR, immunoglobulin-albumin ratio, and SII, respectively. The results showed that postoperative albumin and PLR were significantly reduced than in the preoperative period ($p < 0.01$). Furthermore, no significant changes were observed in pre- and postoperative CRP. Postoperative values had significant results in NLR ($p<0.05$), CAR ($p<0.05$), and SII ($p<0.01$) than in the preoperative period. The significant post-operative values are shown in Table II and Figure 1.

The role of hematologic indices in predicting survival on age, sex, preoperative and postoperative albumin, preoperative NLR, PLR and SII, tumor localization, the operative procedure, differentiation,

number of positive lymph nodes, and tumor size exhibited no significant predictive ability in terms of survival in the univariate model ($p > 0.05$). In contrast, preoperative CRP and CAR, and postoperative CRP, NLR, PLR, CAR, and SII values showed significant effects on predictors of survival ($p < 0.05$). Whereas, in the multivariate reduced model, pre-operative CRP, postoperative NLR, PLR, and stage exhibited a significant and independent effect in the prediction of survival ($p < 0.05$), as shown in Table III.

Survival Analysis Results: the Kaplan-Meier method (Lang-Park) was used for survival analysis, and the results showed that the predicted median survival time was significantly shorter in the CRP >10 group [9.23 months (8.65-9.82)] than in the CRP> 10 group [15.57 months (12.44-18.69)]. The predicted mean survival in the NLR >6 group [8.07 months (2.66-13.47)] was significantly shorter span than in the NLR ≤6 group [15.57 months (13.23-17.91)]. A significantly shorter predicted median survival time was also observed in the PLR >250 group [9.43 months (4.34-14.53)] than in the PLR <250 group [14.73 months (12.34-17.13)]. The predicted median survival time in the CAR >0.4 group [9.13 ay (4.49-3.78)] was significantly shorter than in the CAR ≤0.4 group [15.07 months (12.79-17.35)]. Significantly shorter predicted median survival time was also detected in the SII >2500 group [4.73 months (3.03-6.44)] compared to the SII≤ 2500 group [15.43 months (13.19-17.68)]. Furthermore, the predicted median survival time in stage III [12.30 months (6.30-18.30)] was significantly shorter than that in the CAR> 2500 group [15.63 months (11.97-19.29)] (Table IV, Figure 2)

When cumulative survival rates were examined within a range of 6-60 months, early mortality was more pronounced in patients with PLR values above the cutoff point compared to the other groups. Additionally, none of those patients survived beyond 24 months. The highest survival rate, 8.4%, was observed in stage I-II patients (Table V).

DISCUSSION

The current study showed that changes were observed in inflammatory and nutritional markers in patients with GC over time. Their relationship with patient outcomes and compared both the pre-and post-operative conditions including CRP, albumin, NLR, and PLR which show significant alterations after NACT and operation thereby pointing out their dynamic nature as measures for response to therapy or recovery. The current analysis could contribute over time towards a broader understanding of the prognostication of GC while also helping to establish guidelines for treatment plans and individual care.

Previous studies established the relationship between age with the risk of GC and showed that age plays an important role in inflammatory reactions (15). Whereas other demographic variables including NLR and the ratio of lymphocytes to monocytes (LMR) for inflammation-based prognostication in GC are significantly influenced by the age of the patient (16). An independent predictor of survival, the prognostic nutritional index can be used on systemic inflammation and has strong associations between aging, inflammation, and nutrition status in elderly (<80 years) persons (17). The complexity of these factors has a significant effect on the development of diseases and health management. Therefore, the current study monitored the marker levels are critically important in terms of prognosis with age for appropriate therapeutic strategies.

A study showed that a genetic risk model can predict GC risk in a very vast healthcare (18). However, very limited literature is available on genetic screening but not available in support of the current study's methodology. Whereas, a study showed that using specific genetic signatures is associated with a poor prognosis among similar high-risk groups (19). The current study also uses noninvasive genetic markers in identifying patients with higher chances of death. This will make sure that while we do not use any form of direct gene scanning, alternative methods remain relevant and useful for predicting outcomes among different individuals (18, 19).

The previous studies reported that systematic inflammation plays a significant role in the progression of the tumor, including systematic inflammatory markers including CRP, NLR, and PLR (1, 2, 20, 21). Parallel to that, the previous

studies have reported various reactions towards surgeries/ chemotherapy as in indication differ greatly in prognostic markers for example; survival ***can be predicted by considering baseline systemic inflammation and immune status measured through pretreatment NLR, Δ-LMR and showed treatment response heterogeneity at the individual level (16). Contrary to that, a study identified NLR and PLR (predictors of poor prognosis) in GC and showed that NLR has*** adverse effects on survival and OS(22, 23). Whereas, CRP/albumin ratio and NLR are identified as an independent prognostic indicator (24) widely used in subsequent studies. Other than that, only CAR(α) has a significant association with prognosis but no effect in albumin also reflects inflammation in addition to the patient's nutritional status (1, 24). However, albumin in this context has an association with chronic inflammation reaction and is used as an inflammation marker. The current study found similar results, CAR is significantly correlated with prognosis and has no association with albumin. Therefore, the current study showed that the preoperative and postoperative albumin levels of most patients were within our hospital's normal reference values.

The rise in CRP was probably caused by the effect of the inflammatory microenvironment contributing to aggressive cancer behavior (24, 25). The current study obtained similar results, a significant independent poor prognostic effect in terms of survival time was observed in the staging with preoperative CRP and postoperative NLR and PLR. Another study showed that low NLR and PLR indicated a positive prognosis in GC and that high NLR represented an independent poor prognostic factor(26, 27). However, a study found it unable to confirm the prognostic effect of NLR and PLR (10). The current results show that biomarkers obtained from noninvasive peripheral blood analysis may be useful in the evaluation of the tumor microenvironment and in predicting prognosis (10). Whereas, a study confirmed that patients with high NLR exhibited lower survival rates (6), associated with low lymphocyte value. Lymphocytes produce an anti-tumor immuno-response by inducing cytotoxic cell death and limiting the proliferation and migration of tumor cell (4, 5, 28). Neutrophils support tumor growth, development, and metastasis by inhibiting acute and chronic inflammation according to the cytokines and chemokines they release (2, 5, 9, 17)

Previous studies showed that high SII is associated with poor prognosis in many types of malignancies including GC (2, 5, 8). In contrast, low SII survived longer and exhibited better clinical results (9). These reported results are consistent with the current study. Studies on a specific cut-off point for SII have generally not reported or documented survival rates, and have usually addressed only the relationship between the cut-off point and tumor differentiation or stage or the risk of mortality (21). However, the present study showed a high SII also emerged as a poor prognostic factor.

The TNM staging system is widely used and acceptable to evaluate prognosis and help with treatment decisions (29). The current study showed in a univariate model age, sex, tumor localization, operative procedure, differentiation, number of positive lymph nodes, and tumor size did not show significant effectiveness in predicting survival length of survival. However, stage, lymphovascular invasion, and perineural invasion significantly predicted survival in the same model. In the multivariate reduced model, stage III exhibited significant independent effectiveness in predicting survival duration.

The current study undermines the strengths of the proposed study due to its retrospective nature and the limited number of patients. However, argues that the criticisms regarding cutoff values in the literature are not entirely valid. Since there is no specific cut-off point in the international standards, each study determines values by itself. However, despite this variation in cut-off points, the findings of these studies still exhibit significant predictive power. The number of division of cells is one of the known parameters used, may be affected by several events in the body and can exhibit rapid abnormal changes. The individual-specific immune system or the degree of disease can also have an effect. This also suggests that the cutoff values may be community-specific.

CONCLUSION

This study concluded that systematic markers including CRP, PLR, and NLR are capable of being used as independent prognostic factors in predicting survival in GC patients by comparing various inflammatory indices, nutritional markers, and serum tumor markers. These findings may contribute to the development of new, more patient-specific therapeutic strategies in cases with a poor prognosis.

The current study is rare because it examines the efficacy of novel neoadjuvant chemotherapy in the treatment of cancer and postoperative periods in terms of estimating prognosis. A comprehensive investigation of all periods is important in terms of identifying the most effective period to determine the prognosis of cancer. The inflammatory process can increase significantly during neoadjuvant therapy and the postoperative period. Further studies focusing on this period, considering the effects of these increases on prognosis and yielding results similar to those of other studies may yield more reliable and significant findings in predicting prognosis.

DECLARATION AND STATEMENT

Ethics Approval and Consent to Participate: The current study is registered at Health Sciences University, Adana City Training, and Research Hospital, Turkey under the rregistration No. 2717 on 20th July 2023.

Consent for Publication. Written consent will be shared upon request.

Availability of Data and Materials. The respective data and materials are available, and will be shared upon request.

Competing Interests. NA

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Authors' Contributions

Conceptualization, YD, AS; Methodology, YD, AS; Validation, YD.; Formal Analysis, YD; Draft preparation, YD, AS; writing – review and editing, YD, AS; visualization, YD, AS; supervision, YD, AS.

Conflicts of Interest

The Author(s) declares no conflicts of interest concerning the research, authorship, and/or publication of this article. They also do not have relevant or non-financial interests to disclose.

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Table I. Clinicopathologic characteristics of patients.

		Min-Max			Median	Mean±sd/n-%		
Age		27.00	-	87.00	63.00	61.97	±	45627
Gender	Female					36		26.1%
	Male					102		73.9%
Tumor Localization	Lower					50		36.2%
	Middele					33		23.9%
	Upper					55		39.9%
Operation Procedure	ST					49		35.5%
	TG					89		64.5%
Differentiation	Poor					49		35.5%
	Moderate					68		49.3%
	Well					21		15.2%
Stage	2A					70		50.7%
	2B					25		18.1%
	3A					20		14.5%
	3B					15		10.9%
	3C					8		5.8%
Positive Lymphnode	(-)					38		27.5%
	(+)					100		72.5%
Lymphovascular Invasion	(-)					45		32.6%
	(+)					93		67.4%
Perinoral Invasion	(-)					66		47.8%
	(+)					72		52.2%
Positive Lymphnode #		0.00	-	29.00	1.00	46082	±	45413
Tumor Diameter		1.00	-	18598	4.00	20180	±	18660
Survival Time (M)		41334	-	105.00	14.37	20.25	±	17.40

Table II. [w]Wilcoxon test analysis results of markers in the preoperative and postoperative periods.

	Preop				Postop				p	
	Mean±sd			Median	Mean±sd			Median		
Albumin	37.2	±	5.10	37.2	33.9	±	5.70	34.1	***0.000***	w
CRP	6.80	±	11.38	2.91	6.76	±	11.97	3.45	0.140	w
NLR	3.25	±	1.84	3.00	4.39	±	10.14	2.13	***0.031***	w
PLR	185.6	±	93.5	167.0	164.7	±	124.5	129.7	***0.000***	w
CAR	0.17	±	0.32	0.08	0.21	±	0.41	0.10	***0.026***	w
SII	952.5	±	626.4	779.8	1055.1	±	2246.8	532.3	***0.002***	w
Immunoglobulin -Albumin Ratio	1.2 ± 0.2			1.2	1.1 ± 0.3			1.1	***0.850***	w

Table III. Univariate and Multivariate Overall Survival Analyses of Inflammatory Biomarkers Associated with Survival in Gastric Cancer Patients Using Cox Regression (Forward LR) Analysis.

	Univariate Model	Multivariate Model

		HR	% 95 CI			p	HR	% 95 CI			p
Age		0.993	0.979	-	1.007	0.303					
Gender		1.128	0.768	-	1.658	0.539					
Albumin	Preop	0.969	0.938	-	1.002	0.063					
	Postop	0.990	0.963	-	1.018	0.495					
CRP	Preop	1.024	1.010	-	1.038	0.001	1.027	1.012	-	1.042	0.000
	Postop	1.016	1.002	-	1.031	0.027					
NLR	Preop	1.071	0.988		1.161	0.097					
	Postop	1.034	1.017	-	1.052	0.000	1.027	1.012	-	1.042	0.000
PLR	Preop	1.001	0.999	-	1.002	0.197					
	Postop	1.002	1.001	-	1.003	0.006	1.027	1.012	-	1.042	0.000
CAR	Preop	2.256	1.411	-	3.608	0.001					
	Postop	1.667	1.124	-	2.471	0.011					
SII	Preop	1.000	1.000		1.000	0.275					
	Postop	1.000	1.000	-	1.000	0.003					
Tumor Localization		1.088	0.898	-	1.319	0.388					
Operation Procedure		1.171	0.825	-	1.662	0.378					
Differantiation		0.845	0.666	-	1.073	0.167					
Stage		1.731	1.193	-	2.511	0.004	1.883	1.277	-	2.776	0.001
Positive Lymphnode #		1.025	0.997	-	1.054	0.076					
Tumor Diameter		1.022	0.956	-	1.093	0.521					
Lymphovascular Invasion		1.774	1.226	-	2.569	0.002					
Perinoral Invasion		1.552	1.094	-	2.202	0.014					

Table IV. Kaplan-Meier Survival Analysis of Inflammatory Biomarkers

		Survival Time (Month)				p
		Median	95% Confidence Interval			
CRP	≤10	15.57	12.44	-	18.69	***0.002***
	>10	9.23	8.65	-	9.82	
NLR	≤6	15.57	13.23	-	17.91	***0.005***
	>6	8.07	2.66	-	13.47	
PLR	≤250	14.73	12.34	-	17.13	***0.005***
	>250	9.43	4.34	-	14.53	
CAR	≤0.4	15.07	12.79	-	17.35	***0.002***
	>0.4	9.13	4.49	-	13.78	
SII2	≤2500	15.43	13.19	-	17.68	***0.000***
	>2500	4.73	3.03	-	6.44	
Stage	I-II	15.63	11.97	-	19.29	***0.003***
	III	12.30	6.30	-	18.30	
Overall		14.33	12.22	-	16.44	

Kaplan Meier (Log Rank)

Table V. Cumulative survival ratio %.

		Cumulative Survival Ratio %							
		6.Month	12.Month	18.Month	24.Month	30.Month	36.Month	48.Month	60.Month
Total		84.8%	60.9%	39.9%	31.0%	23.6%	20.5%	19.2%	16.8%
Evre	I-II	88.4%	65.3%	44.2%	34.7%	25.3%	21.9%	20.5%	18.4%
	III	***76.7%***	***51.2%***	***30.2%***	***16.3%***	***7.0%***	***7.0%***	***0.0%***	***0.0%***
NLR	≤6	88.3%	64.2%	42.5%	30.8%	20.8%	17.5%	8.3%	6.7%
	>6	***61.1%***	***38.9%***	***22.2%***	***16.7%***	***11.1%***	***0.0%***	***0.0%***	***0.0%***
CRP	≤10	86.3%	64.1%	44.4%	32.5%	22.2%	17.9%	8.5%	6.8%
	>10	***75.0%***	***40.0%***	***15.0%***	***10.0%***	***5.0%***	***0.0%***	***0.0%***	***0.0%***
PLR	≤250	86.5%	62.7%	42.9%	31.7%	21.4%	16.7%	7.9%	6.3%
	>250	***66.7%***	***41.7%***	***8.3%***	***0.0%***	***0.0%***	***0.0%***	***0.0%***	***0.0%***
CAR	≤0.4	86.3%	64.5%	42.7%	31.5%	21.8%	16.9%	8.1%	6.5%
	>0.4	***71.4%***	***28.6%***	***14.3%***	***7.1%***	***0.0%***	***0.0%***	***0.0%***	***0.0%***
SII	≤2500	89.1%	64.1%	42.2%	30.5%	20.3%	16.4%	7.8%	6.3%
	>2500	***30.0%***	***20.0%***	***10.0%***	***10.0%***	***10.0%***	***0.0%***	***0.0%***	***0.0%***

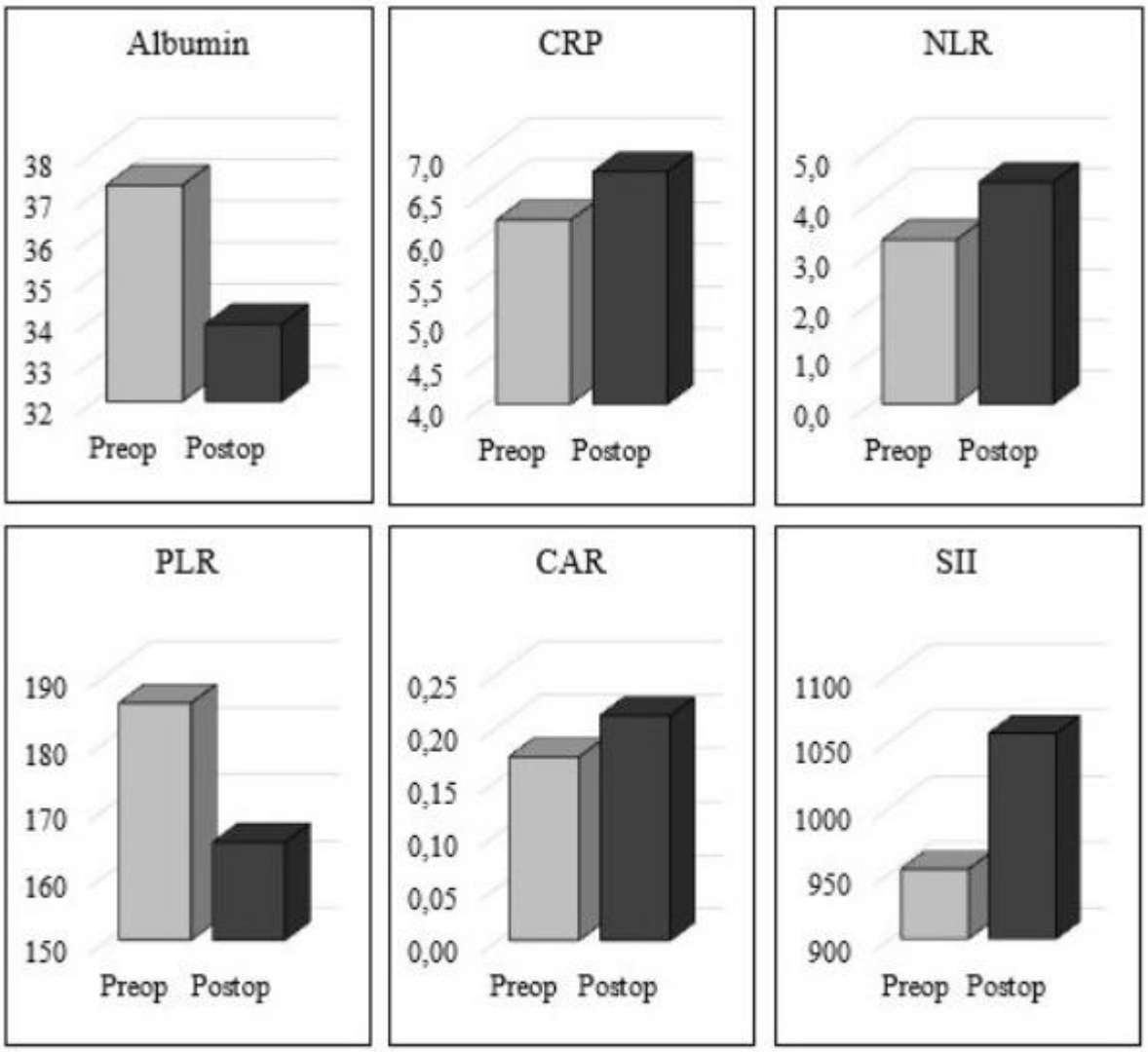

Figure 1. Numerical Data Changes for Inflammatory and Nutritional Markers Preoperative and Postoperative Values. (A) Albumin level, (B) CRP, (C) NLR levels, (D)PLR levels, (E) CAR levels, (F) SII levels. [Wilcoxon test; $p<0.01$ and $p<0.05$ (A, C, D, E, F), $P>0.05$ (B)].

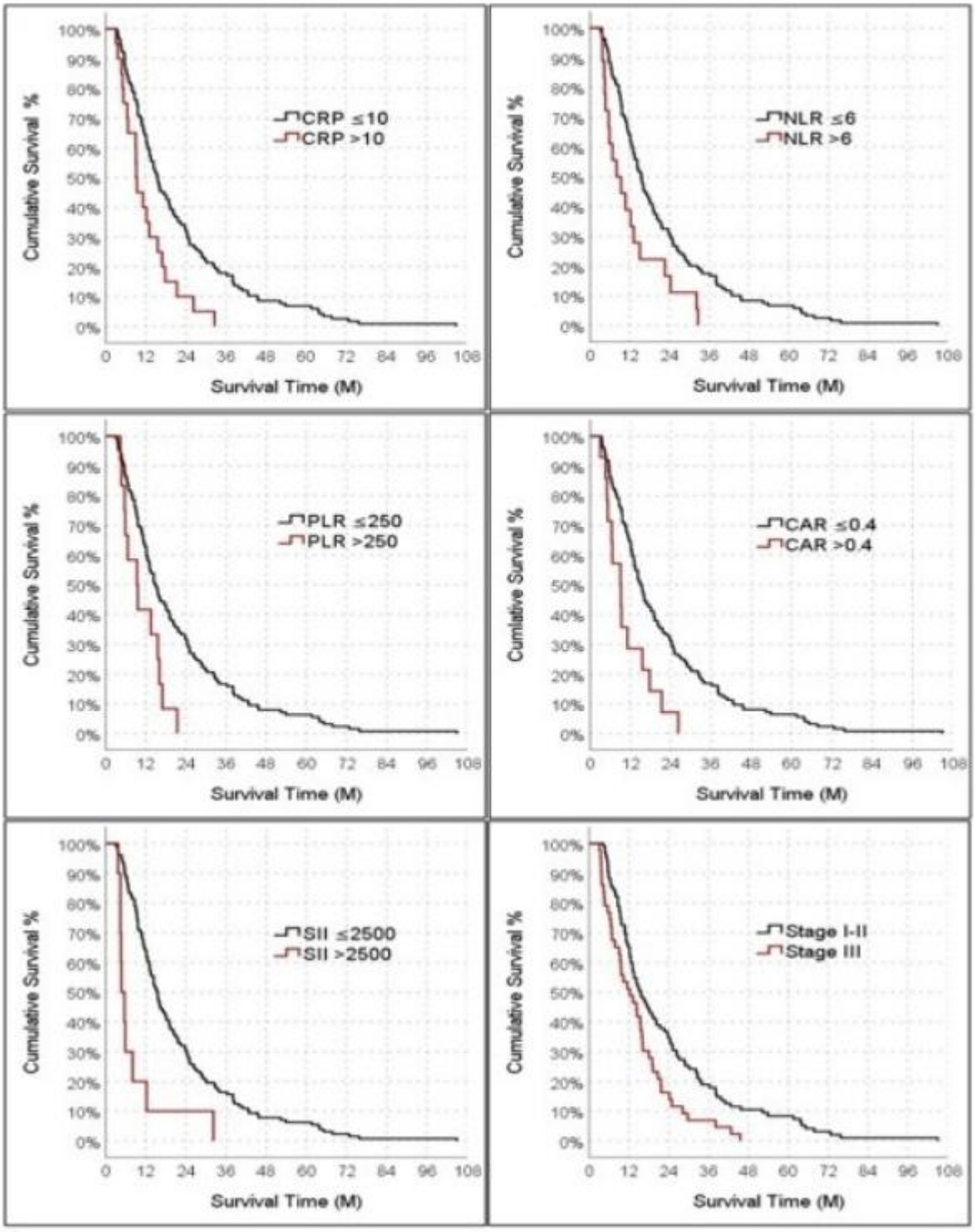
Cumulative Survival %
Survival Time (M)
CRP ≤10
CRP >10
NLR ≤6
NLR >6
PLR ≤250
PLR >250
CAR ≤0.4
CAR >0.4
SII ≤2500
SII >2500
Stage I-II
Stage III

Figure 2. Kaplan–Meier survival curves according to hematologic indexes associated with overall survival (OS) when divided into 2 groups (high/low). OS outcomes according to indexes including CRP, NLR, PLR, CAR, SII and stage ($P < 0.05$).

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