



# Prognostic Significance of Systemic Immune Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI) in Patients with Locally Advanced Gastric Cancer Treated with Perioperative FLOT Therapy

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## ABSTRACT

**Objective:** In recent years, studies have demonstrated the prognostic importance of the systemic immune inflammation index (SII) and the systemic inflammation response index (SIRI) in gastric cancer. We aimed to determine the prognostic significance of SII and SIRI in patients with locally advanced gastric cancer who underwent perioperative fluorouracil, leucovorin, oxaliplatin, and docetaxel therapy at our center.

**Material and Methods:** Our study was a retrospective, single-center study that included 167 patients with locally advanced gastric cancer between June 2019 and December 2023.

**Results:** The SII parameter demonstrated very high discriminatory power [area under the curve (AUC)=0.963; 95% confidence interval (CI): 0.938-0.988]. For a cut-off value of  $\geq 664.00$ , the sensitivity was 87.1% and, the specificity was 87.8%, and the result was statistically significant ( $p < 0.001$ ). Similarly, the SIRI value exhibited high predictive performance (AUC=0.952; 95% CI: 0.922-0.982). For a cut-off value of  $\geq 1.27$ , the sensitivity was 88.2%, and the specificity was 89.2%, establishing this parameter as a strong predictor of mortality ( $p < 0.001$ ). In patients with SII  $< 664.00$ , the 2-year and 5-year overall survival (OS) rates were 94.7% and 83.7%, respectively, while in the SII  $\geq 664.00$  group, the 2-year OS dropped to 13.9%, and the 5-year OS could not be calculated ( $p < 0.001$ ). A similar trend was observed in terms of SIRI; In patients with SIRI  $< 1.27$ , the 2-year OS was 88.1% and the 5-year OS was 85.3%, while in the SIRI  $\geq 1.27$  group, the 2-year OS decreased to 19.4% ( $p < 0.001$ ). According to the multivariate Cox regression analysis results, having an SII  $\geq 664.00$  increased the risk of death 8.49 times [Hazard ratio (HR): 8.49; 95% CI: 4.35-16.57;  $p < 0.001$ ], and having a SIRI  $\geq 1.27$  increased the risk of death 7.88 times (HR: 7.88; 95% CI: 3.99-15.60;  $p < 0.001$ ). Similarly, having an SII  $\geq 664.00$  increased the risk of progression 5.13 times (HR: 5.13; 95% CI: 3.14-8.39;  $p < 0.001$ ) and having a SIRI  $\geq 1.27$  increased the risk of progression 3.89 times (HR: 3.89; 95% CI: 2.39-6.31;  $p < 0.001$ ).

**Conclusion:** There is a need for biomarkers that can be used clinically for prognostic and predictive purposes in gastric cancer patients. Lower SII and SIRI levels are significantly associated with improved OS and disease-free survival in patients with gastric cancer. More comprehensive analyses that combine it with other markers have been and continue to be conducted.

**Keywords:** Systemic immune inflammation index; systemic inflammation response index; prognostic significance; locally advanced gastric cancer; perioperative FLOT therapy

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## INTRODUCTION

Gastric cancer ranks highly among malignancies in terms of both incidence and mortality. It is the 5<sup>th</sup> most common malignancy worldwide and the 4<sup>th</sup> leading cause of cancer-related mortality.<sup>1</sup> Although surgical resection is the primary treatment for stomach cancer, half of the patients die within 5 years after radical surgery.<sup>2</sup>

Because symptoms appear late and there is usually no pathognomonic sign, patients are often diagnosed at an advanced stage. Therefore, the importance of neoadjuvant therapy in gastric cancer has increased over the years. Neoadjuvant therapy has been shown to improve pathological and radiological response.<sup>3,4</sup> According to guidelines, the recommended approach to the medical treatment of locally advanced gastric cancer is perioperative therapy, consisting of neoadjuvant and adjuvant chemotherapy. Perioperative systemic therapy utilizes the fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) regimen.<sup>5</sup> Recent studies have demonstrated a survival benefit of perioperative durvalumab treatment combined with the FLOT regimen in certain patients, and the guidelines have been revised.<sup>6</sup>

Systemic inflammation is a predictor of cancer prognosis, playing a critical role in proliferation, migration, invasion, and metastasis. Many studies have investigated the prognostic significance of systemic inflammation markers in patients with malignancy.<sup>7-9</sup> In recent years, the literature contains studies demonstrating the prognostic importance of the systemic immune inflammation index (SII) and the systemic inflammation response index (SIRI) in gastric cancer.<sup>10,11</sup>

In our study, we aimed to determine the prognostic significance of SII and SIRI in patients with locally advanced gastric cancer who received perioperative FLOT therapy at our center.

## MATERIAL AND METHODS

Our study was conducted retrospectively and as a single-center study, and included 167 patients with locally advanced gastric cancer between June 2019 and December 2023. Pathological staging was done using the 7<sup>th</sup> edition of the tumour, node, and metastasis staging system.<sup>12</sup> Patients with incomplete data, those with metastatic disease, those diagnosed with more than one primary malignancy, and individuals under 18 years of age were excluded from the analysis.

For all patients, tumor localization, tumor grade, histopathology, tumor type (diffuse or intestinal), T and N stages, and counts of neutrophils, lymphocytes, monocytes, and platelets were recorded from their medical records at the

time of diagnosis. SII and SIRI were calculated for all patients at the time of diagnosis. Staging of all patients was performed using thoracic, abdominal, and pelvic computed tomography with intravenous and oral contrast, followed by laparoscopic staging. Additionally, radiological and pathological responses to neoadjuvant therapy, development of recurrence or distant metastasis during treatment or follow-up, overall survival (OS), and disease-free survival (DFS) were assessed.

Radiological response evaluation after 4 cycles of neoadjuvant FLOT was performed using the Response Evaluation Criteria in Solid Tumors.<sup>13</sup> All patients received a total of 8 cycles of FLOT treatment, consisting of 4 neoadjuvant cycles and 4 adjuvant cycles. All patients included in the study received full doses of neoadjuvant and adjuvant therapy. Patients who underwent dose reduction or were unable to complete adjuvant therapy due to toxicity were excluded from our study. OS was defined as the time from diagnosis to death or to the date of the last follow-up. DFS was defined as the time from the last adjuvant chemotherapy to the detection of recurrence/metastasis. Pathological response to neoadjuvant therapy was assessed using the College of American Pathologists (CAP) score, which measures the tumor regression grade after surgery.<sup>14</sup> All patients included in our study were microsatellite-stable, human epidermal growth factor receptor 2-negative, and had a histopathologic diagnosis of adenocarcinoma with a tumor grade of 2-3. The SII was calculated using the formula: platelet count  $\times$  neutrophil count/lymphocyte count. The SIRI was calculated using the formula: monocyte count  $\times$  neutrophil count/lymphocyte count. The parameters included in these indices were derived from peripheral blood samples.

All patients underwent routine follow-ups every 3 months for the first 2 years after completion of adjuvant chemotherapy and every 6 months between the 2<sup>nd</sup> and 5<sup>th</sup> years. During these follow-ups, thoracic, abdominal, and pelvic computed tomography scans with intravenous and oral contrast were performed, and carcinoembryonic antigen (CEA) and CA19-9 levels were recorded.

The study was conducted according to the principles outlined in the Declaration of Helsinki and was approved by the University of Health Sciences Türkiye, Prof. Dr. Cemil Taşcıoğlu City Hospital Ethics Committee (approval number: 388, date: 21.10.2025).

## Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (Statistical Package for the Social Sciences; IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as n and % for categorical variables, and mean  $\pm$  standard deviation and median (minimum-maximum) for continuous variables. Receiver operating characteristic

(ROC) curve analysis was used to predict mortality using various indices. Optimal cut-off values were determined using the Youden index, which identifies the threshold that maximizes the sum of sensitivity and specificity. The Kaplan-Meier method was used to compare OS and DFS between clinical groups. Finally, multivariate Cox regression results for mortality and progression risk associated with various clinical variables are presented;  $p < 0.05$  was considered statistically significant.

## RESULTS

A total of 167 patients were included in the study. The mean age of the patients was  $58.50 \pm 11.02$  years, with a median age of 61 (26-78). Regarding gender distribution, 70.1% of the patients were male, and 29.9% were female. Tumor localization was most frequent in the cardia (35.9%), followed by the antrum (29.9%) and the corpus (19.2%). The distributions of patients' socio-demographic and clinical variables are shown in Table 1. The mean SIRI was  $1.60 \pm 1.05$  (median, 1.35), and the mean SII was  $826.58 \pm 531.96$  (median, 685.00). Median SII values were 646.0 (257.0-1233.0) in stage 2 patients and 717.0 (342.0-3681.0) in stage 3 patients. The median SIRI values were 1.15 (0.45-2.90) in stage 2 patients and 1.47 (1.11-6.80) in stage 3 patients. On radiological response evaluation, a complete response was observed in 16.2% of patients, a partial response in 57.5%, and stable disease in 26.3%. The mean follow-up period was  $29.83 \pm 17.50$  months, with a median follow-up period of 24 months. During follow-up, 67.1% of patients experienced recurrence, 55.7% died, and 44.3% survived.

**TABLE 1: Distributions of socio-demographic and clinical variables.**

Variables	n	%
<b>Age</b>		
Mean $\pm$ SD	58.50 $\pm$ 11.02	
Median (min-max)	61.0 (26-78)	
<60	76	45.5
>60	91	54.5
<b>Gender</b>		
Male	117	70.1
Female	50	29.9
<b>Tumor localization</b>		
Cardia	60	35.9
Corpus	32	19.2
Antrum	50	29.9
Diffuse	9	5.4
<b>Tumor type</b>		
Diffuse	42	25.1
Intestinal	125	74.9

**TABLE 1: Continued.**

Variables	n	%
<b>Clinical T stage</b>		
T2	27	16.2
T3	81	48.5
T4	59	35.3
<b>Clinical N stage</b>		
N0	12	7.2
N1	56	33.5
N2	56	33.5
N3	43	25.7
<b>CA19-9</b>		
Mean $\pm$ SD	443.48 $\pm$ 4322.22	
Median (min-max)	9.90 (0.30-55730.0)	
<b>CEA</b>		
Mean $\pm$ SD	7.24 $\pm$ 13.34	
Median (min-max)	3.00 (0.33-79.00)	
<b>SIRI</b>		
Mean $\pm$ SD	1.60 $\pm$ 1.05	
Median (min-max)	1.35 (0.18-6.80)	
<b>SII</b>		
Mean $\pm$ SD	826.58 $\pm$ 531.96	
Median (min-max)	685.00 (121.00-3681.00)	
<b>Radiological response</b>		
Complete response	27	16.2
Partial response	96	57.5
Stable disease	44	26.3
<b>CAP score</b>		
0	21	12.6
1	39	23.4
2	58	34.7
3	49	29.3
<b>Recurrence</b>		
No	55	32.9
Yes	112	67.1
<b>Mortality</b>		
Alive	74	44.3
Dead	93	55.7
<b>Follow-up time (months)</b>		
Mean $\pm$ SD	29.83 $\pm$ 17.50	
Median (min-max)	24.00 (6.00-66.00)	
SD: Standard deviation; CEA: Carcinoembryonic antigen; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CAP: College of American Pathologists.		

The performance of various biochemical and inflammatory parameters in predicting mortality in patients was evaluated by ROC curve analyses (Table 2). The area under the curve (AUC) for CA19-9 was 0.535 [95% confidence interval (CI): 0.447-0.623], indicating low predictive ability. With a cut-off value of  $\leq 9.95$ , the sensitivity was 54.8% and, the specificity was 55.4%, and the result was not statistically significant ( $p=0.436$ ). Similarly, for CEA, the AUC was 0.535 (95% CI: 0.446-0.624), with a cut-off of  $\geq 2.99$ , sensitivity of 57.0%, and specificity of 56.8%, showing no significant predictive power ( $p=0.438$ ). When inflammatory indices were analyzed, the SII demonstrated excellent discriminatory power (AUC=0.963; 95% CI: 0.938-0.988). For a cut-off value of  $\geq 664.00$ , the sensitivity was 87.1% and, the specificity was 87.8%, and the result was statistically significant ( $p<0.001$ ). Similarly, the SIRI value also exhibited high predictive performance (AUC=0.952; 95% CI: 0.922-0.982). For a cut-off value of  $\geq 1.27$ , the sensitivity was 88.2%, and the specificity was 89.2%, establishing this parameter as a strong predictor of mortality ( $p<0.001$ ). These findings demonstrate that inflammatory markers SII and SIRI are the most powerful predictors of mortality, whereas CA19-9 and CEA show limited discriminatory ability.

Table 3 shows that, when the relationships between inflammatory indices and radiological response, and between

inflammatory indices and CAP treatment response scores were evaluated in patients, significant differences were observed between the SII and SIRI groups (all  $p<0.001$ ). The radiological complete response rate was 33.8% in patients with SII  $<664.0$ , while this rate was only 1.1% in the group with SII  $\geq 664.0$ . Similarly, the radiological complete response rate was 33.8% in the SIRI  $<1.27$  group, while it decreased to 1.1% in the group with SIRI  $\geq 1.27$ . High SII and SIRI levels were associated with significant increases in partial response rates and, in particular, stable disease rates. When evaluated according to the CAP score, the complete response rate was determined to be 26.0% in the SII  $<664.0$  group and 1.1% in the SII  $\geq 664.0$  group. Similarly, for SIRI, a complete response was observed in 26.0% at low SIRI levels, whereas it decreased to 1.1% at high SIRI levels. Conversely, the rate of poor responses increased significantly in groups with a high inflammatory index. Poor response was recorded at 51.2% in the SII  $\geq 664.0$  group, and at 50.0% in the SIRI  $\geq 1.27$  group. These findings indicate that high SII and SIRI values are associated with a significantly lower treatment response as measured by both radiological responses and CAP scores, suggesting that an increased inflammatory load can negatively affect treatment efficacy.

**TABLE 2: Analysis of the predictive value of various clinical parameters in differentiating mortality in patients.**

Variables	AUC	95% CI	Cut-off	Sensitivity (%)	Specificity (%)	p
CA19-9	0.535	0.447-0.623	$\leq 9.95$	54.8	55.4	0.436
CEA	0.535	0.446-0.624	$\geq 2.99$	57.0	56.8	0.438
SII	0.963	0.938-0.988	$\geq 664.00$	87.1	87.8	<b>&lt;0.001</b>
SIRI	0.952	0.922-0.982	$\geq 1.27$	88.2	89.2	<b>&lt;0.001</b>

AUC: Area under the curve; CI: Confidence interval; CEA: Carcinoembryonic antigen.

**TABLE 3: Comparison of radiological response and CAP score with SII and SIRI groups.**

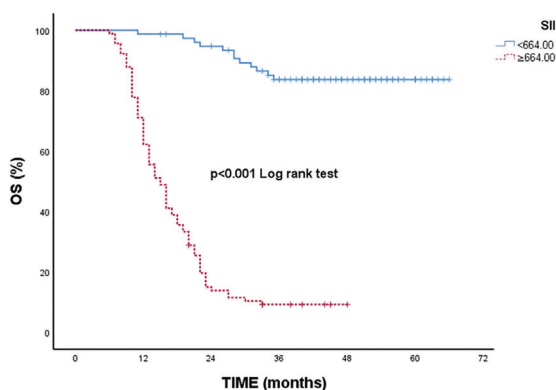
Variables	SII		p	SIRI		p
	$<664.0$ (n=77)	$\geq 664.0$ (n=90)		$<1.27$ (n=77)	$\geq 1.27$ (n=90)	
<b>Radiological response</b>						
Complete response	26 (33.8)	1 (1.1)	<b>&lt;0.001</b>	26 (33.8)	1 (1.1)	<b>&lt;0.001</b>
Partial response	39 (50.6)	57 (63.3)		41 (53.2)	55 (61.1)	
Stable disease	12 (15.6)	32 (35.6)		10 (13.0)	34 (37.8)	
<b>CAP score</b>						
0	20 (26.0)	1 (1.1)	<b>&lt;0.001</b>	20 (26.0)	1 (1.1)	<b>&lt;0.001</b>
1	35 (45.5)	4 (4.4)		31 (40.3)	8 (8.9)	
2	19 (24.7)	39 (43.3)		22 (28.6)	36 (40.0)	
3	3 (3.8)	46 (51.2)		4 (5.1)	45 (50.0)	

Pearson's chi-square test,  $p<0.05$  statistically significant.  
 SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CAP: College of American Pathologists.

As shown in Table 4, the 2-year and 5-year OS rates were 51.1% and 43.5%, respectively, with a median OS of 27 months (95% CI: 19.98-34.02). The most significant survival differences emerged in subgroup analyses based on inflammatory indices. In patients with SII <664.00, the 2-year and 5-year OS rates were 94.7% and 83.7%, respectively, while in the SII ≥664.00 group, the 2-year OS dropped to 13.9%, and the 5-year OS could not be calculated ( $p < 0.001$ ). Similarly, the median OS was not reached in the low SII group, whereas the median OS was 15 months in the high SII group. A similar trend was observed in terms of SIRI; In patients with SIRI <1.27, the 2-year OS was 88.1% and the 5-year OS was 85.3%, while in the SIRI ≥1.27 group, the 2-year OS decreased to 19.4% ( $p < 0.001$ ). The median OS was not reached in the

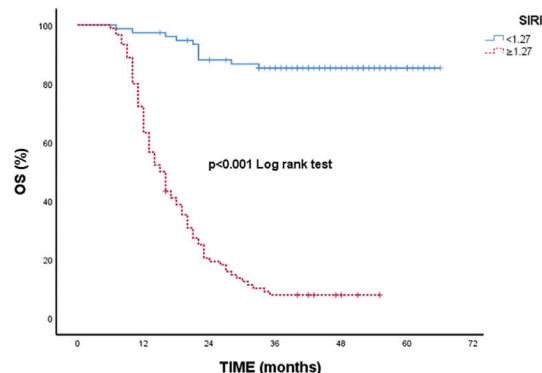
low SIRI group, whereas it was 15 months in the high SIRI group. Figures 1 and 2 show the Kaplan-Meier curves for OS according to SII and SIRI levels, respectively.

As shown in Table 5, when all study patients were evaluated, the 2-year DFS rate was 33.5% and the 5-year DFS rate was 32.9%. The median DFS was calculated as 12 months (95% CI: 9.69-14.30). Inflammatory indices were found to be the strongest predictors of DFS. In patients with an SII value <664.00, the 2-year and 5-year DFS rates were 66.2% and 64.9%, respectively, while in the SII ≥664.00 group, the 2-year DFS was only 5.6%, and the 5-year DFS could not be calculated ( $p < 0.001$ ). While the median DFS was not reached in the low SII group, it was only 9 months in the high SII group. Similarly, the 2-year DFS rate was 64.9% in patients with SIRI <1.27,



**FIGURE 1:** The Kaplan-Meier curves for OS according to SII levels.

OS: Overall survival; SII: Systemic immune inflammation index.



**FIGURE 2:** The Kaplan-Meier curves for OS according to SIRI levels.

OS: Overall survival; SIRI: Systemic inflammation response index.

**TABLE 4:** Patient OS comparisons.

Variables	2 years %	5 years %	Median (months) (95% CI)	p
General	51.1	43.5	27.00 (19.98-34.02)	
<b>Age</b>				
<60	56.2	47.7	30.00 (-)	0.377
>60	46.9	39.9	23.00 (16.85-29.4)	
<b>Gender</b>				
Male	48.5	38.8	23.00 (17.04-28.95)	0.055
Female	57.0	54.8	-	
<b>SII</b>				
<664.00	94.7	83.7	-	<0.001
≥664.00	13.9	-	15.00 (12.85-17.14)	
<b>SIRI</b>				
<1.27	88.1	85.3	-	<0.001
≥1.27	19.4	-	15.00 (12.67-17.32)	

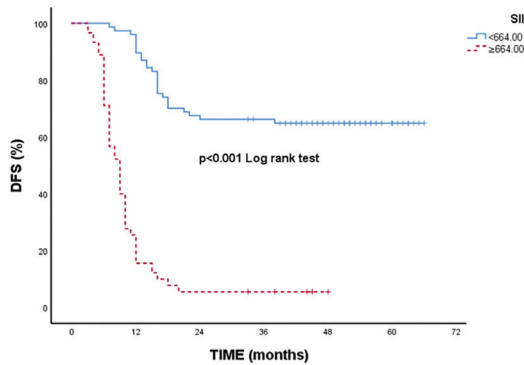
Kaplan Meier, Log rank test,  $p < 0.05$  statistically significant.

OS: Overall survival; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CI: Confidence interval.

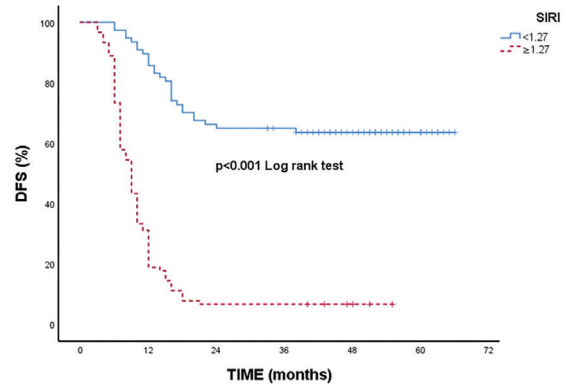
while it was only 6.7% in the SIRI  $\geq 1.27$  group ( $p < 0.001$ ). The median DFS was 9 months in the high SIRI group, but was not reached in the low SIRI group. Figures 3 and 4 show the Kaplan-Meier curves for DFS according to SII and SIRI levels, respectively.

SII and SIRI were significant in univariate analyses. Variables found to be significant in univariate analyses were included in the multivariate Cox regression model. According to the model results, having an SII  $\geq 664.00$  increased the risk of

death 8.49 times [Hazard ratio (HR): 8.49; 95% CI: 4.35-16.57;  $p < 0.001$ ] and having a SIRI  $\geq 1.27$  increased the risk of death 7.88 times (HR: 7.88; 95% CI: 3.99-15.60;  $p < 0.001$ ) (Table 6). Similarly, according to the results of the multivariate Cox regression analysis, having an SII  $\geq 664.00$  increased the risk of progression 5.13 times (HR: 5.13; 95% CI: 3.14-8.39;  $p < 0.001$ ) and having a SIRI  $\geq 1.27$  increased the risk of progression 3.89 times (HR: 3.89; 95% CI: 2.39-6.31;  $p < 0.001$ ) (Table 7).



**FIGURE 3:** The Kaplan-Meier curves for DFS according to SII levels.  
DFS: Disease-free survival; SII: Systemic immune inflammation index.



**FIGURE 4:** The Kaplan-Meier curves for DFS according to SIRI levels.  
DFS: Disease-free survival; SIRI: Systemic inflammation response index.

**TABLE 5: Patient DFS comparisons.**

Variables	2 years %	5 years %	Median (months) (95% CI)	p
General	33.5	32.9	12.00 (9.69-14.30)	
<b>Age</b>				
<60	38.2	36.7	14.00 (10.94-17.05)	0.436
>60	29.7	29.7	12.00 (8.89-15.10)	
<b>Gender</b>				
Male	30.8	29.9	12.00 (9.88-14.11)	0.142
Female	40.0	40.0	16.00 (10.06-21.93)	
<b>SII</b>				
<664.00	66.2	64.9	-	<0.001
$\geq 664.00$	5.6	-	9.00 (7.78-10.21)	
<b>SIRI</b>				
<1.27	64.9	63.6	-	<0.001
$\geq 1.27$	6.7	-	9.00 (7.58-10.41)	

Kaplan Meier, Log rank test,  $p < 0.05$  statistically significant.

DFS: Disease-free survival; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CI: Confidence interval.

**TABLE 6: Multivariate Cox regression results on the mortality risk of various clinical variables.**

Variables	HR (95% CI)	p
<b>SII</b>		
<664.00	ref	<0.001
≥664.00	8.49 (4.35-16.57)	
<b>SIRI</b>		
<1.27	ref	<0.001
≥1.27	7.88 (3.99-15.60)	

HR: Hazard ratio; ref: Reference; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CI: Confidence interval.

**TABLE 7: Multivariate Cox regression results on the progression risk of various clinical variables.**

Variables	HR (95% CI)	p
<b>SII</b>		
<664.00	ref	<0.001
≥664.00	5.13 (3.14-8.39)	
<b>SIRI</b>		
<1.27	ref	<0.001
≥1.27	3.89 (2.39-6.31)	

HR: Hazard ratio; ref: Reference; SII: Systemic immune inflammation index; SIRI: Systemic inflammation response index; CI: Confidence interval.

## DISCUSSION

The medical treatment of locally advanced gastric cancer has long been the perioperative FLOT regimen. Some studies published in the last two years have investigated the benefit of adding immunotherapies to this conventional treatment regimen, and current guidelines have shown that adding durvalumab to the FLOT regimen, as well as neoadjuvant/perioperative immunotherapies in microsatellite instability-high patients, contributes to survival.<sup>15-17</sup>

On the other hand, the effect of inflammation on cancer development and progression has been studied for years, and many inflammatory parameters and scores are associated with malignancy. The common conclusion from these studies is that inflammatory scores are predictive in cancer patients and closely related to survival.<sup>18-20</sup> While data show a link between inflammation and many types of cancer, the literature has also examined the relationship between SIRI and SII and disease recurrence, OS, and DFS in gastric cancer.<sup>21-23</sup> Our study, which included a similar number of patients, demonstrated that low SIRI levels significantly contributed to 3-year and 5-year survival.

A meta-analysis of 7 studies conducted between 2017 and 2023 showed that high SIRI values were associated with poorer OS and DFS in patients with gastric cancer. The accepted cut-off values for SIRI in these studies ranged from 0.58 to 1.35. Our study is similar to this meta-analysis in that the cut-off value calculated using a ROC curve for SIRI is 1.27.<sup>24</sup> In a study with a similar number of patients to our research, it was shown that low SIRI levels contributed statistically significantly to 3-year and 5-year survival.<sup>25</sup> In another study of 107 patients receiving neoadjuvant chemotherapy, SIRI levels were shown to be predictive of OS and DFS.<sup>26</sup> Our study is similar to the studies mentioned above and consistent with the literature. We also found that low SIRI levels had a statistically significant positive effect on both OS and DFS; this positive effect persisted in multivariate Cox regression analyses of mortality and progression. Our study showed that high SIRI values predicted mortality, with sensitivity of 88.2% and specificity of 89.2%, which are among the highest rates reported in the literature.

The significance of SII, similar to that of SIRI, in patients with gastric cancer has been examined in numerous recent studies. In another study that included patients who received perioperative FLOT therapy and were similar to those in our study, high SII values were statistically significant predictors of poor OS and DFS. The number of patients and the SII cut-off value in that study were nearly identical to those in our study.<sup>27</sup> A meta-analysis of data from 30 studies again found a close association between high SII values and worse OS and DFS.<sup>28</sup> As in patients receiving perioperative chemotherapy, in patients with stage 1-2 resectable gastric cancer, lower SII levels were found to be significantly associated with higher 5-year survival.<sup>29</sup> Another study, which examined data from 5995 gastric cancer patients across 16 studies, showed that high SII levels were statistically significantly associated with worse OS.<sup>30</sup> In our study, consistent with the literature, we found that high SII levels were significantly associated with worse OS and DFS, and that SII had a sensitivity of 87.1% and a specificity of 87.8% for predicting mortality.

In addition to its role as a prognostic indicator, studies in the literature also investigate the diagnostic role of SII<sup>31</sup> and its importance in evaluating the response to neoadjuvant therapy. There are limited studies demonstrating a relationship between the CAP score, which is particularly used to assess pathological response to neoadjuvant therapy, and SII.<sup>32</sup> In this respect, our study will make a significant contribution to the literature.

## Study Limitations

Limitations of our study include its single-center, retrospective design and a relatively small number of patients.

## CONCLUSION

In conclusion, there is a need for biomarkers that can be used clinically for prognostic and predictive purposes in gastric cancer patients. These indices have both advantages and disadvantages. Although both indices (SII and SIRI) are easy to use and inexpensive, the parameters included in these indices can also be affected by non-malignant factors. More comprehensive analyses have been and continue to be conducted by combining it with other markers.

## Ethics

**Ethics Committee Approval:** The study was conducted according to the principles outlined in the Declaration of Helsinki and was approved by the University of Health Sciences Türkiye, Prof. Dr. Cemil Taşcıoğlu City Hospital Ethics Committee (approval number: 388, date: 21.10.2025).

**Informed Consent:** Retrospective study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: M.E., Concept: K.E., Design: M.E., Data Collection or Processing: S.B.Ş., Analysis or Interpretation: M.E., Literature Search: K.E., Writing: M.E.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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