

# Does systemic immune inflammation index have predictive value in gastric cancer prognosis?

 Hakan Uzunoglu,  Selcuk Kaya

Department of General Surgery, Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Turkiye

## ABSTRACT

**OBJECTIVE:** Some studies have reported that the systemic immune inflammatory index (SII) and neutrophil/lymphocyte ratio (NLR) provide predictive data on prognosis in gastric cancer patients. In the present study, it was aimed to examine the diagnostic and prognostic values of SII and NLR in gastric cancer.

**METHODS:** A total of 152 patients, operated with the diagnosis of gastric cancer and followed up in the General Surgery Department of our hospital between January 2012 and April 2018, and 152 healthy controls were included in the study.

**RESULTS:** The mean SII ( $989\pm685$ ) and the mean NLR ( $3.9\pm5.2$ ) were significantly higher in gastric cancer patients than the healthy control group ( $433\pm203$  and  $1.9\pm0.8$ , respectively) ( $p<0.001$  for both). In the receiver operating characteristic analyzes, a threshold value of 892 for SII had a sensitivity of 66.7% and a specificity of 62.7% in terms of predicting 5-year survival (AUC: 0.637;  $p=0.076$ ; LB: 0.475; UB: 0.799; CI 95%). The 5-year survival rate was found to be significantly higher in those with a SII of above 892 than those with a SII of 892 and below ( $p=0.026$ ). The 5-year mortality risk was 0.67-fold lower in those with SII above 892 ( $p=0.111$ ; 95% CI 0.4–1.1).

**CONCLUSION:** The present study findings show that SII and NLR are far from providing reliable data on gastric cancer prognosis.

*Keywords:* Gastric cancer; N ratio; neutrophil/lymphocyte ratio; systemic immune inflammatory index.

**Cite this article as:** Uzunoglu H, Kaya S. Does systemic immune inflammation index have predictive value in gastric cancer prognosis? *North Clin Istanbul* 2023;10(1):24–32.

Gastric cancer is the fourth most common cancer in the world and is the second most common cause of cancer-related deaths. Early diagnosis and treatment significantly affect survival in gastric cancer cases. In these cases, the standard staging determined by evaluating tumor diameter, lymph node involvement and the presence of distant metastases provides the most important information about prognosis [1, 2].

Several researches have been conducted on many markers to have predictive information about the prognosis in cancer cases, and to make evaluation with more easily obtainable data. In particular, some indexes have been established with various formulas and some calculations of the hematological and inflammatory parameters

obtained from routine complete blood count. It has been suggested that these indexes, such as the systemic immune inflammatory index (SII), neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte ratio, and platelet/lymphocyte ratio, provide very valuable information in the diagnosis of cancer or in predicting prognosis [3–5]. However, the counts of these cells are significantly affected by numerous events in the body and can rapidly show abnormal changes. Therefore, the ability of these indexes to directly provide highly reliable information about cancer prognosis may depend on many factors [3–5]. In some studies, it has been reported that SII and NLR provide reliable data about poor prognosis in gastric cancer cases [6–11].



Received: April 21, 2021 Revised: June 22, 2021 Accepted: July 08, 2021 Online: February 08, 2023

Correspondence: Hakan UZUNOGLU, MD, Kartal Dr. Lutfi Kirdar Sehir Hastanesi, Genel Cerrahi Klinigi, Istanbul, Turkiye.  
Tel: +90 535 723 27 61 e-mail: drhakanuzunoglu@gmail.com

© Copyright 2023 by Istanbul Provincial Directorate of Health - Available online at [www.northclinist.com](http://www.northclinist.com)

In the present study, it was aimed to analyze the diagnostic and prognostic values of SII and NLR in gastric cancer.

## MATERIALS AND METHODS

The present study was approved by the Kartal Dr. Lutfi Kırdar City Hospital Clinical Research Ethics Committee (date: November 25, 2020/no: 514/190/15) and was planned retrospectively.

### Patients and Tests

A total of 152 patients operated and followed up with the diagnosis of gastric adenocarcinoma in the general surgery department of our hospital between January 2012 and April 2018 were included in the study. In addition, 152 healthy individuals who admitted to our clinic for various control purposes were included as the control group. Demographic information, pathology results, and laboratory findings of the patients were obtained from the records of the hospital automation system.

Patients with autoimmune diseases, those who received neoadjuvant chemotherapy, those with a diagnosis of gastric lymphoma and gastrointestinal stromal tumor, and those with a history of metastatic or other tumors were excluded from the study.

### Statistical Analysis

All statistical analyses in the study were done using SPSS 25.0 software (IBM SPSS, Chicago, IL, USA). Descriptive data are given as numbers and percentages. In terms of categorical variables, comparisons between groups were made with Pearson's Chi-square test and Fisher's Exact Test. Whether continuous variables are suitable for normal distribution was confirmed by the Kolmogorov–Smirnov Test. The differences between the groups in terms of continuous variables were analyzed using Student's *t*-test, and the comparison of mean values between multiple groups was made using variance analysis. The relationship between continuous variables was tested using Spearman's correlation analysis. The ability of SII and NLR to predict the presence of gastric cancer was analyzed using receiver operating characteristic (ROC) curve analysis. The 5-year mortality risks of the variables were found by univariate Cox regression analysis. The results were evaluated within the 95% confidence interval, and  $p < 0.05$  values were considered significant. Bonferroni correction was made where appropriate.

Some values are calculated using the following formulas [3, 5, 12, 13].

### Highlight key points

- SII and NLR values can provide important information in the diagnosis of gastric cancer.
- SII and NLR values are far from providing reliable predictive data about the prognosis in gastric cancer.
- It does not seem reliable to provide a cutoff value for SII in predicting gastric cancer prognosis.

$SII = \text{Platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$ .

$NLR = \text{Neutrophil count} / \text{lymphocyte count}$

$N \text{ ratio} = \text{Number of metastatic lymph nodes} / \text{number of lymph nodes resected during the operation}$ .

## RESULTS

The mean age of the patients was  $63.8 \pm 11.5$  (min-max: 21–88) years. The mean follow-up time was  $33.4 \pm 21.6$  months, the mean 5-year overall survival (OS) was  $25.1 \pm 20.9$  months, and the mean 5-year disease-free survival (DFS) was  $22.3 \pm 21.2$  months. The mean number of resected lymph nodes was  $20.4 \pm 10$ , the mean number of metastatic lymph nodes was  $6.5 \pm 9$ , and the mean N ratio was  $29.3 \pm 30.3\%$ . The mean SII was  $989 \pm 685$ , and the mean NLR was  $3.9 \pm 5.2$  (Table 1).

The mean SII ( $989 \pm 685$ ) and the mean NLR ( $3.9 \pm 5.2$ ) were significantly higher in gastric cancer patients than the healthy control group ( $433 \pm 203$  and  $1.9 \pm 0.8$ , respectively) ( $p < 0.001$  for both) (Table 1).

A total of 98 (64.5%) of the patients were male. Sixty-seven (78.8%) patients died within the 5-year follow-up. Five-year OS was 21.1% and 5-year DFS was 51.3%. Five-year OS was found to be significantly higher in those with SII above 892 than those with SII of 892 and below ( $p = 0.026$ ). Five-year OS rates were similar between gender ( $p = 0.81$ ), gastrectomy type ( $p = 0.229$ ), tumor differentiation ( $p = 0.157$ ), stage (0.051), and N ratio ( $p = 0.06$ ) groups (Table 2).

The mean 5-year OS duration ( $p = 0.022$ ) and the mean 5-year DFS duration ( $p = 0.047$ ) were found to be significantly lower in stage 3 patients compared to that in stages 1 and 2. There were no significant differences between the differentiation, N ratio and SII groups in terms of the mean 5-year OS and DFS durations ( $p > 0.05$  for each) (Table 3).

In the correlation analyzes, SII was found to be correlated with N ratio ( $p = 0.042$ ;  $r = 0.165$ ). In addition, SII ( $p < 0.001$ ;  $r = 0.29$ ) and NLR ( $p = 0.02$ ;  $r = 0.188$ )

**TABLE 1.** The mean values of some variables and comparison of the mean values of some variables between the patient group and the controls

	Mean±SD	Minimum	Maximum
Age (years)	63.8±11.5	31	88
Follow-up duration (months)	33.4±21.6	1	83
OS (months)	33.5±21.6	1	83
5-year OS (months)	25.1±20.9	1	60
DFS (months)	30.7±22.6	1	83
5-year DFS (months)	22.3±21.2	1	60
Number of resected lymph nodes	20.4±10.0	3	53
Number of metastatic lymph nodes	6.5±9.0	0	50
N ratio (metastatic/resected)	29.3±30.3	0.0	100.0
Tumor diameter (cm)	6.1±3.1	0	17
Systemic immune inflammation index	988.8±685.2	104	4797
Pre-op platelets (10 <sup>3</sup> /mL)	288.3±97.6	81.0	651.0
Pre-op lymphocytes (10 <sup>9</sup> /L)	1.8±0.7	0.5	3.7
Pre-op neutrophils (10 <sup>9</sup> /L)	5.3±2.1	2.1	15.9
Neutrophil/lymphocyte ratio	3.9±5.2	0.01	60.0
	Patients	Controls	P
Age (years)	63.8±11.5	63.6±11.6	0.913
Systemic immune inflammation index	988.8±685.2	433.1±203.9	<0.001
Neutrophil/lymphocyte ratio	3.9±5.2	1.9±0.8	<0.001

Independent Samples' t-test was used. SD: Standard deviation; OS: Overall survival; DFS: Disease-free survival.

were both found to be significantly correlated with tumor diameter (Table 4).

In the univariate Cox regression analysis, the 5-year mortality risk was 0.67-fold lower in those with SII above 892 ( $p=0.111$ ; 95% CI 0.4–1.1) (Table 5).

Five-year OS, 5-year DFS, differentiation and stage groups were found to be similar in terms of the mean SII and the mean NLR ( $p>0.05$  for each).

In the ROC analyzes, a threshold value of 503.5 for SII was found to have a sensitivity of 79.6% and a specificity of 77.3% in the diagnosis of gastric cancer (AUC: 0.840;  $p<0.001$ ; LB: 0.794; UB: 0.886; CI 95%). A threshold value of 2.11 for NLR was found to have a sensitivity of 80.3% and a specificity of 73.0% in the diagnosis of gastric cancer (AUC: 0.805;  $p<0.001$ ; LB: 0.755; UB: 0.855; CI 95%).

In the ROC analyzes, a threshold value of 892 for SII was found to have a sensitivity of 66.7%; and a specificity of 62.7% in terms of predicting 5-year OS (AUC: 0.637;  $p=0.076$ ; LB: 0.475; UB: 0.799; CI 95%). A threshold value of 3.05 for NLR was found to have a sensitivity of

54.1% and a specificity of 61.2% in terms of predicting 5-year OS (AUC: 0.576;  $p=0.108$ ; LB: 0.485; UB: 0.667; CI 95%). A threshold value of 10.9% for N ratio had a sensitivity of 66.7% and a specificity of 41.8% in terms of predicting 5-year OS (AUC: 0.329;  $p=0.026$ ; LB: 0.177; UB: 0.481; CI 95%).

## DISCUSSION

Gastric cancer cases are mostly with poor prognosis, and they do not have very long overall survival in most cases. Numerous parameters have been investigated to predict the prognosis in gastric cancer [1, 2]. Recently, some formulas have been created with some calculations from the relationships between some hematological and inflammatory parameters obtained from the complete blood count, and it has been reported that these index values provide significant data about cancer prognosis. In this way, it has been suggested that the prognosis of the patient can be predicted with a non-invasive and easily calculated method [3, 5, 6]. Among these, values such as NLR and SII have been reported to be used as prognostic indicators in these cases [6–11].

**TABLE 2.** Distributions of the variables according to the prognostic groups (%)

	OS		5-year OS		DFS		5-year DFS	
	Dead	Alive	Dead	Alive	Metastasis or recurrence	Disease free	Metastasis or recurrence	Disease free
<b>Gender</b>								
Male (n=98)	43.9	56.1	79.6	20.4	24.5	75.5	79.6	20.4
Female (n=54)	44.4	55.6	77.4	22.6	29.6	70.4	77.4	22.6
P	0.946		0.81		0.491		0.81	
<b>Type of gastrectomy</b>								
Total (n=95)	35.8	64.2	73.9	26.1	22.1	77.9	73.9	26.1
Subtotal (n=57)	57.9	42.1	84.6	15.4	33.3	66.7	84.6	15.4
P	<b>0.008</b>		0.229		0.128		0.229	
<b>Differentiation</b>								
Well (n=15)	33.3	66.7	55.6	44.4	26.7	73.3	55.6	44.4
Moderately (n=60)	48.3	51.7	78.4	21.6	28.3	71.7	78.4	21.6
Poorly (n=77)	42.9	57.1	84.6	15.4	24.7	75.3	84.6	15.4
P	0.552		0.157		0.89		0.157	
<b>Stage</b>								
1A (n=12)	41.7	58.3	71.4	28.6	25	75	71.4	28.6
1B (n=15)	40	60	60	40	26.7	73.3	60	40
2A (n=16)	43.8	56.3	63.6	36.4	18.8	81.3	63.6	36.4
2B (n=28)	46.4	53.6	76.5	23.5	32.1	67.9	76.5	23.5
3A (n=35)	51.4	48.6	94.7	5.3	31.4	68.6	94.7	5.3
3B (n=25)	44	56	91.7	8.3	16	84	91.7	8.3
3C (n=21)	33.3	66.7	77.8	22.2	28.6	71.4	77.8	22.2
P	0.925		0.238		0.825		0.238	
<b>Stage</b>								
1A/1B (n=27)	40.7	59.3	64.7	35.3	25.9	74.1	64.7	35.3
2A/2B (n=44)	45.5	54.5	71.4	28.6	27.3	72.7	71.4	28.6
3A/3B/3C (n=81)	44.4	55.6	90	10	25.9	74.1	90	10
P	0.923		0.051		0.985		0.051	
<b>SII</b>								
≤892 (n=62)	51.2	48.8	87.5	12.5	29.3	70.7	87.5	12.5
>892 (n=80)	35.7	64.3	67.6	32.4	22.9	77.1	67.6	32.4
P	0.055		<b>0.026</b>		0.371		<b>0.026</b>	
<b>No. of lymph node resected</b>								
≤16 (n=48)	50	50	85.7	14.3	20.8	79.2	85.7	14.3
16–30 (n=82)	41.5	58.5	75.6	24.4	32.9	67.1	75.6	24.4
≥30 (n=22)	40.9	59.1	75	25	13.6	86.4	75	25
P	0.607		0.552		0.11		0.552	
<b>N ratio</b>								
≤10.9 (n=61)	45.9	54.1	70	30	29.5	70.5	70	30
>10.9 (n=81)	42.9	57.1	86.7	13.3	24.2	75.8	86.7	13.3
P	0.711		0.06		0.464		0.06	
<b>NLR</b>								
≤3.05 (n=80)	51.2	48.8	82.0	18.0	30.0	70.0	82.0	18.0
>3.05 (n=70)	36.1	63.9	74.3	25.7	22.2	76.8	74.3	25.7
P	0.061		0.392		0.277		0.392	

Chi square test was used. OS: Overall survival; DFS: Disease-free survival; SII: Systemic immune inflammation index; NLR: Neutrophil/lymphocyte ratio.

**TABLE 3.** Comparison of the mean values of some prognosis variables according to the tumor differentiation and stage groups

	OS (months)	5-year OS (months)	DFS (months)	5-year DFS (months)
<b>Differentiation</b>				
Well differentiated	47.1±22.3	48.9±29.1	49.1±22.8	52.2±29.5
Moderately differentiated	39.5±26.5	38.1±28.8	51.7±29.3	54.7±29.9
Poorly differentiated	39.5±27.1	37.7±31.3	49.6±27.5	52.2±31.1
P	0.149	0.32	0.184	0.198
<b>Stage</b>				
1A	38.7±22.4	28±22.3	36.3±22.9	26.4±23.1
1B	42.9±23.9	36.4±24.2	39.1±25	34.4±23.9
2A	36.7±25.5	30.5±24.8	35±27	28±26.3
2B	36.7±23.4	28.9±22.3	33±25.2	22.9±23.1
3A	31±18.4	20±14.8	28.4±19	17.1±14.3
3B	25.5±18.8	13.1±16	24.8±19.3	11.6±16
3C	30.5±20.2	23.3±21.1	26±22.7	22.3±21.7
P	0.181	0.143	0.36	0.201
<b>Stage</b>				
Stage 1A/1B	41±22.9	32.9±23.1	37.8±23.7	31.1±23.2
Stage 2A/2B	36.7±23.9	29.5±22.9	33.8±25.6	24.9±24
Stage 3A/3B/3C	<b>29.2±18.9</b>	<b>18.7±16.7</b>	<b>26.7±19.9*</b>	<b>16.6±16.7*</b>
P	<b>0.022</b>	<b>0.023</b>	<b>0.047</b>	<b>0.043</b>
<b>N ratio</b>				
≤10.9	36±22.7	28.3±22.1	32.8±23.9	24.9±22.8
>10.9	30.1±19.6	19.9±18	27.9±20.8	17.9±17.9
P	0.097	0.073	0.185	0.143
<b>SII</b>				
≤892	30.6±19.5	21.8±17.6	28.5±20.6	19.8±18.1
>892	37.5±23.8	30.1±24.6	33.8±25.1	26±25.1
P	0.053	0.071	0.16	0.187

Independent Samples' t Test and one-way ANOVA test were used. \*: Significantly different only from stage 1A/1B; OS: Overall survival; DFS: Disease-free survival; SII: Systemic immune inflammation index.

However, the findings obtained in the present study show that these two indexes do not provide reliable data regarding prognosis in gastric cancer patients.

NLR is an indicator claimed to provide useful information in the diagnosis of some diseases or in predicting their prognosis [5]. In the present study, the mean NLR ( $3.9\pm 5.2$ ) was found to be significantly higher in gastric cancer patients than that in the control group ( $1.9\pm 0.8$ ), and a threshold value of 2.11 for NLR had a the sensitivity of 80.3%, and a specificity of 73.0% in the diagnosis of gastric cancer. These findings show that the NLR value can be used as a marker with an accuracy rate between 70 and 80% in the diagnosis of gastric cancer.

It has been suggested that NLR values provide information about prognosis in gastric cancer cases [6–11]. Gu et al. [6] reported that the mortality risk increased 1.69-fold in cases with a NLR value of 2.5 and above. Longer survival was reported in patients with NLR values lower than a threshold determined as 2.2 by Zhu et al. [11], as 2.07 by Jomrich et al. [7], as 1.3 by Shi et al. [8] 1.3, and as 2.1 by Wang et al. [9]. In contrast of these, Zhu et al. [14] reported that the pre-operative NLR value was not valuable in terms of lymph node metastasis and prognosis in patients with early gastric cancer. Aldemir et al. [15] also reported that NLR had no prognostic value in early stage local gastric cancer cases.



**TABLE 4.** Correlation analyzes between some markers and prognosis variables

	Age	OS	5-year OS	DFS	5-year DFS	Number of resected lymph	Number of metastatic lymph nodes	N ratio (metastatic /resected)	Tumor diameter	Systematic immune inflammation index
Number of resected lymph nodes										
r	0.036	0.060	0.106	0.031	0.093					
P	0.656	0.463	0.332	0.707	0.397					
Number of metastatic lymph nodes										
r	-0.042	-0.081	-0.121	-0.087	-0.088					
P	0.609	0.322	0.271	0.285	0.424					
N ratio (metastatic/resected)										
r	-0.091	-0.163	-0.233	-0.160	-0.202					
P	0.265	<b>0.045</b>	<b>0.032</b>	<b>0.049</b>	0.063					
Tumor diameter										
r	0.090	0.042	0.035	0.018	0.031	0.153	0.139	0.217		
P	0.271	0.604	0.747	0.822	0.777	0.059	0.088	<b>0.007</b>		
Systemic immune inflammation index										
r	0.067	0.116	0.132	0.100	0.120	0.037	0.069	0.165	0.290	
P	0.409	0.153	0.229	0.222	0.274	0.652	0.398	<b>0.042</b>	<b>&lt;0.001</b>	
Neutrophil/lymphocyte ratio										
r	0.019	0.027	-0.048	0.036	-0.062	-0.059	0.010	0.100	0.188	0.849
P	0.814	0.741	0.660	0.657	0.572	0.471	0.900	0.222	<b>0.020</b>	<b>&lt;0.001</b>

Spearman's correlation analysis was used. OS: Overall survival; DFS: Disease-free survival.

In the present study, although a significant correlation was found between NLR and tumor size; 5-year OS, 5-year DFS, differentiation, and stage groups were found to be similar in terms of the mean NLR. In the ROC analysis, a threshold value of 3.05 for NLR was found to have a sensitivity of 54.1% and a specificity of 61.2% in terms of predicting 5-year OS. There was no significant difference in terms of 5-year OS rate among those with NLR values below or above 3.05. These findings show that the NLR value does not provide very reliable data in predicting the prognosis of gastric cancer.

It has been stated that the SII index can be used in the diagnosis of some cancers [3–11]. In the present study, the mean SII ( $989 \pm 685$ ) was found to be significantly higher in gastric cancer patients than the healthy control group ( $433 \pm 203$ ). In the ROC analyzes, a threshold value of 503.5 for SII was found to have a sensitivity of 79.6% and a specificity of 77.3% in the diagnosis of gastric cancer. These findings show that

SII value can be used as a marker with an accuracy rate between 75 and 80% in the diagnosis of gastric cancer.

It has been suggested that the SII value provides useful information in determining the prognosis of some cancers such as cervical cancer [16], germ cell carcinoma [17], colorectal carcinoma [18, 19], hepatocellular carcinoma [20], and seminoma [21]. It has been reported that SII can also be used as a prognostic marker in gastric cancer cases [4, 7–11, 22]. Accordingly, it has been stated that the increase in the SII value indicates that the inflammatory process worsens in the patient, and the prognosis may be poor [6–11]. Gu et al. [6] reported that the mortality risk increased 1.94-fold in patients with an SII value of 556 and above. Huang et al. [22] reported that SII values of 572 and above decreased the mean OS duration and caused a 1.8-fold increased risk of the mortality. Poor prognosis was reported to be associated with an SII above 644 by Jomrich et al. [7], above 322 by Shi et al. [8], above 600 by Wang and Zhu [10], and above

**TABLE 5.** Univariate cox regression analyzes

	HR	95% CI	p
Age (years)			
≤60	1		
>60	0.82	0.5–1.33	0.41
Gender			
Male	1		
Female	0.85	0.51–1.4	0.521
Type of gastrectomy			
Total	1		
Subtotal	1.01	0.63–1.64	0.955
Differentiation			
Well differentiated	1		
Moderately differentiated	1.88	0.73–4.86	0.193
Poorly differentiated	2.04	0.79–5.22	0.139
P			
Stage			
Stage 1A/1B	1		
Stage 2A/2B	1.19	0.57–2.49	0.639
Stage 3A/3B/3C	2.15	1.09–4.24	<b>0.028</b>
P			
N ratio (%)			
≤10.9	1		
>10.9	1.78	1.09–2.9	<b>0.022</b>
SII			
≤892	1		
>892	0.67	0.4–1.1	0.111

Univariate Cox regression analysis was used. HR: Hazard ratio; CI: Confidence interval; SII: Systemic immune inflammation index.

660 by Wang et al. [9]. However, unlike these studies, Hirahara et al. [23] reported that SII was not an independent prognostic factor for survival in gastric cancer patients under 65 years of age, and they could not find a significant relationship between SII and survival time in non-elderly patients. Guner et al. [24] also did not find a direct relationship between SII and overall survival.

In the present study, a threshold value of 892 for SII was found to have a sensitivity of 66.7%; and a specificity of 62.7% in terms of predicting 5-year OS, and SII values “below” this threshold value were determined to indicate poor prognosis. The 5-year OS rate for those with an SII above 892 was found to be significantly higher than those with an SII 892 and below. SII was also found to be positively significantly correlated with tumor diameter. In addition, there was no significant difference between the

SII groups in terms of mean 5-year OS and DFS. Five-year OS, 5-year DFS, differentiation, and stage groups were found to be similar in terms of mean SII. There was a significant positive correlation between SII and N ratio. The 5-year mortality risk was found to be 0.67-fold lower in those with an SII above 892. All these findings show that the SII value is not a very reliable marker in determining the prognosis in gastric cancer patients, and the increase in the SII value may not be an indicator of poor prognosis in all cases. The fact that the counts of neutrophils, platelets, and lymphocytes used in the SII formula are sensitive parameters that can change rapidly by being affected by numerous factors in the organism may prevent the SII value from predicting the prognosis reliably in gastric cancer. Therefore, SII values should not be evaluated alone in gastric cancer cases.

NLR and SII values are affected by numerous metabolic events in the body. In particular, patients who received neoadjuvant chemotherapy, those underwent blood transfusion, those with the tumor acting aggressive, those with a very low lymphocyte count, or those with autoimmune diseases, have been excluded from the studies, as in the present study, due to the consideration that these factors would affect these indexes and cause erroneous evaluation [3–11]. Since survival is poor even after adequate lymphadenectomy and curative surgery in gastric cancer, the use of preoperative adjuvant chemotherapy is increasing gradually to improve results in many cases [1–3, 25]. Considering all these reasons, NLR and SII values do not seem to be practically applicable as pre-operative prognostic indicators in most gastric cancer patients.

Several studies determined very different cutoff values for SII in predicting gastric cancer prognosis. Yang et al. [3] reported in their meta-analysis that SII cutoff values varying between 330 and 1600 were determined in 22 different studies in different cancer types. In studies conducted with gastric cancer cases, the prognostic cutoff value for SII was determined as 556 by Gu et al. [6], as 572 by Huang et al. [22], as 644 by Jomrich et al. [7], as 322 by Shi et al. [8], as 600 by Wang and Zhu [10], as 660 by Wang et al. [9], and as 527 by Zhu et al. [11]. These results show that there is no ideal cutoff value for SII values, and that SII does not provide very reliable data in terms of prognosis in these patients. Furthermore, Zhu et al. [11] reported that the sensitivity and specificity rates of the cutoff value they determined were both below 45%. In addition, in most of the studies that provide a cutoff value for SII, survival rates were not

reported or documented; only the association between the cutoff value and tumor differentiation or stage or risk coefficient in terms of mortality has been reported. This suggests that there are doubts about the reliability level of SII value on survival. In addition, this index value was found to be ineffective in predicting prognosis in the present study, and even showed a reverse significance contrary to what was suggested for SII. This finding supports that SII does not provide very healthy data in predicting prognosis in gastric cancer patients.

There were some limitations in the present study. The fact that the number of patients whose 5-year follow-up was completed was not very high in the present study may have affected the level of significance in the analyzes. In addition, since the present study was not planned long-term and prospectively, it was not possible to analyze the future prognosis of the patients who were still alive.

## Conclusion

The findings obtained from the present study show that SII and NLR values can provide important information in the diagnosis of gastric cancer, but that they are far from providing reliable predictive data about the prognosis.

**Ethics Committee Approval:** The Kartal Dr. Lutfi Kirdar City Hospital Clinical Research Ethics Committee granted approval for this study (date: 25.11.2020, number: 514/190/15).

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

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Authorship Contributions:** Concept – HU, SK; Design – HU, SK; Supervision – HU, SK; Fundings – HU, SK; Materials – HU, SK; Data collection and/or processing – HU, SK; Analysis and/or interpretation – HU, SK; Literature review – HU, SK; Writing – HU; Critical review – HU, SK.

## REFERENCES

- Guggenheim DE, Shah MA. Gastric cancer epidemiology and risk factors. *J Surg Oncol* 2013;107:230–6. [CrossRef]
- Ang TL, Fock KM. Clinical epidemiology of gastric cancer. *Singapore Med J* 2014;55:621–8. [CrossRef]
- Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of systemic immune-inflammation index in cancer: a meta-analysis. *J Cancer* 2018;9:3295–302. [CrossRef]
- Huang Y, Gao Y, Wu Y, Lin H. Prognostic value of systemic immune-inflammation index in patients with urologic cancers: a meta-analysis. *Cancer Cell Int* 2020;20:499. [CrossRef]
- Guthrie GJ, Charles KA, Roxburgh CS, Horgan PG, McMillan DC, Clarke SJ. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol* 2013;88:218–30. [CrossRef]
- Gu L, Wang M, Cui X, Mo J, Yuan L, Mao F, et al. Clinical significance of peripheral blood-derived inflammation markers in advanced gastric cancer after radical resection. *BMC Surg* 2020;20:219. [CrossRef]
- Jomrich G, Paireder M, Kristo I, Baierl A, Ilhan-Mutlu A, Preusser M, et al. High systemic immune-inflammation index is an adverse prognostic factor for patients with gastroesophageal adenocarcinoma. *Ann Surg* 2021;273:532–41. [CrossRef]
- Shi H, Jiang Y, Cao H, Zhu H, Chen B, Ji W. Nomogram based on systemic immune-inflammation index to predict overall survival in gastric cancer patients. *Dis Markers* 2018;2018:1787424. [CrossRef]
- Wang K, Diao F, Ye Z, Zhang X, Zhai E, Ren H, et al. Prognostic value of systemic immune-inflammation index in patients with gastric cancer. *Chin J Cancer* 2017;36:75. [CrossRef]
- Wang Q, Zhu D. The prognostic value of systemic immune-inflammation index (SII) in patients after radical operation for carcinoma of stomach in gastric cancer. *J Gastrointest Oncol* 2019;10:965–78.
- Zhu Z, Cong X, Li R, Yin X, Li C, Xue Y. Preoperative Systemic Immune-Inflammation Index (SII) for predicting the survival of patients with stage I-III gastric cancer with a Signet-Ring Cell (SRC) Component. *Biomed Res Int* 2020;2020:5038217. [CrossRef]
- Marchet A, Mocellin S, Ambrosi A, de Manzoni G, Di Leo A, Marrelli D, et al; Italian Research Group for Gastric Cancer Study (GIRCG). The prognostic value of N-ratio in patients with gastric cancer: validation in a large, multicenter series. *Eur J Surg Oncol* 2008;34:159–65.
- Marchet A, Mocellin S, Ambrosi A, Morgagni P, Garcea D, Marrelli D, et al; Italian Research Group for Gastric Cancer (IRGGC). The ratio between metastatic and examined lymph nodes (N ratio) is an independent prognostic factor in gastric cancer regardless of the type of lymphadenectomy: results from an Italian multicentric study in 1853 patients. *Ann Surg* 2007;245:543–52. [CrossRef]
- Zhu GS, Tian SB, Wang H, Ma MG, Liu Y, Du HS, et al. Preoperative neutrophil lymphocyte ratio and platelet lymphocyte ratio cannot predict lymph node metastasis and prognosis in patients with early gastric cancer: a single institution investigation in China. *Curr Med Sci* 2018;38:78–84. [CrossRef]
- Aldemir MN, Turkeli M, Simsek M, Yildirim N, Bilen Y, Yetimoglu H, et al. Prognostic value of baseline neutrophil-lymphocyte and platelet-lymphocyte ratios in local and advanced gastric cancer patients. *Asian Pac J Cancer Prev* 2015;16:5933–7. [CrossRef]
- Huang H, Liu Q, Zhu L, Zhang Y, Lu X, Wu Y, et al. Prognostic value of preoperative systemic immune-inflammation index in patients with cervical cancer. *Sci Rep* 2019;9:3284. [CrossRef]
- Albany C. Systemic immune-inflammation index in germ-cell tumours: search for a biological prognostic biomarker. *Br J Cancer* 2018;118:761–2. [CrossRef]
- Chen JH, Zhai ET, Yuan YJ, Wu KM, Xu JB, Peng JJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. *World J Gastroenterol* 2017;23:6261–72. [CrossRef]
- Xie QK, Chen P, Hu WM, Sun P, He WZ, Jiang C, et al. The systemic immune-inflammation index is an independent predictor of survival for metastatic colorectal cancer and its association with the lymphocytic response to the tumor. *J Transl Med* 2018;16:273. [CrossRef]
- Hu B, Yang XR, Xu Y, Sun YE, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res* 2014;20:6212–22.



21. Imamoglu GI, Eren T, Baylan B, Karacin C. May high levels of systemic immune-inflammation index and hematologic inflammation markers suggest a further stage in testicular tumours? *Urol Int* 2019;103:303–10. [\[CrossRef\]](#)
22. Huang L, Liu S, Lei Y, Wang K, Xu M, Chen Y, et al. Systemic immune-inflammation index, thymidine phosphorylase and survival of localized gastric cancer patients after curative resection. *Oncotarget* 2016;7:44185–93. [\[CrossRef\]](#)
23. Hirahara N, Tajima Y, Matsubara T, Fujii Y, Kaji S, Kawabata Y, et al. Systemic immune-inflammation index predicts overall survival in patients with gastric cancer: a propensity score-matched analysis. *J Gastrointest Surg* 2021;25:1124–33. [\[CrossRef\]](#)
24. Guner A, Kim SY, Yu JE, Min IK, Roh YH, Roh C, et al. Parameters for predicting surgical outcomes for gastric cancer patients: simple is better than complex. *Ann Surg Oncol* 2018;25:3239–47. [\[CrossRef\]](#)
25. Coccolini F, Nardi M, Montori G, Ceresoli M, Celotti A, Cascinu S, et al. Neoadjuvant chemotherapy in advanced gastric and esophago-gastric cancer. Meta-analysis of randomized trials. *Int J Surg* 2018;51:120–7.