Association of Inflammatory Parameters with Survival in Gastric Cancer Patients Underwent Subtotal and Total Gastrectomy

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SUMMARY

This study aimed to assess the differences in inflammatory markers and modified Glasgow prognostic score (mGPS) among patients diagnosed with gastric cancer who underwent subtotal or total gastrectomy and to evaluate the diagnostic performance of these markers in predicting prognosis. The study included 103 patients diagnosed with gastric cancer who had undergone subtotal (n:48) or total gastrectomy (n:55). The inflammatory indices were respectively calculated as follows: neutrophil to lymphocyte ratio (NLR) = neutrophil count/lymphocyte count, platelet to lymphocyte ratio (PLR) = platelet count/lymphocyte count, systemic *immune-inflammatory index (SII) = platelet count × neutrophil count/* lymphocyte count, C-reactive protein (CRP) to albumin ratio (CAR) = \hat{CRP} / albumin levels. The mGPS was determined using established criteria based on CRP and albumin levels. The endpoint was the 3-year survival outcomes for all patients. The mean age of the patients included in the study was 65.9±9.7 years, and the vast majority were male (68.9%). The results of the inflammatory indices were not statistically significant between the subtotal and total gastrectomy groups. Multiple *Cox regression analysis showed that elevated* SII (HR = 1.12, p < 0.001) were independent predictors of the 3-year mortality. In predicting the 3-year mortality, SII demonstrated superior diagnostic performance compared to other inflammatory indices (Area under the curve: 0.843, Sensitivity: 90.5%, and Specificity = 67.1%). SII could be an essential screening tool for predicting long-term prognosis, regardless of the surgical procedure in patients with gastric cancer who have undergone subtotal and total gastrectomy.

Key Words: Gastric cancer, gastrectomy, inflammation, prognosis.

Mide Kanseri Hastalarında İnflamatuvar Parametrelerin Subtotal ve Total Gastrektomi Sonrası Sağkalımla İlişkisi

ÖΖ

Bu çalışma, subtotal veya total gastrektomi uygulanmış mide kanseri tanılı hastalarda inflamatuar belirteçlerin ve modifiye Glasgow prognostik skorunun (mGPS) farklılık gösterip göstermediğini ve bu belirteçlerin prognozu tahmin etmedeki tanısal performansını değerlendirmeyi amaçlamıştır. Çalışmaya, subtotal (n: 48) veya total gastrektomi (n: 55) uygulanmış mide kanseri tanılı 103 hasta dahil edildi. İnflamatuar belirteçler sırasıyla şu şekilde hesaplandı: nötrofillenfosit oranı (NLR) = nötrofil sayısı / lenfosit sayısı, trombositlenfosit oranı (PLR) = trombosit sayısı / lenfosit sayısı, sistemik immün-inflamatuar indeks (SII)= trombosit sayısı × nötrofil sayısı / lenfosit sayısı, C-reaktif protein (CRP) - albümin oranı (CAR) = CRP / albümin düzeyleri. mGPS, CRP ve albumin düzeylerine göre belirlenen kriterlere göre belirlendi. Sonlanım noktası, tüm hastaların 3 yıllık sağkalım sonuçları idi. Çalışmaya dahil edilen hastaların yaş ortalaması 65.9±9.7 yıldı ve çoğunluğu erkekti (%68.9). İnflamatuar belirteçler, subtotal ve total gastrektomi grupları arasında anlamlı farklılık göstermedi. Çoklu Cox regresyon analizi, yüksek SII'nin (HR = 1.12, p < 0.001) 3 yıllık mortalitenin bağımsız belirleyicisi olduğunu gösterdi. 3 yıllık mortaliteyi tahmin etmede, SII düzeyleri diğer inflamatuar belirteçlere göre üstün tanısal performans sergiledi (Eğri altı alan: 0.843, Duyarlılık: %90.5 ve Özgüllük = %67.1). Subtotal ve total gastrektomi uygulanmış mide kanseri hastalarında, SII cerrahi prosedürden bağımsız olarak uzun vadeli prognozu tahmin etmede önemli bir tarama aracı olarak hizmet edebilir.

Anahtar Kelimeler: Mide kanseri, gastrektomi, iltihaplanma, prognoz.

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INTRODUCTION

Worldwide, gastric cancer emerges as the third most prevalent cancer type and is the fourth leading cause of cancer-related mortality, underscoring a significant health concern globally (Bray, 2018). Although survival rates for many cancers have markedly improved over the years, the death rate related to gastric cancer is still high (Shin, 2016). Gastric cancer treatments encompass subtotal or total gastrectomy, immunotherapy, chemotherapy, radiation therapy, and palliative care (Joshi and Badgwell, 2021).

Despite surgical procedures, a significant portion of patients after gastric cancer resection are at risk of morbidity and mortality related to perioperative risk factors and comorbidity (Papenfuss, 2014). The primary prognostic factors for gastric cancer are tumour, node and metastasis (TNM) staging and the pathological type of the tumor (Zhu, 2016). However, it has been reported that the clinical outcomes of patients can be heterogeneous even within the same tumor stage (Shah and Ajani, 2010). Therefore, using additional parameters to predict prognosis can increase the likelihood of accurate estimation. Numerous studies suggest that inflammatory markers may be a valuable prognostic biomarker for gastric cancer patients (Liang, 2020; Fu, 2021). The modified Glasgow prognostic score (mGPS), taking into account C-reactive protein (CRP) and albumin concentrations, is increasingly being recognized as a predictive indicator for morbidity and survival in gastrointestinal malignancies (Wu, 2023), suggesting its potential significance in gastric cancer too (Zhang, 2022). On the other hand, previous studies involving gastric cancer patients have indicated inconsistent findings between prognosis and the systemic immuneinflammatory index, a novel inflammation marker based on neutrophil, lymphocyte, and platelet counts (Qiu, Zhang, and Chen, 2021; Uzunoglu and Kaya, 2023). Besides, there are few studies comparing the diagnostic performance of inflammatory markers and mGPS in predicting the prognosis of patients who have undergone subtotal and total gastrectomy (Szor, 2020; Tinoco, 2020).

This study aimed to assess the differences in inflammatory markers and mGPS levels in patients diagnosed with gastric cancer who underwent subtotal or total gastrectomy and to evaluate the diagnostic performance of these markers in predicting prognosis.

MATERIALS AND METHODS

Following the principles outlined in the Declaration of Helsinki, this retrospective study was conducted at Kutahya Health Sciences University General Surgery Clinic between January 2015 and December 2022. The study has been approved by the Kutahya Health Sciences University Clinical Research Ethics Committee (Date: 08.09.2023, Decision No: 105466).

A total of 154 patients diagnosed with gastric cancer who had undergone subtotal or total gastrectomy in General Surgery Clinic between January 2015 and December 2022 were evaluated retrospectively. Patients who received neoadjuvant therapy, those deemed inoperable or unresectable based on preoperative and intraoperative evaluations, those treated with palliative medical or surgical treatments without tumor resection, patients operated on in outside centers, and those with additional diseases such as diabetes mellitus, hypertension, rheumatoid arthritis, chronic kidney failure, and liver failure were excluded. After the exclusion process, 103 patients diagnosed with gastric cancer who had undergone subtotal or total gastrectomy were included in the analysis.

Study Protocol

The hospital's electronic information system and patient files were used to gather demographic and clinical data. D2 dissection was applied to all N1 and N2 group lymph nodes, while D3 dissection was performed on all N1, N2, and N3 group lymph nodes. A previously defined N-ratio (NR) classification was used to determine the cut-off values for the ratio of metastatic lymph nodes to the total number of removed lymph nodes (Asoglu, 2009). Accordingly, the NR classification was categorized as NR0 (0%), NR1 (1-10%), NR2 (11-25%), and NR3 (26-100%). The endpoint was the 3-year survival outcomes for all patients.

Laboratory Parameters

Blood samples were taken from all patients before surgery, and complete blood counts and biochemical parameters were measured. The calculation of the inflammatory indices is as follows: neutrophil to lymphocyte ratio (NLR) = neutrophil count/ lymphocyte count, platelet to lymphocyte ratio (PLR) = platelet count/lymphocyte count, SII = platelet count × neutrophil count/lymphocyte count, C-reactive protein (CRP) to albumin ratio (CAR) = CRP / albumin levels (Qiu, Zhang, and Chen, 2021; Uzunoglu and Kaya, 2023; Alkurt, 2022).

The mGPS was determined using established criteria based on CRP and albumin levels. In brief, a score of 2 was given for elevated CRP (>10 mg/L) and low albumin (<35 g/L), a score of 1 for elevated CRP alone, and a score of 0 for normal CRP, irrespective of albumin levels (Jiang, 2012).

Statistical Analysis

All data were analyzed with STATA/MP v.16 software (StataCorp LLC, Texas, USA). Numerical data determined to be normally distributed based on the results of Kolmogorov-Smirnov tests are given as mean \pm standard deviation values. Student T-test and Mann-Whitney U test were used to compare the two groups. Categorical variables were presented as numbers and percentages, and comparisons between

groups were performed using Chi-square and Fisher exact tests. Cox regression analyses were conducted to establish any possible factors independently associated with mortality. The Variance Inflation Factor (VIF) was used to assess multicollinearity among the variables in multivariable regression model. A VIF value greater than 2.5 was considered to indicate multicollinearity (Johnston, Jones, and Manley, 2018). The receiver operating characteristic (ROC) curve analysis was applied to assess diagnostic performance. Threshold values were determined by the Youden index method. Comparison of the area under curve (AUC) curves was performed with a nonparametric approach using the theory of generalized U-statistics to generate an estimated covariance matrix previously reported by DeLong et al. (DeLong, DeLong, and Clarke-Pearson, 1988). Significance was accepted at P < 0.05 (*) for all statistical analyses.

RESULTS AND DISCUSSION

The mean age of the study participants was 65.9 years, with a standard deviation of 9.7 years (42 - 83 years), and the vast majority were male (68.9%). Total gastrectomy was performed on 55 patients, while 48 underwent subtotal gastrectomy. The distributions of age, gender, or histological pattern did not show significant differences between the subtotal and total gastrectomy groups. In the subtotal gastrectomy group, the tumor was primarily located in the antrum (68.8%), while in the total gastrectomy group, it was in the cardia (45.5%). In comparison, the median number of removed lymph nodes was higher in the total gastrectomy group than in the subtotal gastrectomy group (22 vs. 14, p = 0.018), while the NR was similar between the groups (p = 0.449). Both surgical groups showed comparable hospitalization durations and 3-year mortality rates (Table 1).

Variables population n = 103 Subtotal n = 48 Total $n = 55$ Age, years 65.9 ± 9.7 67.7 ± 9.8 64.4 ± 9.5 Male gender, n (%) $71 (68.9)$ $29 (60.4)$ $42 (76.4)$ Histology, n (%) 67.7 ± 9.8 67.7 ± 9.8 67.7 ± 9.8	p 0.079 0.092	
Male gender, n (%) 71 (68.9) 29 (60.4) 42 (76.4)		
	0.092	
Histology, n (%)		
Adenocarcinoma 72 (69.9) 33 (68.8) 39 (70.9)	0.999	
Signet ring cell carcinoma 21 (20.4) 10 (20.8) 11 (20.0)		
Other 10 (9.7) 5 (10.4) 5 (9.1)		
Tumor localization, n (%)		
Antrum 33 (32.0) 30 (62.5) 3 (5.5)		
Cardia 27 (26.2) 2 (4.2) 25 (45.5)		
Corpus 19 (18.4) 7 (14.6) 12 (21.8)		
Small curvature 14 (13.6) 7 (14.6) 7 (12.7)	<0.001*	
Greater curvature 4 (3.9) 0 4 (7.3)		
Diffuse 4 (3.9) 1 (2.1) 3 (5.5)		
Gastroenterostomy line 2 (1.9) 1 (2.1) 1 (1.8)		
Dissection, n (%)		
D2 87 (84.5) 45 (93.8) 42 (76.4)	- 0.027*	
D3 16 (15.5) 3 (6.3) 13 (23.6)		
Number of removed LNs 20 (12-28) 14 (9.5-26) 22 (15-29)	0.018*	
Number of metastatic LNs 3 (0-9) 1 (0-8) 5 (0-10)	0.225	
N ratio, n (%)		
NR0 36 (35.0) 19 (39.6) 17 (30.9)	- 0.449	
NR1 10 (9.7) 6 (12.5) 4 (7.3)		
NR2 13 (12.6) 4 (8.3) 9 (16.4)		
NR3 44 (42.7) 19 (39.6) 25 (45.5)		
Duration of hospital stay, day 15 (11-21) 15 (11-20) 14 (11-21)	0.698	
Mortality, n (%) 21 (20.4) 10 (20.8) 11 (20.0)	0.999	
Median follow-up time, months 36 (16-36) 36 (16-36) 36 (20-36)	0.934	

Table 1. Demographic and clinical characteristics of patients diagnosed with gastric cancer who had undergone subtotal or total gastrectomy.

Data are mean \pm standard deviation or median (IQR) or number (%). *p<0.05 indicates statistical significance. LNs, lymph nodes; NR, Ratio of dissected lymph nodes to metastatic lymph nodes.

The distribution of laboratory parameters did not show significant differences between the subtotal and total gastrectomy groups (Table 2).

Table 2. Comparison of laboratory findings based on subtotal or total gastrectomy groups in patients with gastric cancer.

Variables		Gastre			
	All population n = 103	Subtotal n = 48	Total n = 55	р	
Hemoglobin, g/dL	11.7 ± 2.3	11.7 ± 2.2	11.8 ± 2.4	0.939	
Hematocrit, %	36.4 ± 6.4	36.8 ± 5.9	36.2 ± 6.8	0.656	
WBC, x10³/μL	7.5 ± 2.3	7.4 ± 1.9	7.6 ± 2.5	0.673	
Neutrophils, x10 ³ /µL	4.6 (3.8-6.0)	4.5 (3.3-5.9)	4.7 (4.0-6.1)	0.348	
Platelets, x10 ³ /µL	252.6 ± 75.0	239.4 ± 66.8	264.1 ± 80.3	0.960	
Lymphocytes, x10 ³ /µL	1.7 (1.2-2.2)	1.8 (1.4-2.2)	1.7 (1.2-2.3)	0.773	
PLR	139 (110-191)	131 (112-164)	146 (107-214)	0.383	
NLR	2.4 (1.9-4)	2.4 (1.8-3.5)	2.8 (2-4.2)	0.156	
SII, x10 ²	6.6 (4.5-10.2)	6.2 (4.1-9.4)	7.0 (4.5-11.0)	0.130	
Total protein, g/L	6.1 ± 0.6	6.1 ± 0.7	6.2 ± 0.6	0.537	
CRP, mg/L	7.9 (4-22.3)	7.1 (3-19.8)	8.4 (4.3-29.1)	0.271	
Albumin, g/L	3.4 ± 0.5	3.4 ± 0.6	3.4 ± 0.5	0.596	
CAR	2.5 (1.1-6.6)	2.2 (0.8-5.7) 2.7 (1.2-9.2)		0.275	
mGPS, n (%)					
0	60 (58.3)	28 (58.3)	32 (58.2)		
1	13 (12.6)	5 (10.4)	8 (14.5)	0.783	
2	30 (29.1)	15 (31.3)	15 (27.3)		

Data are mean \pm standard deviation or median (IQR) or number (%). *p<0.05 indicates statistical significance. Abbreviations: CAR, C-reactive protein to albumin ratio; CRP, C-reactive protein; mGPS, modified Glasgow prognostic score; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; SII, systemic immune inflammation index. Increased age, NR3, high neutrophil counts, low lymphocyte counts, high PLR, high NLR, high SII, high CRP level, low albumin level, and high CAR and mGPS 2 scores were found to be associated with increased mortality risk (Table 3 and 4).

Variables	Sur	Survival		Univariable Cox Regression		
	Alive n = 82	Exitus n = 21	HR	95% CI	р	
Age, years	64.9 ± 9.8	70.0 ± 7.8	1.05	1.01-1.11	0.036*	
Male gender, n (%)	59 (72.0)	12 (57.1)	0.55	0.23-1.31	0.175	
Gastrectomy, n (%)						
Subtotal	38 (46.3)	10 (47.6)	ref			
Total	44 (53.7)	11 (52.4)	0.94	0.40-2.21	0.883	
Histology, n (%)						
Adenocarcinoma	56 (68.3)	16 (76.2)	ref			
Signet ring cell carcinoma	16 (19.5)	5 (23.8)	1.07	0.39-2.93	0.889	
Other	10 (12.2)	0	0.01	0.01-12.60	0.977	
Tumor localization, n (%)						
Antrum	25 (30.5)	8 (38.1)	ref			
Cardia	18 (22.0)	9 (42.9)	1.40	0.54-3.64	0.486	
Corpus	18 (22.0)	1 (4.8)	0.20	0.02-1.58	0.126	
Other			0.50	0.13-1.87	0.300	
N ratio, n (%)						
NR0	32 (39.0)	4 (19.0)	ref			
NR1-2	20 (24.4)	3 (14.3)	2.84	0.64-12.7	0.172	
NR3	30 (36.6)	14 (66.7)	3.08	1.01-9.37	0.047*	
Duration of hospital stay, day	14 (11-20)	16 (11-24)	1.01	0.96-1.06	0.685	

Table 3. Demographic and clinical characteristics associated with mortality.

Data are mean \pm standard deviation or median (IQR) or number (%). *p<0.05 indicates statistical significance. Abbreviations: LNs, lymph nodes; NR, the ratio of dissected lymph nodes to metastatic lymph nodes.

Variables	Sur	Survival		Univariable Cox Regression		
	Alive n = 82	Dead n = 21	HR	95% CI	р	
Hemoglobin, g/dL	12.0 ± 2.3	10.9 ± 2.0	0.84	0.70-1.01	0.066	
Hematocrit, %	37.1 ± 6.4	34.1 ± 5.8	0.94	0.89-1.01	0.073	
WBC, x10³/μL	7.4 ± 2.4	8.0 ± 2.0	1.09	0.93-1.29	0.279	
Neutrophils, x10 ³ /µL	4.4 (3.6-5.5)	5.9 (4.9-7.2)	1.32	1.10-1.58	0.003*	
Platelets, x10 ³ /µL	250.0 ± 79.3	262.7 ± 55.7	1.00	0.98-1.01	0.526	
Lymphocytes, x10³/µL	1.8 (1.3-2.3)	1.2 (0.9-1.4)	0.14	0.05-0.41	<0.001*	
PLR	126 (107-165)	199 (146-349)	1.07	1.04-1.10	<0.001*	
NLR	2.3 (1.8-3.3)	5.5 (3.5-6.8)	1.55	1.32-1.81	<0.001*	
SII, x10 ²	5.7 (3.8-8.2)	11.3 (7.9-20.4)	1.13	1.07-1.18	<0.001*	
Total protein, g/L	6.2 ± 0.6	6.0 ± 0.7	0.97	0.85-1.09	0.264	
CRP, mg/L	7 (3.8-17.6)	26.6 (7-81.1)	1.02	1.01-1.03	<0.001*	
Albumin, g/L	3.5 ± 0.5	3.1 ± 0.6	0.28	0.13-0.61	0.001*	
CAR	2.2 (0.9-5.3)	8.6 (2.5-29.5)	1.06	1.04-1.09	<0.001*	
mGPS						
0	54 (65.9)	6 (28.6)	ref			
1	10 (12.2)	3 (14.3)	2.47	0.62-9.88	0.201	
2	18 (22.0)	12 (57.1)	4.54	1.7-12.13	0.003*	

Data are mean \pm standard deviation or median (IQR) or number (%). *p<0.05 indicates statistical significance. Abbreviations: CAR, C-reactive protein to albumin ratio; CRP, C-reactive protein; mGPS, modified Glasgow prognostic score; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; SII, systemic immune inflammation index.

Parameters associated with mortality were included in the multivariable Cox regression analysis with the backward-Wald method. There was multicollinearity between the CAR and CRP (VIF = 22.5), albumin (VIF = 3.8) levels, as well as the mGPS (VIF = 2.9). In addition, multicollinearity was found between SII and neutrophil counts (VIF = 7.8), platelet counts (VIF = 5.4), lymphocyte counts (VIF = 4.5),

PLR (VIF = 14.2), and NLR (VIF = 25.4). Therefore, the components of CAR and SII were not included in the multivariable regression model. Multiple Cox regression analysis showed that increased age (HR = 1.08, p = 0.015), NR3 (HR = 3.56, p = 0.036), and elevated SII (HR = 1.12, p < 0.001) were independent predictors of mortality (Table 5).

Variables	Mu	VIE		
	HR	95% CI	р	VIF
Age	1.08	1.02-1.15	0.015*	1.11
N ratio				1.07
NR0	ref			
NR1-2	1.13	0.235-5.11	0.872	
NR3	3.56	1.09-11.65	0.036*	
SII	1.12	1.06-1.18	<0.001*	1.53
CAR	1.04	0.98-1.08	0.085	1.59
	-2Log			

Table 5. Independent predictors of mortality.

*p<0.05 indicates statistical significance. Abbreviations: CAR, C-reactive protein to albumin ratio; NR, ratio of dissected lymph nodes to metastatic lymph nodes; SII, systemic immune inflammation index; VIF, variance inflation factor.

In predicting the 3-year mortality, SII demonstrated superior diagnostic performance compared to other inflammatory indices (Figure 1).

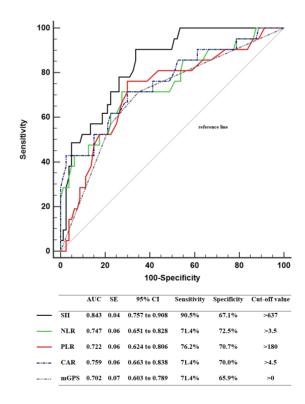


Figure 1. Diagnostic performance of inflammatory indices in predicting mortality

In the prognosis of gastric cancer, increasing age, especially over 60, is considered a significant risk factor (Bilici, 2010; Jaworski, 2011). Even though gastric cancer occurs approximately twice as often in men than in women, the influence of gender on its prognosis remains a matter of debate (Bilici et al., 2010; Jaworski et al., 2011). In the current study, most patients with gastric cancer were both in the geriatric age group and male. In surgical treatment for gastric cancer, a critical decision revolves around the extent of stomach removal. Although routinely performing a total gastrectomy is often recommended, it has been demonstrated that such a procedure elevates morbidity without significantly affecting survival. Nevertheless, it is reported that when the surgical approach is tailored based on the specific case, the choice of gastrectomy does not play a pivotal role in determining survival outcomes (Patel and Kooby, 2011). Consistent with the existing literature, the type of gastrectomy was not associated with prognosis.

In gastric cancer, the presence or number of metastatic lymphadenopathies are significant determinants of prognosis (Adachi, 2000). Additionally, a previous study has shown that in gastric cancer, the number of lymph nodes removed in gastric cancer is a more important predictor of longterm survival than the type of surgery. (Palaj, 2021). In some studies, rather than focusing on the number of metastatic lymph nodes, an NR nodal assessment is proposed based on the ratio of metastatic nodes to excised nodes (Sano, 2000; Wang, 2021). Furthermore, this assessment has been indicated as an independent prognostic factor (Persiani, 2008; Wang et al., 2021). Evaluating the efficacy of lymphadenectomy, NR is a straightforward method and can be applied even when fewer than 15 lymph nodes are removed or in cases of non-curative resection (Marchet, 2007). An optimal threshold value for NR scores has yet to be established. However, the classification by Asoğlu et al. (Asoglu et al., 2009) is frequently utilized. The present study determined that the NR3 category had an independent association with increased mortality risk.

Tumor progression is not only driven by the inherent characteristics of the tumor itself but also

by the inflammatory response (Alifano, 2014). The relationship between cancer and inflammation is manifested through the infiltrative nature of inflammatory cells, the production of inflammatory factors during tumorigenesis, tissue remodeling and angiogenesis (Singh, 2019). Furthermore, it has been reported that tumor-associated neutrophils in regional lymph nodes promote the invasion of these nodes by cancer cells through enhanced lymphangiogenesis, contributing to the progression of the tumor (Tokumoto, 2014). On the other hand, neutrophils, influenced by the secretion of specific cytokines and chemokines, may curtail immediate and persistent inflammation while fostering tumor progression and spread (Tan, 2013). Through the discharge of adenine nucleotides, platelets facilitate the epithelialmesenchymal transition (EMT) in circulating tumor cells (Labelle, Begum, and Hynes, 2014). Meanwhile, lymphocytes are instrumental in moderating tumor progression by producing cytokines and facilitating robust cellular immune responses (Ogiya, 2016).

In this regard, many studies have shown that inflammatory indices such as NLR, PLR, and CAR can be used as prognostic biomarkers in patients with gastric cancer (Liang et al., 2020; Fu et al., 2021; Nechita, 2023; Alkurt et al., 2022). Previous studies have shown that CAR is a better prognostic indicator than mGPS (Lee, 2020; Liu, 2015). Besides, a comprehensive evaluation of immune cells might provide a more explicit depiction of the inflammatory state. In line with limited studies, elevated SII levels served as an independent indicator of prognosis (Qiu, Zhang, and Chen, 2021; Uzunoglu and Kaya, 2023; Wang and Zhu, 2019). The inflammatory indices did not demonstrate significant differences between the subtotal and total gastrectomy groups. For forecasting the 3-year mortality, SII outperformed other inflammatory markers regarding diagnostic efficacy. To the best of our knowledge, this was the first study comparing SII with mGPS and CAR in predicting prognosis for gastric cancer patients. SII levels can be an essential screening tool in gastric cancer patients that is simple, inexpensive, and exhibits high sensitivity in predicting prognosis, independent of the surgical procedure.

The strength of this study is the combined evaluation of both old and new inflammatory indices in predicting the prognosis of patients with gastric cancer. However, this study has some significant limitations. The primary limitation was the singlecenter retrospective design and limited sample size. Secondly, postoperative changes in inflammatory indices could not be examined. Thirdly, due to the study's retrospective nature, information regarding patient relapses was unavailable and could not be assessed. Finally, crucial prognostic parameters, such as data on locoregional recurrence and diseasefree survival, were unavailable. This limitation may reduce the significance of overall survival since it is challenging to establish the cause of death as diseaserelated.

CONCLUSION

Preoperative SII level was a significant prognostic indicator in patients with gastric cancer who have undergone subtotal and total gastrectomy, regardless of the surgical procedure. Furthermore, SII exhibited superior diagnostic performance compared to other inflammatory indices. SII could serve as an important screening tool in the long-term follow-up of gastric cancer patients.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION STATEMENT

Concept – BIU, Design- BIU and SZ; Supervision - BIU and MFE; Data collection and/or processing – BIU, MAT, HEA, MFE and SZ; Analysis and/ or interpretation - BIU, MAT, HEA, MFE and SZ; Writing – BIU; Critical review- MAT, HEA, MFE and SZ. All authors read and approved the final version of the manuscript.

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