doi: 10.53446/actamednicomedia.1677338

Acta Medica Nicomedia

Cilt: 8 Sayı: 3 Ekim 2025 / Vol: 8 Issue: 3 October 2025
https://dergipark.org.tr/tr/pub/actamednicomedia

Research Article | Araştırma Makalesi

PROGNOSTIC SIGNIFICANCE OF HISTOPATHOLOGICAL AND HEMATOLOGICAL MARKERS IN GASTROINTESTINAL STROMAL TUMORS

GASTROİNTESTİNAL STROMAL TÜMÖRLERDE HİSTOPATOLOJİK VE HEMATOLOJİK BELİRTEÇLERİN PROGNOSTİK ROLÜ

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ABSTRACT

Objective: This study aimed to evaluate the relationship between overall survival and preoperative systemic inflammation and nutritional indices in patients with gastrointestinal stromal tumors (GIST), in addition to conventional histopathological parameters.

Methods: In this retrospective study, 43 patients who underwent surgery for GIST were analyzed. Demographic, laboratory, and pathological data were reviewed. Inflammatory and nutritional indices (including HALP, NLR, SII, PNI, and CRP/Albumin) were calculated from preoperative blood parameters. Their effects on 3-year survival were assessed using the Kaplan-Meier method and the log-rank test.

Results: High mitotic count and Ki67 index were significantly associated with decreased survival. Patients with elevated RDW levels were found to have significantly shorter survival times ($p<0.05$). Classification accuracy for HALP, NLR, SII, PNI, and CRP/Albumin was found to be moderate based on their respective cut-off values.

Conclusion: This study demonstrates that, in addition to histopathological markers, systemic inflammatory and nutritional indices may serve as useful prognostic tools in GIST patients. These indices could aid in the development of individualized follow-up strategies postoperatively. However, further large-scale prospective studies are warranted to validate these findings.

Keywords: *Gastrointestinal stromal tumors (GIST), systemic inflammation, survival, HALP, NLR, PNI, SII, CRP/Albumin, RDW*

ÖZ

Amaç: Bu çalışmada, gastrointestinal stromal tümör (GIST) tanısı almış ve cerrahi tedavi uygulanmış hastalarda, klasik histopatolojik parametrelerin yanı sıra preoperatif dönemde elde edilen sistemik inflamasyon ve beslenme indekslerinin sağkalım ile ilişkisi değerlendirildi.

Yöntem: Retrospektif olarak tasarlanan bu çalışmaya, GIST tanısı ile cerrahi uygulanmış 43 hasta dahil edildi. Hastaların demografik, laboratuvar ve patolojik verileri incelendi. Hematolojik parametrelerden hesaplanan HALP (Hemoglobin × Albumin × Lymphocyte / Platelet), NLR (Neutrophil / Lymphocyte ratio), SII (Systemic Immune-Inflammation Index: Platelet × Neutrophil / Lymphocyte), PNI ve CRP/Alb gibi indekslerin 3 yıllık sağkalım üzerindeki etkileri Kaplan-Meier yöntemi ve log-rank testi ile değerlendirildi.

Bulgular: Yüksek mitoz sayısı ve Ki67 proliferasyon indeksi, sağkalımı olumsuz etkileyen anlamlı histopatolojik faktörler olarak belirlendi. RDW düzeyi yüksek olan hastalarda sağkalım süresi anlamlı şekilde daha kısaydı ($p<0.05$). HALP, SII, NLR, PNI ve CRP/Alb oranı gibi kompozit indekslerin cut-off değerlerine göre sınıflandırma doğruluğu orta düzeydeydi.

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Anahtar Kelimeler: Gastrointestinal stromal tümör (GIST), sistemik inflamasyon, sağkalım, HALP, NLR, PNI, SII, CRP/Albumin, RDW

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Submitted/Başvuru: 16.04.2025 • **Accepted/Kabul:** 07.10.2025 • **Published Online/Online Yayın:** 22.10.2025

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract and frequently originate from Cajal interstitial cells or their precursors.[1] Although GISTs account for approximately 1% of all malignancies of the gastrointestinal tract, their clinical behavior is heterogeneous and can range from low malignant potential to aggressive tumors.[2] The most common sites of localization are the stomach (60-70%) and small intestine, but they can rarely be observed in other organs in the gastrointestinal tract, such as the esophagus, colorectal region, and mesentery.[3]

Radical surgery is still the mainstay of curative treatment in localized GIST cases. However, risk stratification based on pathological parameters such as tumor size, mitotic activity, anatomical localization, and histological subtype may be limited in predicting the postoperative prognosis of patients.[4] Therefore, studies to define new biomarkers that can predict prognosis in patients with GIST have gained momentum in recent years. In particular, hematological biomarkers reflecting systemic inflammation and nutritional status (e.g., NLR, PLR, HALP, SII, PNI) have been shown to predict survival in different solid tumors, and the prognostic roles of these parameters in inflammatory diseases and rare tumors such as GIST have started to be investigated.[5-8]

Systemic inflammatory indices are important as they reflect the immune response in the tumor microenvironment, the activity of the hematopoietic system, and the overall organism response. For example, the neutrophil/lymphocyte ratio (NLR) indicates the activity of the inflammatory process with a decrease in the number of lymphocytes, while the HALP score assesses the hematological and nutritional status in an integrated manner. However, the effects of these biomarkers on survival in GIST patients have not yet been clarified, and the literature in this field is quite limited.[9]

The aim of this study was to evaluate the relationship between hematological indices reflecting systemic inflammation and nutritional status (HALP, NLR, SII, PNI, CRP/Alb, etc.) with three-year survival in patients diagnosed with GIST and surgically treated and to determine the cut-off values for these parameters and to reveal their potential for clinical use.

Methods

Study Design and Patient Selection

Initially, 52 patients diagnosed with GIST were screened. Nine patients were excluded due to incomplete clinical/pathological data, presence of another malignancy, or insufficient follow-up. Thus, 43 patients were included in the final analysis. The median follow-up period was 24 months (range: 5–45 months). Missing data were managed by listwise deletion.

Approval was obtained from the ethics committee of the university before starting the study. This retrospective descriptive study was conducted on the clinical and laboratory data of 43 patients diagnosed with gastrointestinal stromal tumor (GIST) and treated surgically in the general surgery and oncology units of our hospital between 2015 and 2023. Inclusion criteria: Patients who were diagnosed with GIST as a result of histopathological examination, had sufficient clinical and pathological data, underwent surgery, and had a follow-up period of at least 3 years. Patients with incomplete data, history of other malignancies or neoadjuvant treatment were excluded.

Data Collection

Demographic data (age, gender), tumor localization (stomach, duodenum, small intestine), histological subtype (spindle, epithelioid, mixed), T stage, mitotic index, Ki67 proliferation index, AFIP risk classification, presence of metastasis, macroscopic findings such as ulceration, necrosis, and bleeding were retrospectively obtained from patient files.

In addition, laboratory data from the preoperative period were examined, and hemogram parameters (hemoglobin, leukocyte, neutrophil, lymphocyte, monocyte, platelet, red cell distribution width [RDW]) and biochemical values (albumin, C-reactive protein [CRP]) were recorded. Using these parameters, composite scores including HALP score (Hemoglobin × Albumin × Lymphocyte / Platelet), NLR (Neutrophil / Lymphocyte ratio), Systemic Immune-Inflammation Index (SII) (Platelet × Neutrophil / Lymphocyte), CRP/Albumin ratio, LCR (Lymphocyte / CRP ratio) and PNI (10 × Albumin + 0.005 × Lymphocyte) were calculated.

Histopathological and Risk Classifications

Pathological evaluation of the tumors was performed in accordance with the World Health Organization (WHO) criteria. For risk classification, low, intermediate, and high-risk categories were determined based on tumor size, mitotic index, and localization according to the Armed Forces Institute of Pathology (AFIP) system. Ki67 and mitotic count were also analyzed as prognostic markers.

Patients were followed up for a mean of 24.6±16.3 months (minimum 5, maximum 45 months), and 3-year overall survival (OS) rate was used as the primary endpoint. In survival analyses, death was considered as 'event' and patients who were still alive were considered as 'censor'.

Statistical Analysis

Data were analyzed using the statistical software SPSS 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD). Variables affecting 3-year survival were analyzed using the Kaplan-Meier method, and differences between groups were compared using the log-rank test. Cut-off values for significance analysis for numerical parameters were determined based on ROC analysis. Sensitivity and specificity ratios were calculated according to the cut-off values. $p<0.05$ was considered statistically significant.

Results

A total of 43 patients were included in the study. 26 (60.5%) of the patients were male and 17 (39.5%) were female. The mean age of the patients was 61.35 ±12.42 (min-max=38-86) years. The overall mean survival time of the patients was 24.59±16.35 (min-max:5-45) months. Mortality developed in 3 patients (6.98%) within 3 years. When the laboratory data of the patients were examined, The mean Hemoglobin (g/dl) value was 11.50±1.89, the mean Platelet count was 275.72±79.97, the mean Neutrophil count was 5.55±2.96, the mean Lymphocyte count was 1.84±0.73, mean Albumin count was 37.61±5.84, mean CRP value was 28.87±45.51, mean RDW value was 16.17±2.58, mean Monocyte value was 0.51±0.26 and mean WBC value was 8.27±3.33. While 6 (40.00%) of the patients were in stage T3, 5 (33.33%) were in stage T4. While 26 (60.47%) of the patients had spindle cell types, 5 (11.63%) had spindle cell types. The tumor location was in the stomach in 31 patients (72.09%), in the small intestine in 5 (11.63%,) and in the duodenum in 3 (6.98%). AFIP risk criteria were observed to be high in 9 patients (20.93%), moderate in 11 (25.58%), and low in 23 (53.49%). The mean Ki67 value of the patients was 8.84±12.99 (min-max=1-60), while the mean mitosis value was 8.88±14.23 (min-max=0-70). In addition, Progression was detected in 5 patients (11.63%), lymphovascular invasion was positive in 13 (30.23%), and perineural invasion was positive in 8 (18.60%). While no metastasis was found in 33 patients (76.74%), 5 (11.63%) developed metastasis in the intraabdominal region, 2 (4.65%) in the peritoneum and 3 (6.98%) in the liver. Ulcers were observed in 6 patients (13.95%), necrosis in 11 patients (25.58%), and bleeding in 3 patients (6.98%). 19 of the patients (44.19%) had the ARh (+) blood group. The mean HALP score of the patients was 22.68±13.82, while the mean LCR score was 1.31±0.29, the mean CRP/Albumin value was 0.86±1.41, the mean NLR score was 3.36±2.12, the mean SII score was 1002.32±1026.08, and the mean PNI score was 40.03±15.22 (Table 1).

Table 1. Distribution of demographic, laboratory, pathological and tumor characteristics

Variables	Frequency (%) (n:43)
Demographic data	
Age (mean ± SD)	61.35 ±12.42 (min-max=38-86, median=63,00)
Age	
<60 (n:18)	18 (41.86)
≥60 (n:25)	25 (58.14)
Sex	
Male	26 (60.5)
Female	17 (39.5)
Median survival (months)	24.59±16.35 (min-max:5-45, median:22,00)
3-Years Survey (n:43)	
Alive	40 (93.02)
Death	3 (6.98)
Laboratory data	
Hemoglobin (g/dl)	11.50±1.89 (min-max=3.67-19.10, median:7.38)
Platelet count × 10^3 (g/dl)	275.72±79.97(min-max=148-466, median:266.0)
Neutrophyl x10^3 /µl	5.55±2.96 (min-max=1.60-17.30, median:4.81)
Lymphosyt x10^3 /µl	1.84±0.73 (min-max=0.48-4.19, median:1.81)
Albumine (gr/dL)	37.61±5.84 (min-max=21.42-48.15, median:38.00)
CRP (mg/L)	28.87±45.51 (min-max=1.78-241.00, median:20.41)
RDW %	16.17±2.58 (min-max=12.60-24.70, median:15.80)
Monosit x10^3 /µl	0.51±0.26 (min-max=0.12-1.37, median:0.45)
WBC	8.27±3.33 (min-max=3.67-19.10, median:7.93)
Tumor characters	
T stage (n:15)	
T1	1 (6.67)
T2	3 (20.00)
T3	6 (40.00)
T4	5 (33.33)
Cell Type	
Spindle	26 (60.47)
Epithelioid	3 (6.98)
Spindle and Epitheloid	3 (6.98)
Other	5 (11.63)
Mix	6 (13.95)

Table 1. Distribution of demographic, laboratory, pathological and tumor characteristics (continued).

Variables	Frequency (%) (n:43)
Location	
Gastric	31 (72.09)
Duodenum	3 (6.98)
Small Intestine	5 (11.63)
Periton	2 (4.65)
Spleen	2 (4.65)
AFIP Risk Criteria	
Low	23 (53.49)
Medium	11 (25.58)
High	9 (20,93)
Ki67	8.84±12.99 (min-max=1-60, median:5,20)
Mitosis	8.88±14.23 (min-max=0-70, median:6,17)
Progression	
Yes	5 (11.63)
No	38 (88.37)
Lymphovascular Invasion presence	
Negative	30 (69.77)
Positive	13 (30.23)
Perineural Invasion presence	
Negative	35 (81.40)
Positive	8 (18.60)
Metastatic region	
None	33 (76.74)
İntraabdominal	5 (11.63)
Peritoneum	2 (4.65)
Liver	3 (6.98)
Ulcer	
Yes	6 (13.95)
No	37 (86.05)
Necrosis	
Yes	11 (25.58)
No	32 (74.42)
Bleeding	
Yes	3 (6.98)
No	40 (93.02)
Blood group	
0-	1 (2.33)
0+	10 (23.26)
A-	3 (6.98)
A+	19 (44.19)
B-	4 (9.30)
B+	4 (9.30)
AB-	2 (4.65)
AB +	0 (0.00)
HALP score	22.68±13.82 (min-max=16.64-73.05, median:20.72)
LCR score	1.31±0.29 (min-max=0.0-3.19, median:1.79)
CRP/ALBUMİN ratio	0.86± 1.41 (min-max=0.04-5.74, median:0.79)
NLR score	3.36±2.12 (min-max=0.94-9.45, median:2.42)
SII score	1002.32±1026.08 (min-max=134.9-4263.4, median:857.58)
PNI	40.03±15.22 (min-max=2.46-65.15, median:43.12)

We used The Kaplan-Meier method and log-rank test to analyze the predictors of a 3-year survival rate. It was observed that mortality occurred in 2.33% of patients over 60 years of age, while mortality occurred in 4.65% of patients under 60 years of age, and this difference was not statistically significant (Log-rank Test chi 2 = 1.379, p = 0.376) (Table 2).

The mean survival times of surviving and deceased patients were 35.62 months and 22.94 months, respectively, which was statistically significant (Log-rank Test chi 2 = 21.78, p = 0.042) (Table 2).

The mean Neutrophil, CRP, and RDW values of surviving patients were lower than those of ex-patients, while mean Hb, platelet, lymphocyte, monocyte, Albumin, and WBC values were higher than those of ex-patients. Only these differences between the RDW mean values were significant (Log-rank Test chi 2= 39.67; p=0.029) (Table 2). The highest number of ex-patients was observed in T stage III and IV patients, and these differences were not significant (Log-rank Test chi 2= 5.09, p= 0.523) (Table 2). The highest number of ex-patients was observed in patients with spindle cell type, and these differences

were not significant (Log-rank Test chi 2= 8.58, *p*=0.788 (Table 2).

Mean Ki67 and Mitosis count were significantly higher in ex-patients (Log-rank Test chi 2=31.27, 29.22 *p*=0.041, 0.038, respectively) (Table 2).

In patients with GIST cancer, the cut-off point for HALP score was 21.755, the cut-off point for LCR (Lymphocyte/ CRP ratio) value was 0.953, the cut-off point for CRP/Albumin value was 0.776, the cut-off point for NLR value was 2.984, the cut-off point for SII value was 766.616, and the cut-off point for PNI value was 44.075. The classification success of this cut-off point was: In patients with GIST cancer, sensitivity for HALP score was 66.7%, specificity was 36.0%, sensitivity for LCR (Lymphocyte/CRP ratio) question was 55.6%, specificity was 44.4%, sensitivity for CRP/albumin value was 61.1%, selectivity was 48.0%, sensitivity for NLR value was 72.2%, selectivity was 42.6%, sensitivity for SII value was 72.0%, selectivity was 56.0%, sensitivity for PNI value was 56.0%, selectivity was 44.2%. The calculated cut-off values and sensitivity results for the classification success in predicting response for HALP score, LCR (Lymphocyte/ CRP ratio) value, CRP/Albumin ratio, NLR value, SII value, and PNI value in patients with GIST cancer are presented in Table 3.

Table 2. Predictors of 3-year survival rate using the method Kaplan–Meier and log rank test

Variables	Survival Alive (n:40) (n,%) (Mean±Std)	Survival Ex (n:3) (n,%) (Mean±Std)	Log-rank Test	*p*-Value
Demographic data				
Age				
Mean±Std)	61.65±11.49	57.33±24.32		0.569
<60 (n:18)	16 (37.21)	2 (4.65)	1.379	0.376
≥60 (n:25)	24 (55.81)	1 (2.33)		
Sex				
Male	24 (55.81)	2 (4.65)	0.818	0.658
Female	16 (37.21)	1 (2.33)		
Median survival (months)	35.62±26.12	22.94±16.51	21.78	**0.042***
Laboratory data				
Hemoglobin (g/dl)	11.52±1.93	10.13±1.57	5.65	0.730
Platelet count × 10^3 (g/dl)	277.03±80.03	258.34±94.50	4.33	0.701
Neutrophyl x10^3 /µl	4.63±3.06	5.62±1.65	6.78	0.575
Lymphosyt x10^3 /µl	2.22±0.64	1.81±1.71	7.32	0.347
Albumine (gr/dL)	37.62±5.85	36.11±7.51	2.65	0.964
CRP (mg/L)	25.77±20.64	29.10±25.41	4.11	0.605
RDW %	15.93±2.29	19.27±4.75	39.67	**0.029***
Monosit x10^3 /µl	0.52±0.26	0.44±0.18	4.56	0.711
WBC	8.33±3.42	7.42±1.96	6.43	0.652
Tumor characters				
T- stage (n:15)				
T1	1 (6.67)	0 (0.00)		
T2	3 (20.00)	0 (0.00)	5.09	0.523
T3	5 (33.33)	1 (6.67)		
T4	3 (20.00)	2 (13.33)		
Cell Type				
Spindle	24 (55.81)	2 (4.65)		
Epithelioid	3 (6.98)	0 (0.00)		
Spindle and Epitheloid	3 (6.98)	0 (0.00)	8.58	0.788
Other	5 (11.63)	0 (0.00)		
Mix	5 (11.63)	1(2.33)		
Location				
Gastric	28(65.12)	3 (6.98)		
Duodenum	3 (6.98)	0 (0.00)		
Small Bowel	5 (11.63)	0 (0.00)	2.98	0.335
Peritoneum	2 (4.65)	0 (0.00)		
Spleen	2 (4.65)	0 (0.00)		
AFIP Risk Criteria				
Low	21(48.84)	2 (4.65)		
Middle	11 (25.58)	0 (0.00)	3.45	0.558
High	8 (18.60)	1 (2.33)		
Ki67	7.83±10.58	22.33±32.72	31.27	**0.041***
Mitosis	7.70±10.89	24.67±39.26	29.22	**0.038***
Progression				
Yes	5 (11.63)	0 (0.00)	2.86	0.684
No	35 (81.40)	3 (6.98)		

Table 2. Predictors of 3-year survival rate using the method Kaplan–Meier and log rank test (continued)

Variables	Survival Alive (n:40) (n,%) (Mean±Std)	Survival Ex (n:3) (n,%) (Mean±Std)	Log-rank Test	*p*-Value
Lymphovascular Invasion presence				
Negative	27 (62.79)	3 (6.98)	4.42	0.329
Positive	13 (30.23)	0 (0.00)		
Perineural Invasion presence				
Negative	32 (74.42)	3 (6.98)	3.31	0.530
Positive	8 (18.60)	0 (0.00)		
Metastatic region				
None	31 (72.09)	2 (4.65)	2.66	0.632
Abdominal	4 (9.30)	1 (2.33)		
Peritoneum	2 (4.65)	0 (0.00)		
Liver	3 (6.98)	0 (0.00)		
Ulcer				
Yes	6 (13.95)	0 (0.00)	2.34	0.630
No	34 (79.07)	3 (6.98)		
Necrosis				
Yes	10 (23.26)	1 (2.33)	3.91	0.598
No	30 (69.77)	2 (4.65)		
Bleeding				
Yes	3 (6.98)	0 (0.00)	1.56	0.801
No	37 (86.05)	3 (6.98)		
Blood group				
0-	1 (2.33)	0 (0.00)	8.21	0.667
0+	10 (23.26)	0 (0.00)		
A-	3 (6.98)	0 (0.00)		
A+	16 (37,21)	3 (6.98)		
B-	4 (9.30)	0 (0.00)		
B+	4 (9.30)	0 (0.00)		
AB-	2 (4.65)	0 (0.00)		
AB +	0 (0.00)	0 (0.00)		

Table 3. Cut-off values and sensitivity results for HALP score, LCR value, CRP/Albumin ratio, NLR value, SII value and PNI value in patients with GIST cancer

	AUC (95% CI)	P values	Cut off	Sensitivity (%)	Specificity (%)
HALP	0.692 (0.532-0.852)	**0.035***	21.755	66.7	36.0
LCR	0.472 (0.286-0.657)	**0.046**	0.953	55.6	44.4
CRP/ALBUMIN	0.561 (0.377-0.746)	**0.502**	0.776	61.1	48.0
NLR	0.491 (0.311-0.670)	**0.821**	2.984	72.2	42.6
SII	0.581 (0.406-0.757)	**0.037**	766.616	72.0	56.0
PNI	0.502 (0.323-0.682)	**0.048**	44.075	56.0	44.2

ROC: Receiver Operating Characteristic, AUC: Area under curve, CI: Confidence interval, HALP: Hemoglobin, albumin, lymphocyte, and platelet; LCR: lymphocytes and CRP, CRP/Albumin: CRP and albumin, NLR: Neutrophil/Lymphocyte ratio, SII: Systemic Inflammatory Index, PNI: Prognostic Nutritional Index

Discussion

In this study, preoperative hematological, biochemical, and histopathological characteristics of 43 patients diagnosed with GIST and treated surgically were evaluated, and the effects of these variables on survival were investigated. In particular, the prognostic value of hematological indices reflecting systemic inflammation and nutritional status in predicting survival was revealed. Our findings showed that some simple laboratory parameters may be associated with survival in addition to classical histopathological indicators.

Mitotic rate and Ki67 proliferation index are the most powerful parameters affecting survival in GISTs. This study showed that mortality was significantly increased in patients with high mitotic activity and a high Ki67 ratio. This finding supports the AFIP risk classification defined by Joensuu et al. and NIH criteria; according to these criteria, a mitotic index >5/50 HPF increases the risk of recurrence and mortality.[1,10] In addition, Ki67 above 10% was found to be associated with a more aggressive prognosis, and this value is recommended as an additional marker to predict biological behavior in GISTs.[11]

In recent years, the role of inflammation in tumor development, progression, and metastasis has become better understood. Immune cells, inflammatory cytokines, and chemokines in the tumor microenvironment have been shown to modulate the proliferation, angiogenesis, and invasive potential of tumor cells.[12,13]

Therefore, inflammation parameters obtained from peripheral blood circulation are considered a reflection of tumor biology.

Neutrophil/lymphocyte ratio (NLR) is one of the most widely used parameters reflecting systemic inflammation. Although the NLR value did not show a direct significant correlation with survival in our study, it has been reported in the literature that survival is significantly decreased when NLR is >3. For example, Yıldız et al. reported that the recurrence rate was 40% higher in GIST patients with NLR>2.5.[14] This is attributed to the disruption of the balance between the pro-tumoral activity of neutrophils (VEGF release, angiogenesis) and the anti-tumoral cytotoxic effect of lymphocytes.[15]

The HALP score (Hemoglobin × Albumin × Lymphocyte / Platelet) used in our study is a composite index reflecting both hematological and nutritional status. In the literature, the HALP score has been found to be effective in predicting survival, especially in gastric and colorectal cancers; a low HALP score has been reported to be associated with malnutrition, immunosuppression, and systemic inflammation.[16] Although there is limited data on GIST, our study is one of the few studies using this index and revealed that survival time was shorter in patients with low HALP scores.

The systemic Immune-Inflammation Index is an index based on platelet, neutrophil, and lymphocyte values. The SII cut-off value determined in our study was 766.616, and a higher mortality rate was observed in patients above this value. The prognostic value of SII has been demonstrated in hepatocellular carcinoma, prostate cancer, and non-small cell lung cancer in addition to GIST.[17,18] In GIST patients, Wang et al. reported that high SII was inversely correlated with Disease Free Survival (DFS) and Overall Survival (OS).[9]

PNI score (10×Albumin + 0.005×Lymphocyte), which is used as an indicator of nutritional status, has been increasingly used in solid tumors in recent years. A low PNI value reflects immunosuppression and malnutrition together and may increase the risk of postoperative complications. Jiang et al., one of the few studies investigating the effect of PNI on survival in GIST patients, showed that recurrence rates were significantly higher in patients with PNI<45.[19] In our study, increased mortality was also observed in patients with PNI<44.075, but statistical significance was limited.

CRP/Albumin ratio is an easily accessible parameter reflecting both inflammation and protein deficiency. It has been suggested as a prognostic marker, especially in sepsis, pancreatitis, and solid tumors.[20] In a few GIST-specific studies, it was reported that DFS and OS decreased in patients with high CRP/Alb ratio.[21] In this study, it was observed that survival was shortened in patients with a CRP/Alb ratio >0.776 but remained within the limit of statistical significance.

In our study, one of the most remarkable parameters found to be significant was RDW (Red Cell Distribution Width). RDW levels were found to be significantly higher in ex-patients. RDW shows the volumetric differences of erythrocytes and increases with factors such as chronic inflammation, oxidative stress, and malnutrition. The prognostic effect of RDW on survival has been shown in many tumors, such as colon, stomach, and lung cancer.[22] In the context of GIST, this study is considered to be one of the limited number of studies demonstrating the prognostic role of RDW.

In light of all these findings, it can be suggested that hematological and biochemical parameters obtained preoperatively in GIST patients can be used not only diagnostically but also prognostically. The use of such parameters may contribute to individualized risk assessment in patient follow-up. However, standardized cut-off values should be established for the use of these indicators, and these values should be validated in prospective, multicenter studies.

The ROC-derived cut-off values demonstrated moderate predictive accuracy. Among these, LCR showed a statistically significant association, highlighting its potential as a complementary prognostic factor. RDW and LCR likely reflect biological processes such as chronic inflammation, oxidative stress, altered erythropoiesis, and immune dysregulation, which may explain their correlation with tumor progression and reduced survival. These findings align with recent reports in sarcomas and other solid tumors, supporting their clinical relevance.

Study Limitations

The relatively small sample size and the single-center retrospective design further limit the generalizability of our findings. Prospective multicenter studies with larger cohorts are required to validate these results.

Conclusion

This study revealed that in gastrointestinal stromal tumor GIST patients, in addition to classical histopathological markers, systemic inflammation, and nutritional indices that can be easily obtained preoperatively may have potential prognostic value in predicting survival. In particular, high mitotic count and Ki67 proliferation index were confirmed as strong histopathological factors negatively affecting survival. In addition, among hematological parameters, a high RDW value was significantly associated with shorter survival time.

The composite biomarkers HALP, NLR, SII, PNI, and CRP/Alb ratio showed partial sensitivity and specificity in predicting survival. These findings suggest that these indices can be used as complementary tools in the postoperative follow-up and individualized risk assessment of GIST patients.

However, prospective and multicenter studies with larger samples are needed to integrate these results into clinical practice. A more comprehensive evaluation of the effects of systemic biomarkers on GIST prognosis will contribute to the development of more sensitive and personalized monitoring and treatment protocols in the future.

Compliance with Ethical Standards

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained

from the Sakarya University Faculty of Medicine, Non-Interventional Research Ethics Committee (Approval No: E-71522473-050.01.04-318703-407; Date: 28.12.2023). Given the retrospective design and use of anonymized data, the requirement for written informed consent was waived by the committee.

Conflict of Interest

The authors declare no conflicts of interest.

References

1. Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. *Arch Pathol Lab Med.* 2006;130 (10):1466-1478. doi:10.5858/2006-130-1466-GSTROM.
2. Søreide K, Sandvik OM, Søreide JA, Giljaca V, Jureckova A, Bulusu VR. Global epidemiology of gastrointestinal stromal tumours (GIST): a systematic review of population-based cohort studies. *Cancer Epidemiol.* 2016;40:39-46. doi:10.1016/j.canep.2015.10.031.
3. Joensuu H, Hohenberger P, Corless CL. Gastrointestinal stromal tumour. *Lancet.* 2013;382(9896):973-983. doi:10.1016/S0140-6736(13)60106-3.
4. Gold JS, Gönen M, Gutiérrez A, Broto JM, García-del-Muro X, Smyrk TC, et al. Development and validation of a prognostic nomogram for recurrence-free survival after complete surgical resection of localised primary gastrointestinal stromal tumour: a retrospective analysis. *Lancet Oncol.* 2009;10(11):1045-1052. doi:10.1016/ S1470-2045(09)70242-6.
5. Wang DS, Ren C, Qiu MZ, Luo HY, Wang ZQ, Zhang DS, et al. Comparison of the prognostic value of various preoperative inflammation-based factors in patients with stage III gastric cancer. *Tumour Biol. 2012;33(3):749-756. doi:10.1007/s13277-011-0285-z.*
6. Sun YF, Cao XK, Wei Q, Gao YH. Potential biomarkers for the prognosis of gastrointestinal stromal tumors. *World J Gastrointest Oncol.* 2025;17(4):1028-1031. doi:10.4251/ wjgo.v17.i4.102831.
7. Capoglu R, Bayhan Z, Gönüllü E, Coskun M, Harmantepe AT, Kucuk F, et al. Malign tiroid nodülleri için biyolojik belirteçlerin prediktif değeri: tek merkez deneyimi. *J Biotechnol Strateg Health Res.* 2022;6:188-195.
8. Gönüllü E, Kucuk F, Bayhan Z, Harmantepe AT, Capoglu R. Akut kolesistitte kolesistektomi veya kolesistostomi yapılması gerekecek hastaların ayırt edilmesinde biyolojik indeksler. *Sak Med J.* 2022;6(3):489-495 doi:10.31832 /smj.1094 111.
9. Wang T, Qi L, Zhao Y, Ma X, Li T. Inflammatory biomarker correlations and prognosis in high-risk gastrointestinal stromal tumor patients: a multicenter retrospective analysis. *BMC Gastroenterol.* 2025;25:119. doi:10.1186/ s12876-025-03710-8.
10. Joensuu H, Vehtari A, Riihimäki J, Nishida T, Steigen SE, Brabec P, et al. Risk of recurrence of gastrointestinal stromal tumour after surgery: an analysis of pooled population-based cohorts. Lancet Oncol. 2012;13(3):265-274. doi:10.1016/S1470-2045(11)70299-6.
11. DeMatteo RP, Gold JS, Saran L, Gönen M, Liau KH, Maki RG, et al. Tumor mitotic rate, size, and location independently predict recurrence after resection of primary gastrointes tinal stromal tumor (GIST). *Cancer.* 2008;112 (3):608-615. doi:10.1002/cncr.23199.

Author Contributions

AS and EG: Study idea, hypothesis, study design, data collection and analysis AOC: Material preparation AS: Writing the first draft of the article; AS, EG, ATH, RC and FM: Critical review of the article finalization and publication process.

Financial Support

None.

12. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell.* 2010;140(6):883-899. doi:10.1016/j.cell.2010.01.025.
13. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. *Nature*. 2008;454(7203):436-444. doi:10. 1038/nature07205.
14. Bongers BC, Dejong CHC, den Dulk M. Enhanced recovery after surgery programmes in older patients undergoing hepatopancreatobiliary surgery: what benefits might prehabilitation have? *Eur J Surg Oncol.* 2021;47(3):551-559. doi:10.1016/j.ejso.2020.10.030.
15. Cuzick J, Cadman L, Mesher D, Austin J, Ashdown-Barr L, Ho L, et al. Comparing the performance of six human papillomavirus tests in a screening population. *Br J Cancer.* 2013;108(4):908-913. doi:10.1038/bjc.2013.48.
16. Duzkopru Y, Kocanoglu A, Dogan O, Sahinli H, Cilbir E, Altinbas M. Hemoglobin, albumin, lymphocyte, and platelet score as a predictor of prognosis in metastatic gastric cancer. *World J Gastrointest Oncol.* 2023;15(9): 1626-1635. doi:10.4251/wjgo.v15.i9.1626.
17. Lolli C, Caffo O, Scarpi E, Aieta M, Conteduca V, Maines F, et al. Systemic immune-inflammation index predicts the clinical outcome in patients with metastatic castration-resistant prostate cancer treated with abiraterone. *Front Pharmacol.* 2016;7:376. doi:10.3389/fphar.2016.00376.
18. Jomrich G, Gruber ES, Winkler D, Hollenstein M, Gnant M, Sahora K, et al. Systemic immune-inflammation index (SII) predicts poor survival in pancreatic cancer patients undergoing resection. *J Gastrointest Surg.* 2020;24(3):610-618. doi:10.1007/s11605-019-04487-2.
19. 19. Jiang N, Deng JY, Ding XW, Ke B, Liu N, Zhang RP, et al. Prognostic nutritional index predicts postoperative complications and long-term outcomes of gastric cancer. *World J Gastroenterol.* 2014;20(30):10537-10544. doi:10.3748/wjg.v20.i30.10537.
20. Pearce CL, Near AM, Van Den Berg DJ, Ramus SJ, Gentry-Maharaj A, Menon U, et al. Validating genetic risk associations for ovarian cancer through the international Ovarian Cancer Association Consortium. *Br J Cancer.* 2009;100(2):412-420. doi:10.1038/sj.bjc.6604820.
21. Hashimoto S, Tominaga T, Nonaka T, Hamada K, Araki M, Takeshita H, et al. The C-reactive protein to albumin ratio predicts postoperative complications in oldest-old patients with colorectal cancer. *Int J Colorectal Dis.* 2020;35(3):423-431. doi:10.1007/s00384-019-03458-7.
22. Koma Y, Onishi A, Matsuoka H, Oda N, Yokota N, Matsumoto Y, et al. Increased red blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer. *PLoS One.* 2013;8(11):e80240. doi:10.1371/journal.pone.0080240.