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Predictive Role of Halp Score, LCR Value and CRP-Albumin Ratio for Survival and Recurrence in Gastric Cancer

Mide Kanserinde Halp Skoru, LCR Değeri ve CRP-Albumin Oranının Sağkalım ve Nüks için Öngörücü Rolü

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ABSTRACT

Objective: To investigate whether the ratios of biochemical markers such as hemoglobin, albumin, lymphocyte and platelet (HALP) score, lymphocyte-C-reactive protein ratio (LCR) and CRP/Albumin ratio can predict the survival and recurrence of the disease in gastric cancer patients.

Materials and Methods: Adult patients who were operated for gastric cancer in our clinic between January 2014 and December 2023 (n: 85) were included in this retrospective study. HALP and CRP/Albumin scores and LCR ratios were calculated from the preoperative biochemical data of the patients.

Results: Overall survival of patients with a low HALP score was significantly shorter than that of patients with a high HALP score (30.6 vs 35.5 months) ($p<0.05$). In addition, overall survival of patients with low LCR rate was significantly shorter than that of patients with high LCR score (27.9 vs 35.6 months, $p<0.05$), and similarly, the overall survival of patients with low CRP/Albumin value was significantly shorter than that of patients with high CRP/Albumin value (29.9 months vs 32.4 months) ($p<0.05$). There was a strong correlation between HALP, LCR, and CRP/Albumin scores and recurrence (for each $p<0.05$). According to the results of multivariate Cox regression analysis, HALP score, LCR score and CRP/albumin ratio were found to be independent and positive factors for overall survival ($p<0.05$).

Conclusions: Low scores in any of the HALP, LCR, and CRP/Albumin scores were associated with poor postoperative overall survival and recurrence in patients with gastric cancer.

Keywords: Biomarkers, gastric cancer, prognosis, recurrence

ÖZ

Amaç: Hemoglobin, albumin, lenfosit ve trombosit (HALP) skoru, lenfosit-C-reaktif protein oranı (LCR) ve CRP/Albumin oranı gibi biyokimyasal belirteçlerin oranlarının mide kanseri hastalarında hastalığın sağ kalımını ve tekrarını tahmin edip edemeyeceğini araştırmak.

Materyal ve Metot: Ocak 2014 ile Aralık 2023 tarihleri arasında kliniğimizde mide kanseri nedeniyle opere edilen yetişkin hastalar (n: 85) bu retrospektif çalışmaya dahil edildi. Hastaların preoperatif biyokimyasal verilerinden HALP ve CRP/Albumin skorları ve LCR oranları hesaplandı.

Bulgular: Düşük HALP skorlu hastaların genel sağ kalım süresi, yüksek HALP skorlu hastalara göre anlamlı derecede daha kısaydı (30.6'ya karşı 35.5 ay) ($p<0,05$). Ayrıca, düşük LCR oranına sahip hastaların genel sağ kalım süresi, yüksek LCR skorlu hastalara göre anlamlı derecede daha kısaydı (27.9'a karşı 35.6 ay, $p<0,05$) ve benzer şekilde, düşük CRP/Albumin değerine sahip hastaların genel sağ kalımı, yüksek CRP/Albumin değerine sahip hastalara göre anlamlı derecede daha kısaydı (29.9'a karşı 32.4 ay) ($p<0,05$). HALP, LCR ve CRP/Albumin skorları ile tekrarlama arasında güçlü bir korelasyon vardı (her biri için $p<0,05$). Çok değişkenli Cox regresyon analizinin sonuçlarına göre, HALP skoru, LCR skoru ve CRP/albumin oranının genel sağ kalım için bağımsız ve pozitif faktörler olduğu bulundu ($p<0,05$).

Sonuç: HALP, LCR ve CRP/Albumin skorlarından herhangi birinde düşük skorlar, mide kanseri olan hastalarda düşük postoperatif genel sağ kalım ve nüks ile ilişkiliydi.

Anahtar Kelimeler: Biyobelirteçler, mide kanseri, prognoz, nüks

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INTRODUCTION

Gastric Cancer (GC) is a complex disease characterized as a primary epithelial malignancy that originates in the stomach. It develops through multiple stages and is influenced by various risk factors. In recent years, global efforts in prevention, screening, and treatment have led to a general decrease in the disease's incidence and mortality rates. Despite this, GC remains the fifth most common cancer worldwide and ranks fourth in cancer-related deaths.[1]

Precise pathological tumor staging plays a crucial role in assessing survival outcomes for these individuals. While the overall survival rate for GC is 45% at one year, it drops to 26% at five years, and further decreases to 7% in cases of metastatic GC.[2]

Recent research suggests a potential link between systemic inflammation and cancer development, invasion, proliferation, and metastasis.[3] Inflammation, regardless of its cause, contributes to cancer progression by promoting angiogenesis and enhancing apoptosis resistance around the tumor.[4] Elevated levels of neutrophils, leukocytes, platelets, and C-reactive protein (CRP), along with reduced lymphocyte and albumin values in the preoperative period, serve as indicators of systemic inflammatory response.[5] Various prognostic factors based on inflammatory response are derived by combining these biochemical parameters.[6] These factors are utilized not only in determining the prognosis of malignant diseases but also in autoimmune, inflammatory, and infectious conditions where the severity of inflammation is critical.[7]

C-reactive protein (CRP) is a protein produced during the body's response to various inflammatory conditions, including infection, cancer, ischemia, and trauma.[8,9] Other factors known to influence cancer patient prognosis include hemoglobin levels, as well as leukocyte and platelet counts.[10] Serum albumin, the most prevalent protein in human blood plasma, is liver-produced and serves as a crucial prognostic indicator in cancer patients, with low levels (hypoalbuminemia) suggesting a poor outlook.[10] The lymphocyte-to-CRP ratio (LCR) is utilized as a prognostic marker in diverse cancer types.[11] Similarly, a low HALP score, which combines albumin, hemoglobin, platelet, and lymphocyte counts, indicates an unfavourable prognosis in cancer.[10] Research has shown that the CRP/albumin ratio is an independent prognostic indicator for patients with infection, cancer, and comorbidities.[12]

This research aims to explore the connections between CRP/albumin ratio, HALP score, and LCR value and the survival and recurrence rates in GC patients who have undergone surgical treatment.

MATERIALS AND METHODS

Ethics Committee Approval: Our study was approved by the Sakarya University Ethics Committee (Date: 28.12.2023, decision no: E. 318701). The study was carried out following the Helsinki Declaration and international guidelines.

Sample and Study Design: This retrospective observational study included 85 patients who underwent surgery for GC at the Surgical Oncology Clinic of the Sakarya Education and Research Hospital between January 2014 and December 2023. Patient data were obtained from patient files and electronic hospital databases. All laboratory data, including hemogram, CRP, and albumin levels, were obtained from blood samples collected within one week prior to surgery. The same clinical laboratory and standardized protocols were used for all biochemical analyses to minimize measurement variability. As a routine clinical practice in our department, patients were followed up according to a standardized protocol until they died due to disease recurrence. During the follow-up of the patients, control imaging was performed at certain periods (ultrasonography, computed tomography, PET/CT).

Adult patients aged > 18 years who underwent surgery for pathologically confirmed GC were included in this study. Patients with incomplete clinicopathological and follow-up data, those who had been treated for another cancer before Chemoradiotherapy (CRT), those with any inflammatory disease, those who had not undergone surgery, and those with secondary malignancies were excluded.

Variables including chemotherapy regimens, comorbidities, surgical procedures, pathological diagnoses, types of lymph node dissection, tumor size, metastatic site, and patient survival time were recorded and analyzed. Overall survival was defined as the time from surgery to death or last follow-up visit. To calculate inflammation markers, the results of preoperative blood tests were recorded.

HALP Score Calculation: Hemoglobin (gr/dL) x Lymphocyte (count/µl) x Albumin (gr/dL) / Platelet (count/µl).

LCR Calculation: Lymphocyte (count/µl) / CRP (mg/L).

CRP/Albumin Score Calculation: CRP (mg/L)/ Albumin (gr/dL)

Statistical Analysis: Statistical analyses were conducted using SPSS version 27. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as means with standard deviations. The Kolmogorov-Smirnov test was used to assess the normality of continuous data. For comparisons, categorical variables were analyzed using the chi-square test or Fisher's exact

test, whereas independent samples t-tests were applied for continuous variables. The optimal cut-off points were determined based on the minimum P-value from the log-rank $\chi 2$ test and the highest sensitivity and specificity for overall survival. The prognostic significance of CRP/Albumin, LCR, and HALP was evaluated using Receiver Operating Characteristic (ROC) analysis. The area under the curve (AUC) was classified as follows: 0.9–1.0 (excellent), 0.8–0.9 (good), 0.7–0.8 (moderate), 0.6–0.7 (poor), and 0.5–0.6 (unsuccessful). The sensitivity and specificity of the cut-off values were assessed. The optimum cut-off value was calculated by minimizing the sum of the absolute values of the differences between AUC and sensitivity and AUC and specificity, provided that the difference between sensitivity and specificity is minimal. Kaplan-Meier survival curves were compared using the log-rank test, and independent prognostic factors for survival were determined through multivariate Cox regression analysis. A 95% confidence interval was used, with statistical significance defined as $p<0.05$.

RESULTS

In this study, the demographic and clinical characteristics of 85 patients with gastric cancer were evaluated. The mean age of the patients was 62.1±10.8 years, and 60% were male. The average survival time was 31.5±22.6 months. The mean hemoglobin level was 11.4±2.1 g/dL, albumin was 3.24±0.68 g/dL, and lymphocyte count was 1640.1±874.1/mm³. The mean tumor size was 6.1±2.9 cm, with a median lymph node count of 25 (18.5-32) and a median metastatic lymph node count of 6 (1.0-10.0). Lymphovascular invasion was detected in 76.5% of patients, while perineural invasion was present in 60%. Additionally, 30.6% of patients experienced relapse, and 68.2% were deceased. Adjuvant chemotherapy was administered to 90.6% of patients, while 31.8% received neoadjuvant chemotherapy. Among the biochemical markers, the CRP/Albumin ratio was 5.3±9.8, and the HALP score was 37.5±19.4. D2 lymph node dissection was performed in 51.7% of patients, and 27.1% had malignant 8a lymph nodes (Table 1).

Table 1. Demographic and clinical characteristics of patients with gastric cancer (n:85).

Variables	n (%)/Mean±SD/Median (25P, 75P)
Age (Years)	62.1±10.8
Sex (Male/ Female)	51 (60.0) / 34 (40.0)
Survival (Months)	31.5±22.6
Hemoglobin (gr/dL)	11.4±2.1
Albumin (gr/dL)	3.24±0.68
Lymphocyte (/mm^3)	1640.1±874.1
Platelet (µL)	25365.6±94204.4
CRP (mg/L)	20.1±32.7
Fibrinogen (mg/dL)	334.9±143.1
Neutrophil (/mm^3)	7.3±4.6
Monocyte (/mm^3)	0.6±0.3
CEA (ng/mL)	21.2±101.3
CA 19-9 (U/mL)	108.4±288.1
Tumor size (cm)	6.1±2.9
Lymph nodes (n)	25 (18.5. 32.0)
Metastatic lymph nodes (n)	6 (1.0.10.0)
HALP score	37.5±19.4
LCR score	2.8±2.6
CRP/Albumin score	5.3±9.8
LDN (D1 / D2 / D2+) (%)	1(1.2) / 40(47.1) / 44(51.7)
8a LN (benign/ malign)	62 (72.9) / 23 (27.1)
Lymphovascular invasion (Positive/Negative)	65 (76.5) / 20(23.5)
Perineural invasion (Pozitive/Negative)	51 (60.0) / 34(40.0)
Differentiation (Poor/Little/ Moderate/Well)	2 (2.4)/ 32 (37.6) / 35 (41.2)/ 16 (18.8)
Relapse (Yes/No)	26 (30.6) /59 (69.4)
Comorbidity (Yes/No)	44 (51.8) / 41(48.2)
Deceased (Yes/No)	58 (68.2) / 27 (31.8)
Adjuvant Chemotherapy (Yes/No/ Radiotherapy)	77 (90.6)/ 7 (8.2)/ 1 (1.2)
Neoadjuvant Chemotherapy (Yes/No)	27 (31.8) / 58 (68.2)

Descriptive data are given as n (%) or mean±standart deviation; CRP: C-reactive protein; CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; HALP score: Hemoglobin (gr/dL) x Albumin (gr/dL) x Lymphocyte (count/µl) / Platelet (count/µl); LCR score: Lymphocyte (count/µl) / CRP (mg/L); LDN: Lymphadenectomy; LN: Lymph nodes.

The predictive performance of HALP in assessing treatment response for GC patients was analyzed using ROC-derived cut-off values. The optimal cut-off thresholds were determined as follows: 28.61 for HALP, 1.97 for LCR, and 3.41 for CRP/Albumin. At these thresholds, classification performance was as follows: HALP demonstrated a sensitivity of 86.3% and specificity of 76.5%; LCR exhibited a sensitivity of 80.4% and specificity of 64.8%; and CRP/Albumin showed a sensitivity of 82.1% and specificity of 70.6% (respectively, p=0.018, p=0.023, p=0.044). An analysis of the association between clinicopathological parameters and HALP revealed statistically significant relationships with gender (p=0.045), survival duration(p=0.047), haemoglobin (p<0.001), albumin (p<0.001), lymphocyte (p<0.001), platelet (p=0.009), CRP (p=0.041), CEA (p=0.033), Ca19-9 (p=0.009), tumor size (p<0.001), lymphovascular invasion (p=0.029), perineural invasion (p=0.042), 8a lymph nodes involvement (p=0.041), as well as the administration of adjuvant and neoadjuvant therapies (Table 2).

Similarly, the evaluation of LCR in relation to clinicopathological variables showed significant correlations with metastatic lymph nodes, lymphovascular invasion, and perineural invasion, relapse with p-values of 0.035, 0.043, 0.015, 0.049, respectively (Table 3).

Table 2. HALP score and clinical correlations in gastric cancer.

Variables	HALP score [Mean±SD/ n (%)/Median (p25, p75)]			p-values
	Low (≤28.61//N:52)	**High (>28.61//N:33)**		
Age (Years)	63.9±11.5	59.4±8.8	t= 2.149	0.298
Sex (Female. n (%))	25(29.4)	9(10.6)	χ^2=13.641	**0.045**
Survival (Months)	28.9 (21.8-38.2)	32.4 (25.8-39.1)	t=7.231	**0.047**
Hemoglobin (gr/dL)	10.6±1.5	13.4±2.2	t=8.072	**0.001**
Albumin (gr/dL)	2.8±0.7	3.6±0.5	F=19.438	**0.001**
Lymphocyte (/mm^3)	1266.9±0.634	2282.3±0.8838	F=34.008	**0.001**
Platelet (µL)	274.513.5±89.680.9	219.756.3±90.807.4	F=8.192	**0.009**
CRP (mg/L)	18.4 (3.5. 55.7)	13.5(4.5. 67.4)	Z=2.514	**0.041**
Fibrinogen (mg/dL)	343.0±141.4	319.5±152.5	F=0.521	0.318
CEA (ng/mL)	32 (32.0. 57.5)	23.5(15.2. 71.7)	Z=2.359	**0.033**
CA 19-9 (U/mL)	97.0 (33.0. 322.5)	71.4 (42.2.286.3)	Z=3.102	**0.009**
Tumor size (cm)	6.8±3.1	4.7±2.2	F=11.969	**0.001**
Lymph nodes	29.1±10.2	25.3±12.0	F=1.449	0.232
Metastatic lymph nodes	6.0 (3.8-8.3)	6.2 (3.7-8.8)	F=0.114	0.906
T status (T1/T2/T3/T4)	4/5/17/26	3/6/15/9	χ^2=6.125	0.409
N status (N0/N1/N2/N3)	18/11/6/17	12/5/2/14	χ^2 =4.541	0.474
LDN (D1 / D2 / D2+)	1/23/28	0/17/16	χ^2=0.974	0.614
8a LN (Benign/ Malign)	38/14	24/9	t=2.856	**0.041**
Lymphovascular invasion (+)	41/11	24/9	χ^2=8.112	**0.029**
Perineural invasion (+)	34/18	17/16	χ^2=4.415	**0.042**
Differentiation (Poor/Little/ Moderate/Well)	1/22/21/8	1/10/14/8	χ^2=1.740	0.199
Relapse (Yes/No)	16/36	10/23	t =1.964	0.486
Comorbidity (Yes/No)	31/21	13/20	U=2.526	**0.044**
Deceased (Yes/No)	35/17	23/10	U=2.688	**0.042**
Adjuvant Chemotherapy (Yes/No/ Radiotherapy)	46/6	32/1	χ^2=10.993	**0.003**
Neoadjuvant Chemotherapy (Yes/No)	15/37	12/21	t=3.894	**0.031**

Descriptive data are given as n(%); Mean±standart deviation or median (25P,75P); Chi-square (χ^2,) One-way Anova test (F test); Independent sample t-test; Mann Whitney U test (Z test) and Kruskal-Wallis tests (U test); CRP: C-reactive protein; CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; LDN: Lymphadenectomy, LN: Lymph nodes.

Table 3. LCR score and clinical correlations in gastric cancer.

Variables	LCR score [Mean±SD/ n (%)/Median (p25, p75)]			p-values
	Low (≤1.97. n:46)	**High (>1.97. n:39)**		
Age (Years)	63.1±10.2	61.3±11.2	t= 1.172	0.782
Sex (Female. n (%))	25(29.4)	26(30.6)	χ^2 =2.559	0.176
Survival (Months)	27.1 (22.6-34.2)	34.8 (26.3-43.8)	t =6.723	**0.031**
Hemoglobin (gr/dL)	10.1±1.7	13.6±2.2	t=4.124	**0.038**
Albumin (gr/dL)	3.0±0.6	3.5±0.7	F=12.530	**0.003**
Lymphocyte (/mm^3)	1298.1±0.748	2043.5±0.846	F=19.812	**0.001**
Platelet (µL)	269246.1±85667.9	240140.1±98992.1	F=3.926	**0.048**
CRP (mg/L)	18.6 (8.5-38.4)	10.4 (3.1-51.9)	Z=1.429	**0.016**
Fibrinogen (mg/dL)	371.4±158.5	315.7±134.6	F=0.999	0.327
CEA (ng/mL)	29.5 (20.0-54.0)	16.0 (12.9-76.2)	Z=3.126	**0.003**
CA 19-9 (U/mL)	121.0 (43.0-288.0)	85.6 (27.5-319.7)	Z=2.829	**0.009**
Tumor size (cm)	6.3±3.0	4.8±2.8	F=1.277	0.211
Lymph nodes	28.6±11.2	24.5±10.8	F=0.765	0.165

Table 3. Continue.

Metastatic lymph nodes	8.2 (5.22-11.29)	4.3 (2.67-5.92)	F=5.845	**0.035**
T status (T1/T2/T3/T4)	4/5/15/22	3/6/17/13	χ^2 =4.766	0.713
N status (N0/N1/N2/N3)	14/15/4/13	16/1/4/18	χ^2=13.498	**0.021**
LDN (D1 / D2 / D2+)	0/21/25	1/19/19	χ^2 =1.891	0.421
8a LN (Benign/ Malign)	32/14	30/9	t=3.579	0.304
Lymphovascular invasion (+)	38/8	27/12	χ^2 =6.798	**0.043**
Perineural invasion (+)	28/18	23/16	χ^2 11.247	**0.015**
Differentiation (Poor/Little/ Moderate/Well)	1/20/19/6	1/12/16/10	χ^2 =1.063	0.137
Relapse (Yes/No)	12/34	14/25	t =2.104	**0.049**
Comorbidity (Yes/No)	23/23	21/18	U=2.526	0.407
Deceased (Yes/No)	29/16	28/11	U=2.714	**0.048**
Adjuvant Chemotherapy (Yes/No/ Radiotherapy)	41/5	37/2	χ^2 =1.921	0.291
Neoadjuvant Chemotherapy (Yes/No)	17/29	10/29	t =2.510	0.189

Chi-square (χ^2); One-way Anova test (F test); Independent sample t-test; Mann-Whitney U test (Z test) and Kruskal-Wallis tests (U test); CRP: C-reactive protein; CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; LDN: Lymphadenectomy.

A high CRP/Albumin ratio in gastric cancer patients was significantly associated with lower hemoglobin, albumin, and lymphocyte levels, as well as fewer metastatic lymph nodes. Patients with a low CRP/ Albumin ratio had higher rates of lymphovascular and perineural invasion, 8a lymph node malignancy, relapse, and mortality. Additionally, those with a high ratio were more likely to receive adjuvant and neoadjuvant chemotherapy (Table 4).

In the univariate analysis, several factors were identified as predictors of survival, including sex, Adjuvant Chemotherapy, Neoadjuvant Chemotherapy, Mortality, Lymph node, 8aLN, CRP, Hb, Albumin, Platelet, T stage, N stage, tm size, Metastatic LN station, Lymph Vascular Invasion, and recurrence. Univariate Cox regression analysis demonstrated a significant association between HALP, LCR, and CRP/Albumin levels and overall survival time.

Table 4. CRP/Albumin score and clinical correlations in gastric cancer.

Variables	CRP/Albumin ratio [Mean±SD/ n (%)/Median (p25, p75)]			p-values
	Low (≤3.41. n:56)	**High (>3.41. n:29)**		
Age (Years)	63.8±9.6	59.0±12.2	t=2.355	0.466
Sex (Female. n (%))	34(40)	17 (20)	χ^2 =13.035	**0.037**
Survival (Months)	28.7 (23.1-36.7)	31.5(25.4-39.3)	t=0.211	0.647
Hemoglobin (gr/dL)	10.1±2.2	11.6±1.9	t=3.487	**0.046**
Albumin (gr/dL)	2.8±0.6	3.5±0.7	F=17.157	**0.001**
Lymphocyte (/mm^3)	1478.8±0.865	1723.6±0.874	F=14.448	**0.003**
Platelet (µL)	265029.1±88898.9	232079.3±101.630	F=2.361	0.128
CRP (mg/L)	16.0 (3.14-76.0)	11.0 (5.1-58.7)	Z=2.677	**0.047**
Fibrinogen (mg/dL)	370.7±125.9	266.8±155.2	F=3.804	**0.042**
CEA (ng/mL)	38.5 (18.7-56.2)	13.5 (5.7-52.8)	Z=3.504	**0.001**
CA 19-9 (U/mL)	103.0 (55.0-312.5)	97.3 (57.0-272.0)	Z=0.541	0.614
Tumor size (cm)	5.9±2.7	6.2±3.2	F=0.805	0.652
Lymph nodes	27.3±11.2	26.1±10.6	F=1.018	0.641
Metastatic lymph nodes	6.3 (4.66-9.26)	4.2 (2.39-6.57)	F=2.996	**0.031**
T status (T1/T2/T3/T4)	5/7/21/7/23	2/4/11/12	χ^2=3.052	0.802
N status (N0/N1/N2/N3)	20/8/6/22	10/8/2/9	χ^2=2.621	0.758
LDN (D1 / D2 / D2+)	1/30/25	0/10/19	χ^2=11.606	0.149
8a LN (Benign/ Malign)	43/13	19/10	t=3.229	**0.038**
Lymphovascular invasion (+)	43/13	22/7	χ^2=5.674	**0.038**
Perineural invasion (+)	34/22	17/12	χ^2=4.411	**0.042**
Differentiation (Poor/Little/ Moderate/Well)	1/22/22/11	1/10/13/5	χ^2=3.573	0.258
Relapse (Yes/No)	18/38	8/21	t=3.398	**0.027**
Comorbidity (Yes/No)	29/26	14/15	U=1.897	0.437
Deceased (Yes/No)	37/18	20/9	U=2.963	**0.035**
Adjuvant Chemotherapy (Yes/No/ Radiotherapy)	52/4	26/3	χ^2=11.259	**0.016**
Neoadjuvant Chemotherapy (Yes/No)	15/41	12/17	t=2.877	**0.034**

Chi-square (χ^2); One-way Anova test (F test); Independent sample t-test; Mann Whitney U test (Z test) and Kruskal-Wallis tests (U test); CRP: C-reactive protein; CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; LDN: Lymphadenectomy; LN: Lymph nodes.

Multivariate Cox regression analysis identified the HALP score as an independent positive predictor of overall survival (HR = 2.49, 95% CI: 1.294–2.487, p< 0.001). Similarly, LCR was found to be an independent prognostic factor favorably associated with overall survival (HR = 1.298, 95% CI: 1.043–1.757, p = 0.027). The CRP/Albumin ratio was also determined to be an independent useful predictor of overall survival (HR = 2.886, 95% CI: 1.831–4.396, p=0.033) (Table 5).

Table 5. Univariate and multivariate Cox analysis for overall survival of gastric cancer patients in 85 patients.

	Univariate analysis		Multivariate analysis	
Variable	**HR (95%CI)**	**p-values**	**HR (95%CI)**	**p-values**
Age.	1.032 (1.008-1.282)	0.056	1.541 (0.841-3.647)	0.115
Sex: Female vs. Male	1.156 (1.075-1.526)	**0.015**	1.837 (0.953-2.741)	**0.024**
Adjuvant Chemotherapy	1.896 (1.202–3.921)	**0.025**	1.067 (1.012–1.783)	**0.031**
Neoadjuvant Chemotherapy	1.363 (1.132-6.478)	**0.040**	2.134 (1.274-3.416)	**0.047**
Mortality	2.015 (1.532–5.791)	**0.038**	2.711 (1.327-4.673)	**0.001**
Lymph nodes	1.054 (1.012-1.096)	**0.010**	1.819 (1.317-1.928)	**0.001**
8aLN	3.899 (1065-6.273)	**0.037**	2.011(1.231-3.722)	**0.017**
CRP	1.785 (1.465-2.278)	**0.013**	1.907(1.480-2.165)	**0.001**
Hb	1.776 (1.571-3.056)	**0.017**	2.115 (1.709-2.755)	**0.013**
Albumin	0.723(0.334-0.968)	**0.010**	0.944 (0.663-0.999)	**0.006**
Platelet	2.852(1.142-3.877)	**0.042**	2.942 (1.109-5.231)	**0.039**
Differentiation	0.964 (0.535–0.996)	0.171	1.479 (1.075-1.710)	0.124
T Status	2.847 (1.647-5.134)	**0.014**	2.588 (1.368-4.763)	**0.037**
N Status	1.029 (1.001-2.276)	**0.008**	1.632 (1.277-1.927)	**0.022**
HALP ((≤28.61/>28.61)	2.521 (1.583-5.911)	**0.001**	2.497 (1.294-2.487)	**0.001**
LCR (≤1.97/>1.97)	1.266 (1.136-1.701)	**0.037**	1.298 (1.043-1.757)	**0.027**
Crp/Albumin (≤3.41/ >3.41)	2.480 (1.243-2.295)	**0.026**	2.886 (1.831-4.396)	**0.033**
Recurrence	3.184 (1.733-6.911)	**0.001**	3.699 (1.911-6.429)	**0.001**
Metastatic lymph nodes	-1.224 (1.015-2.843)	**0.033**	-3.522 (2.271-4.326)	**0.001**
Tumor size	-0.983 (0.860-0.999)	**0.023**	-2.478(1.012-3.148)	**0.012**
Lymph Vascular Invasion	-2.342 (1.475-3.814)	**0.029**	-2.268 (1.517-2.833)	**0.047**
Perineural invasion	-1.713 (1.122-2.621)	**0.041**	-1.742 (1.245-2.683)	**0.038**

CRP: C-reactive protein; CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; HALP score: Hemoglobin (gr/dL) x Albumin (gr/dL) x Lymphocyte (count/µl) / Platelet (count/µl); LCR score: Lymphocyte (count/µl) / CRP (mg/L); LDN: Lymphadenectomy.

DISCUSSION AND CONCLUSION

The systemic inflammatory response has gained recognition as an influential predictor of cancer prognosis, and hematologic and biochemical markers have been increasingly integrated as prognostic indicators.[13]

In our study, we evaluated 85 patients with GC and demonstrated that the HALP (Hemoglobin, Albumin, Lymphocyte, Platelet) score, LCR (Lymphocyte-to-C-Reactive Protein ratio), and CRP/Albumin ratio can serve as novel prognostic markers for locally advanced GC. Models incorporating these markers effectively identified patients at higher risk of poor survival. We observed that the mean overall survival of the patients was 31.5±22.6 months, aligning well with values reported in the literature.[14]

The HALP score has recently emerged in the literature as a novel prognostic biomarker across various malignancies.[10,15,16] Anemia, often manifesting as a paraneoplastic syndrome in patients with upper gastrointestinal cancers such as gastric and esophageal cancers, is typically exacerbated by oral intake issues and chronic tumor bleeding.[16] Platelets, by secreting vascular endothelial growth factor (VEGF), play a significant role in promoting angiogenesis, which may facilitate tumor metastasis.[17] HALP has been linked to prognosis in various cancers, including pancreatic adenocarcinoma, colorectal, bladder, esophageal, kidney, and small-cell lung cancers.[18] In our study, we found a significant negative correlation between HALP scores and the number of metastatic lymph nodes as well as tumor size (p<0.05). Additionally, we observed significant associations between HALP scores and both lymphovascular invasion and perineural invasion (p<0.05). Numerous studies have underscored the prognostic importance of the HALP score; for instance, Sargın and Düşünceli reported that a low HALP score indicates a poorer prognosis in GC patients.[19]

The LCR, calculated by dividing the lymphocyte count by the CRP level, is significantly associated with prognosis in digestive system cancers.[20] As an inflammation marker, LCR is a reliable predictor of overall survival in GC, with low preoperative LCR values linked to worse survival outcomes and advanced cancer stages.[21] In addition, lymphovascular invasion, defined by the infiltration of tumor cells into lymphatic or blood vessels, is a critical route for tumor dissemination and serves as an independent

prognostic factor in resectable GC, particularly in stage N0 patients.[22] In our study, we observed significant associations between LCR values and lymphovascular invasion ($p<0.05$), as well as between mean LCR scores and survival, tumor size, metastatic lymph nodes count, N 0-1 stages, perineural invasion, mortality, and recurrence ($p<0.05$).

The CRP/Albumin ratio is employed in various prognostic scoring systems to assess survival and treatment efficacy among cancer patients.[23] In our study, we found that the CRP/Albumin ratio represents a promising prognostic marker for locally advanced GC. Toyokawa et al. previously reported that the CRP/Albumin ratio is an independent predictor of overall survival in stage III GC patients.[24] Moreover, Liu et al. observed that higher serum albumin levels reduce mortality among cachectic cancer patients, thus underscoring albumin as a valuable prognostic indicator.[25] Lymph node involvement and metastatic spread are among the most significant prognostic factors in GC.[26] Non-randomized studies conducted in Japan and other countries have indicated that high lymph node involvement (≥20%) is associated with poor prognosis; thus, extensive lymph node dissection could enhance survival by increasing the number of metastatic lymph nodes removed.[27] In our study, we noted that the mean number of lymph nodes removed was 26.9±11.1, with a mean of 6.2±7.7 metastatic nodes, consistent with literature findings that highlight the impact of lymph node positivity on survival.

Considering that CRP elevation is associated with the characteristics of cancer, the most important way to change the CRP/Albumin ratio is to change the albumin value. Low albumin levels due to malnutrition are common in GCs.

Systemic inflammatory responses associated with cancer are critical indicators of tumor progression. Inflammation plays a significant role not only within the local tumor microenvironment but also systemically, influencing tumor biology.[28] These responses often involve changes in the secretion of cytokines, hormones, growth factors, and acute-phase proteins.[29] Recent studies have highlighted that biomarkers such as CRP, complete blood count, albumin, and serum inflammation-based scores can reflect the systemic inflammatory state and predict prognosis in cancer patients.[28] All these molecular pathways support our study.

This study has some limitations. A major limitation is that it is a retrospective and single-center study. In addition, the relatively small sample size and incomplete follow-up records further limit the generalizability of our findings. Nonetheless, our study is significant in that it represents one of the few analyses evaluating the prognostic values of HALP, LCR, and CRP/Albumin inflammatory markers concurrently in relation to recurrence and survival among GC patients. Future prospective multicenter studies are warranted to elucidate better the relationship between these inflammatory markers, postoperative changes, and prognosis in GC.

In conclusion, our findings indicate that the preoperative inflammatory markers HALP, LCR, and Albumin ratios are effective adjunctive tools for predicting postoperative overall survival and recurrence in patients with GC. Integrating these markers with conventional diagnostic tools may enhance prognostic accuracy. Given their low cost, accessibility, and ease of use, these markers hold potential for broader clinical application. However, further prospective, multicenter studies are necessary to confirm their clinical utility and validate their role in routine practice.

Ethics Committee Approval: The study was approved by the Sakarya University Ethics Committee (Date: 28.12.2023, decision no: E. 318701). The study was carried out following the Helsinki Declaration and international guidelines. This study was conducted in accordance with the principles of the Declaration of Helsinki. Since it was a retrospective study, informed consent/consent form was not obtained from the patient/relatives.

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