Prognostic significance of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients undergoing curative resection for colorectal cancer

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BACKGROUND/OBJECTIVE: *In this study, we aimed to determine the relationship between HALP score and postoperative complications (According to Clavien-Dindo classification 3 and above), in patients with colo-rectal cancer who underwent curative surgical resection and to determine its clinical value in predicting prognosis.*
METHODS*: 279 patients who underwent curative surgery for colorectal cancer between 2015-2018 were included in the study. The HALP value was calculated by dividing the product of hemoglobin (g/L), albumin (g/L), lymphocytes (/ L) by the number of platelets (/ L). In order to generate a cut off value for the HALP value, ROC analysis and ROC curve were created. The patients were divided into two groups according to survival, and cut off value was found by ROC analysis: Group 1 (Low HALP) and Group 2 (High HALP). Demographic, clinical characteristics, intraoperative , postoperative results and mean survival were compared between the groups.*
RESULTS*: The patients were divided into two groups according to cut off value of 15.73. Group 1 consisted of 113 patients; Group 2 consisted of 166 patients. Average age was similar in the groups (62vs61, p:0.480). Patients in Group 1 received more neoadjuvant therapy (31%vs21%, p:0.064). CEA levels were higher in Group 1 (7.6vs4.3 p:0.034). Mucinous adenocarcinoma histological type was more common in Group 1 (24%vs13% ,p:0.040). Pathological grade poorly differentiated was more common in Group 1 (27%vs13%). Postoperative outcomes was similar to groups We found the HALP score as a risk factor for survival in multivariate analysis (HR=0.8552 95% (CI:0.6575-1.1125, p:0.007). If the HALP value is below 15.73, it is assumed that the average survival is 28 months with 45.4% sensitivity and 66.938% specificity.*
CONCLUSION*: Our results showed that the HALP score is closely related to clinic pathological features and is an independent prognostic factor for survival. Its value in estimating mean survival is limited.*

KEY WORDS: Colorectal cancer, HALP score, Immunity, Nutrition

Introduction

Cancer remains one of the leading causes of death worldwide and is responsible for 8.8 million deaths per year. In general, it is estimated that one out of three people will have cancer during their lifetime and one out of four people will die from cancer [1,2].
Not only the tumor cell type is associated with the poor course of cancer or the process of metastatic disease, but also the nutritional and immune status of the patient plays an important role in these processes. An individual's immunity or nutritional status can be assessed by some hematological tests. Some studies have reported that peripheral blood cells such as neutrophils, lymphocytes, platelets, and monocytes can support tumor proliferation and metastasis [3-8]. Based on this evidence, seve-

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ral inflammatory index combinations such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and hemoglobin and albumin levels with lymphocyte and platelet number (HALP) combination have been used to predict prognosis [2,9].

Recent evidence has suggested that inflammation may play an important role in the development and progression of CRC. High inflammation increases proliferation, migration, invasion of malignant CRC cells, while silencing of cytokines [interleukin (IL) -21, IL-8 or IL-32] reverses these effects [10,11].

In recent studies, a new composite index named HALP, calculated as Hemoglobin (g/L) × Albumin (g/L) × Lymphocyte (/L)/Platelet (/L) was reported to be related to survival in gastric cancer [12], colorectal cancer [9], bladder cancer [13], and renal cancer [14] patients. However, there is still a lack of evidence in the literature regarding the relationship between HALP prognostic index and postoperative complications.

In this study, we aimed to determine the prognostic significance of the combination of preoperative hemoglobin and albumin levels and lymphocyte and platelet count (HALP) in postoperative complications in patients with colorectal cancer undergoing curative resection.

Material and method

Study Population and Data Collection

After obtaining permission from the Ethics Committee of Cukurova University Faculty of Medicine, dated 04.09.2019 and numbered 91/27, 360 patients who underwent surgery for colorectal cancer between January 2015 and January 2019 were evaluated for this study. Patient files and hospital information system records were examined and a common database was created. Patients were analyzed retrospectively using this database. Patients who underwent palliative surgery, stage 4 disease, patients under eighteen years of age, pregnant patients, chronic inflammatory (tuberculosis, sarcoidosis) and autoimmune disease, patients with hematological disease, steroid treatment and those whose records could not be reached were excluded from the study. The remaining 279 patients were included in the study.

Then, the HALP index was calculated as the following formula: hemoglobin (g/L) × albumin (g/L) × lymphocytes (/L) / platelets (/L).

After the cut-off value was determined by ROC curves, the patients were divided into two groups according to the cut-off value as Group 1 (low HALP) and Group 2 (high HALP). In these two groups, demographic characteristics, body mass index, American Society of Anesthesiologists (ASA) score, tumor marker level, type and nature of the operation, tumor localization, pathological stage of tumors, response to treatment in patients receiving neoadjuvant chemotherapy (NAC), additional non-tumor intervention, stoma status, operation duration, conversion to open surgery, intraoperative complication, postoperative hospital stay, postoperative complications (According to Clavien Dindo classification 3 and above) [15] were analyzed, and also subgroup analysis was performed according to the type of postoperative complications. Unplanned re-admission, re-operation, long-term local recurrence, postoeperative 30 day mortality and distant metastasis were compared in terms of disease-free survival and total survival. Unplanned hospitalization within the first 30 days after discharge was accepted as unplanned re-admission to hospital. Unscheduled reoperation was accepted as a surgical procedure under general, spinal or epidural anesthesia within 30 days of the operative procedure for any reason except follow-up procedures based on pathology results, in accordance with the ACS NSQIP definition [16]. 8th TNM Classification was used as the staging system [17].

Conversion to open surgery was the use of any incision made for anything other than sample extraction or port placement. Extracorporeal anastomosis was not accepted as a conversion to open surgery [18].

Anastomosis leakage was defined as a deterioration of anastomosis integrity determined by combination of clinical, radiological and operative tools.

Wound infection was defined as superficial or deep incisional surgical site infection in the surgical wound according to the definition of the Centers for Disease Control (CDC) (19).

The total blood count was measured by an automated hematology analyzer (Roche Hitachi Cobas® 8000 Roche Diagnostics, Indianapolis, IN, USA While calculating the HALP index conversion was performed in normal value units.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA). When evaluating the data of the study, in addition to descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum), Student's t test was used for the comparison of quantitative data and Mann Whitney U test was used for the evaluation of parameters not showing normal distribution. Pearson's Chi-squared test and Fisher's Exact test were used to compare qualitative data, and logistic regression was used for multivariate evaluations. The patients were divided into two groups according to survival, and cut off value was found by ROC analysis. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curve analysis. To assess the association of HALP with CRC overall survival, multivariate Cox's proportional hazard model was conducted to estimate Hazard ratios (HRs) and their 95% confidence intervals (CIs). Kaplan-Meier and Log Rank tests were used for

survival analysis. A p value of <0.05 was considered statistically significant.

Results

In order to generate a cut off value for the HALP value, ROC analysis and ROC curve were created. As a result of ROC analysis, the area under the ROC curve was calculated as 55.4%. In other words, the cut off value obtained gives the correct answer by 55.4%. According to our cut off value, if the HALP value is below 15.73, it is assumed that the average survival is 28 months with 45.4% sensitivity and 66.938% specificity. It is shown in Table I and Fig. 1.

TABLE I - *Proposed cut-off values for significant parameters in overall survive.*

	HALP
AUC	0.554
Cut-off	<15.73
Specificity	66.38
95%-Cl (%)	57.0-74.9
Sensitive (%)	45.40
95%-Cl (%)	37.6-53.4
PPV	65.5
NPV	46.4
+LR	1.35
-LR	0.82
p	0.125

AUC: Area under the curve PPV: Positive predictive value; NPV: Negative predictive value; OR: Odds ratio; +LR: Positive likelihood ratio; -LR: Negative likelihood ratio.

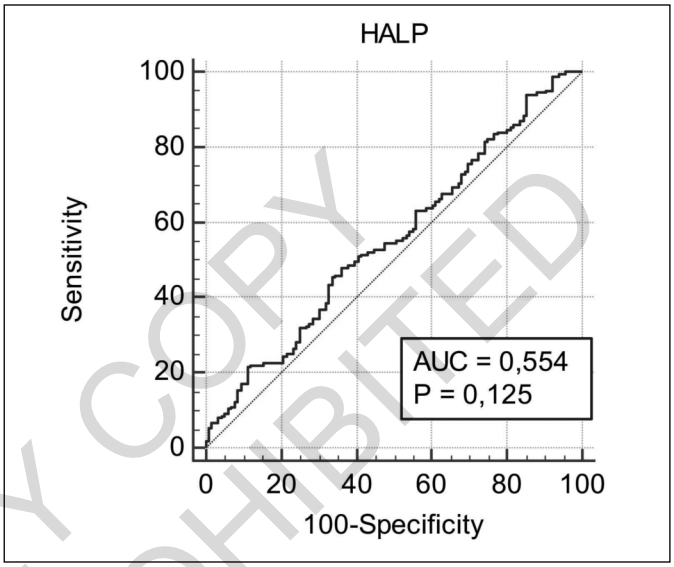

Fig. 1: Receiver operating characteristic (ROC) curve analyses for overall survive.

TABLE II - *Demographic characteristics and preoperative findings of the patients.*

		Low HALP n:113	High HALP n:166	p*
Age (Mean+sd) (Min-max)		62,07+13,1920-107	61.02+11.3827-91	0.480
Sex	Male	67(59.3)	111(66.9)	0.122
	Female	46(40.7)	55(33.1)	
ASA score	1	58(51.3)	77(46.4)	0.664
	2	34(30.1)	58(34.9)	
	3	21(18.6)	31(18.7)	
BMI (Mean+sd) (Min-max)		26,10+4,2718-51	26.50+4.8318-50	0.480
CEA (Mean+sd) (Min-max)		7,69+17,480-146	4.39+7.920-73	0.034
Ca19.9 (Mean+sd) (Min-max)		43,38+170,70-1760	47.38+321.490-4036	0.904
Synchronic lesion	No	98(86.7)	142(85.5)	0.462
	Yes	15(13.3)	24(14.5)	
Neoadjuvant CT (+)	Yes	36(31.9)	36(21.7)	0,039
	No	77(68.1)	130(78.3)	
Tumor localization	Anal canal	1(0.9)	0(0.0)	0.315
	Caecum	6(5.3)	12(7.2)	
	Ascending Colon	21(18.6)	15(9.0)	
	FAP	0(0.0)	3(1.8)	
	Hepatic flexure	7(6.2)	10(6.0)	
	Descending colon	5(4.4)	16(9.6)	
	Multiple	2(1.8)	6(5.4)	
	Rectosigmoid	10(8.8)	13(7.8)	
	Rectum	43(38.1)	59(35.5)	
	Sigmoid colon	10(8.8)	22(13.3)	
	Splenic flexure	4(3.5)	7(4.2)	
	Transvers colon	4(3.5)	3(1.8)	

Fap Familial Adenomatous Polyposis coli

TABLE III - *Intraoperative characteristics.*

		Low HALP n:113	High HALP n:166	p*
Emergency/Elective	Emergency	18(15.9)	16(9.6)	0.083
	Elective	95(84.1)	150(90.4)	
Operation type	Open	71(62.8)	95(57.2)	0.209
	Laparoscopic	42(37.2)	71(42.8)	
Stoma	No	64(56.6)	100(60.2)	0.317
	Yes	49(43.4)	66(39.8)	
Conversion	No	36(85.7)	64(90.1)	0.336
	Yes	6(14.3)	7(9.9)	
Operation duration (min-max)		173,40+31,27 120-250	168.64+33.45 20.0-250.0	0.232
Intraoperative complication	No	108(95.6)	161(97.0)	0.378
	Yes	5(4.4)	5(3.0)	
Additional non-tumor intervention	Cholecystectomy	4(3.5)	0(0.0)	0.153
	Bladder repair	1(0.9)	1(0.6)	
	Cystoscopy	1(0.9)	0(0.0)	
	Splenectomy	0(0.0)	1(0.6)	
	Splenectomy + distal pancreatectomy	0(0.0)	1(0.6)	
	Surrenal biopsy	0(0.0)	1(0.6)	
	TAH+BSO	1(0.9)	0(0.0)	
	Ureter repair	2(1.8)	1(0.6)	
	None	104(92.0)	161(97.0)	

TAH+BSO total abdominal hysterectomy with a bilateral salpingo-oophorectomy

TABLE IV - *Pathological characteristics.*

		Low HALP n:113	High HALP n:166	p*
Histological type	Mucinous	28(24.8)	23(13.9)	0.040
	NOS	83(73.5)	142(85.5)	
	Signet ring	2(1.8)	1(0.6)	
Pathological grade	Poorly differentiated	31(27.4)	22(13.3)	0.012
	Moderately differentiated	50(44.2)	85(51.2)	
	Well-differentiated	32(28.3)	59(35.5)	
Pathological stage	0	2(1.8)	1(0.6)	0.706
	1	22(19.5)	32(19.3)	
	2	0(0.0)	1(0.6)	
	2A	7(6.2)	16(9.6)	
	2B	35(31.0)	41(24.7)	
	2C	1(0.9)	1(0.6)	
	3A	4(3.5)	10(6.0)	
	3B	22(19.5)	40(24.1)	
	3C	20(17.7)	24(14.5)	
Treatment effect (only rectum)	Bad response	8(28.6)	9(37.5)	0.739
	Minimal response	13(46.4)	8(33.3)	
	Moderate response	5(17.9)	4(16.7)	
	Full response	2(7.1)	3(12.5)	

The patients were divided into two groups according to the value of 15.73. Group 1 (less than 15.3; low) consisted of 113 patients, Group 2 (more than 15.73; high) consisted of 166 patients. There was no statistically significant difference between groups in terms of mean age, sex, ASA scores, and body mass index (p>0.05). CEA level was higher in Group 1 than Group 2 (7.69 vs 4.39, p:0.034). Synchronous lesion was similar in the groups (p:0.544). Patients in Group 1 received more neoadjuvant treatment (31.9% vs 21.7%, p:0.039). Tumor localizations were the most common in rectal localizations in both groups, and had similar characteristics (38.1% vs 35.5%, p:0.315). Demographic characteristics and preoperative findings of the patients are shown in Table II.

Elective surgeries were more common in both groups (84.1% vs 90.4%, p:0.083), The rates of laparoscopic surgery were similar in Group 1 and Group 2 (p:0.209).

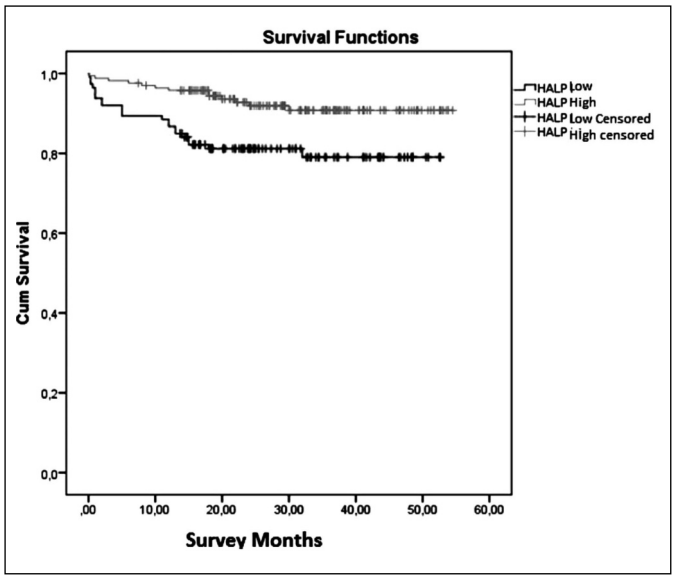

Fig. 2: Total survival according to HALP groups.

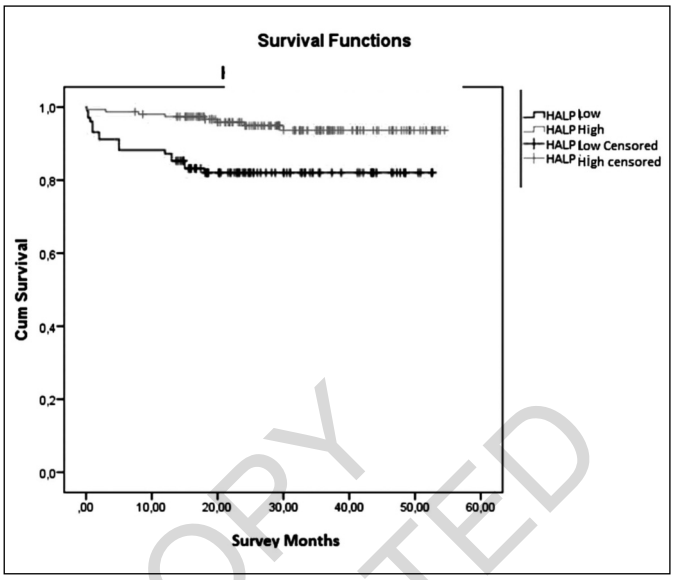

Fig. 3: Disease-free survival according to HALP groups.

TABLE V - *Perioperative and Postoperative Clinical Outcomes, Oncological outcomes.*

		Low HALP n:113	High HALP n:166	p*
Postop duration of hospital stay (Mean+sd)	(Min-max)	9.78+8.302-75	9.25+6.371-49	0.549
Postoperative complication*	Yes	30 (26,5)	31 (18,7)	0,079
	No	83 (73,5)	135 (81,3)	
Wound site infection	Yes	20 (17,7)	19 (11,4)	0,097
	No	93 (82,3)	147 (88,6)	
Intraabdominal abscess	Yes	7 (6,2)	10 (6,0)	0,572
	No	106 (93,8)	156 (94,0)	
Evisceration	Yes	4 (3,5)	3 (1,8)	0,298
	No	109 (96,5)	163 (98,2)	
Ileus	Yes	14 (12,4)	14 (8,4)	0,190
	No	99 (87,6)	152 (91,6)	
Anastomotic leak	Yes	4 (3,5)	3 (1,8)	0,298
	No	109 (96,5)	163 (98,2)	
Reoperation	Yes	6 (5,3)	9 (5,4)	0,596
	No	107 (94,7)	157 (94,6)	
Unplanned readmission to the hospital	Yes	18 (15,9)	19 (11,4)	0,183
	No	95 (94,1)	147 (88,6)	
Postoperative 30 day mortalitiy	Yes	8(7.1)	2(1.2)	0.012
	No	105(92.9)	164(98.8)	
Local recurrence	Yes	7 (6,2)	4 (2,4)	0,101
	No	106 (93,8)	162 (97,6)	
Distant organ metastasis	Yes	10 (8,8)	9 (5,4)	0,190
	No	103 (91,2)	157 (94,6)	

* Clavien-dindo classification 3 and above

Stomatal creation rates were similar (43.4% vs 39.8%, p:0.31). Conversion rates were similar in the groups (p:0.336). Operation durations were similar between the groups (173 vs 168 min, p:0.232). Intraoperative complication rates were similar (4.4% vs 3% p:0.369). Additional non-tumor intervention rates were similar (p:0.153). Intraoperative characteristics are given in Table III.

When we look at the pathological features of tumors, for histological types, mucinous tumors were more common in Group 1 (24.8% vs 13.9%, p:0.040). The rate of poorly differentiated tumors in Group 2 was higher than in Group 1 (27.4% vs 13.3%, p:0.012). Pathological stage distribution was similar between the groups (p:0.706). There was no difference between the groups when we evaluated the response to treatment in patients receiving neoadjuvant chemotherapy (p:0.739). The pathological characteristics of the tumors are shown in Table IV.

TABLE VI - *Univariate and multivariable analysis of factors associated with overall survival in colorectal cancer.*

Measurements		Univariate P	Multivariate HR (95% - Cl)	p
Age group	< 58	<0.001	1.00	
	> 58		1.0361 (0.7992-1.3432)	<0.001
Sex	Male	0.822	1.00	0.4869
	Female		1.0972(0.8447-1.4250)	
Pathological grade	Poorly differentiated	0.335	1.00	
	Moderately differentiated			
	Well-differentiated		1.0990(0.9246-1.3063)	0.2884
Pathological stage	0	0.748	1.00	
	1			
	2			
	2A			
	2B		1.0035 (0.9518-1.0581)	0.8965
	2C			
	3A			
	3B			
	3C			
Histological type	Mucinous	0.677	1.00	0.7477
	NOS			
	Signet ring cell carcinoma		1.0554 (0.7598-1.4660)	
Postoperative complication	Yes	0.931	1.00	0.6874
	No		0.9379 (0.6862-1.2818)	
HALP	<15.73	0.006	1.00	0.007
	>15.73		0.8552 (0.6575-1.1125)	

TABLE VII - *Total survival according to HALP groups.*

		Average (Mean+sd (Min-Max))	p
HALP Group	Low HALP	43.63+1.7440.22-47.04	0.003
	High HALP	50.85+0.9748.94+52.75	

TABLE VIII - *Disease-free survival according to HALP groups.*

		Average (Mean+sd (Min-Max))	p
HALP Group	Low HALP	44.33+1.7940.82-47.82	0.011
	High HALP	52.09+0.8350.46+53.72	

Postoperative duration of hospital stay (p:0.549), postoperative complication rates 26.5% vs 18.7% p:0.079). and.reoperation (p:0.596) and unplanned re-admission (p:0.183) were similar between the groups . Postoerative 30 day mortalitity Group 1 was higher than in Group 2 (%7.1 vs %1.2 p:0,012) In follow-up, local recurrence was 6.2% in Group 1 and 2.4% in Group 2 (p:0.101). Distant organ metastasis was 8.8% in Group 1 and 5,4% in Group 2 (p:0.190). Perioperative and postoperative clinical outcomes, and oncologic outcomes are shown in Table IV.

Univariate and multivariate analyzes of age, sex, pathological grade, pathological stage, histological type, presence of postoperative complications and the relationship between the variables of HALP and survival were evaluated. There were statistically significant differences in univariate and multivariate analyzes in terms of age and HALP groups (p<0.01). There was no statistically significant difference between sex, pathological grade, pathological stage, histological type and postoperative complications (p>0.05). It is shown in Table VI.

Total survival was lower in Group 1 than in Group 2 (43.63 vs 50.85, p:0.003). It is shown in Table VII and Figure 2. Disease-free survival was lower in Group 1 than in Group 2 (44.3 vs 52.09, p:0.011). It is shown in Table VIII and Fig. 3.

Discussion

In this study, we evaluated the prognostic significance of the new index HALP, which combines hemoglobin, albumin levels, lymphocyte and platelet counts, in patients with colorectal cancer who underwent curative resection. HALP was closely associated with clinicopathological features such as histological type and tumor grade. Univariate and multivariate analyzes have shown that HALP is an independent predictor of survival for patients with colorectal cancer undergoing curative surgery. In addition, in our study, we discussed the relationship of HALP score with the incidence of postope-

rative complications and its role in postoperative morbidity and 30-day mortality.

Systemic inflammation and nutritional status are known to play an important role in the prognosis of cancer patients, and the role of nutrition and immunity in predicting the prognosis of cancer patients has recently gained more attention [20-23].

Hemoglobin and albumin are commonly used markers to assess the nutritional status of the patient. With the progression of cancer, hemoglobin and albumin levels drop sharply because malnutrition and the systemic inflammatory response suppress their synthesis [24].

Serum albumin is known as a negative acute phase protein in the liver. In addition, systemic factors such as inflammation and stress may affect serum albumin levels. Therefore, a decrease in serum albumin level represents malnutrition and also a continuous systemic inflammation response. It has also been used to evaluate cancer progression and prognosis. Indeed, low albumin levels correlate with poor survival of cancer patients [25,26].

Serum albumin level can give an idea about retrospective long-term nutritional status. Due to the increase in anaerobic glucose in tumor metabolism in advanced cancer patients, the current energy need is tried to be obtained from fatty acids and muscle tissue. Therefore, protein synthesis decreases and albumin levels decrease as a laboratory reflection. This is the main reason for the occurrence of sarcopenia in tumor patients with a high tumor load. Low levels of albumin are detected in patients with a poor survival (advanced stage and aggressive tumors) [27].

Anemia has an impact on performance status, quality of life, clinical symptoms, and the tolerance and recovery of treatments such as surgical treatment and chemoradiotherapy, and even prognosis. In general, cancer-related anemia (CRA) was detected at the time of diagnosis in 30% of cancer patients, and CRA is associated with a later stage of cancer [28,29].

Major research has shown that anemia and malnutrition can have many negative clinical consequences, such as reduced quality of life, reduced response to treatment, increased risk of chemotherapeutic toxicity, and reduced cancer survival [25,30,31].

The function of lymphocytes is to stimulate the death of cytotoxic cells that inhibit cancer development, and cytokine production [32,33]. Intense intratumoral lymphocyte infiltration in early lesions has been shown to decrease the incidence of metastases and improve the prognosis of patients [34]. Platelets can protect cancer cells by platelet-mediated protective action in blood cells. Some reports have shown that platelets play a role in the protection, growth, tumor angiogenesis, invasion, and metastasis of cancer cells by promoting the release of many types of platelet-derived endothelial cell growth factor [35,36]. In addition, platelets adhering to tumor cells may secrete vascular endothelial growth factor (VEGF), which induces microvessel permeability, promotes extravasation of cancer cells and induces neoangiogenesis [2].

From the above results, it can be concluded that hemoglobin, albumin and lymphocyte may be positive prognostic factors, but platelet may be negative. HALP is an integration of these four hematological and biochemical parameters and has been shown to have a prognostic value in patients with colorectal cancer [9]. Inflammation-based rates are biomarkers representative of the host inflammation response that predicts cancer prognosis.

In their study, Chen XL et al investigated the HALP score in stomach cancer. HALP was associated with many clinicopathological features such as tumor size ($p = 0.003$), and T stage ($p < 0.001$). Low HALP score was significantly associated with tumor progression and served as a negative prognostic factor in gastric cancer patients. In the same study, the mean survival time of the high HALP group was longer and the overall 1- , 2-, 3-year survival rates were higher than the low HALP group [12]. In their study for Renal Cell Carcinoma, Peng et al found that low HALP level was associated with high Fuhrman grade and high T stage, with N and M positive, sarcomatoid transformation, tumor necrosis, and lymphovascular invasion. In their study, they found that preoperative HALP was an independent prognostic factor for cancer specific survival (HR = 1.838, 95% CI: 1.260-2.681, $p = 0.002$) [14]. In their study, Shen X.-B. et al investigate the prognostic significance of the HALP score in patients with small cell lung cancer (SCLC) before first-line treatment with etoposide. However, patients with a high HALP score had also significantly increased progression-free survival (PFS) of ≥6 months. In the groups with a low HALP score, the PFS was significantly shorter compared with a high HALP score group, 5.30±3.08 months and 7.02±3.59 months, respectively (p:0.004). HALP score >25.8 was an independent protective factor that increased PFS in patients with small cell lung cancer (SCLC) undergoing etoposide-based first-line treatment (HR, 0.483; 95% CI, 0.270–0.865) (p:0.014) [37].

In the study of JIANG, Huihong et al. where they evaluated the prognostic value of HALP score in locally advanced colorectal cancer patients, lower HALP exhibited an increased risk of death (HR = 1.46, 95% CI 1.11-1.92; P= 0.007) and cancer-related death (HR = 1.78, 95% CI 1.31-2.43; P< 0.001). Moreover, these patients had lower 5-year OS (60.7% vs. 74.0%; log rank P= 0.001) [9]. Similarly, in our series, we found shorter mean survival (43.63 vs 50.85, p: 0.003) and disease-free survival (44.33 vs 52.09, p: 0.011) in the group with lower HALP. Additionally, we found high levels of tumor markers, another poor prognostic factor, in the low HALP group. The low HALP group received neoadjuvant treatment more frequently, which can be explained by tumor stage and aggressive tumor biologi-

cal variant. Mucinous tumor was one of the more common histological types with a poor prognostic factor (24.8 vs 13.9, p:0.04). Poorly differentiated grade, which is a poor prognostic factor, was detected more frequently in the tumors of the low HALP group (27.4 vs 13.3, p:0.012).

It is well known that malnutrition is a factor closely related to the incidence of postoperative complications, length of hospital stay, quality of life, and increased mortality of malignant tumors [38,39]. In the study of Güldoğan CE et al, where they investigated the relationship between the prognostic nutritional index (PNI) and postoperative complications in colorectal cancer patients, PNI correlated with all postoperative complications. The median PNI values were significantly lower in patients with major complications (CD grade 3 to 5) ($p<0.001$)[31].

In the study of Ihara et al., the patient's nutritional status and immunocompetence status were examined. In this study, BMI, serum albumin level, Onodera's prognostic nutritional index (OPNI) and Glasgow Prognostic Score [GPS] scores were found to be significantly related to overall survive. In addition, preoperative malnutrition has been found to be associated with post-operative complications, tumor progression and poor clinical outcome [40].

In the literature, the HALP score is a newly accepted index, and there are a limited number of conducted studies, and these studies have not addressed the relationship of the HALP score with postoperative complications. In the literature, only Yalav O et al investigated the relationship of HALP score with postoperative complications. In their study, patients with gastric cancer who underwent curative resection were divided into two groups according to their HALP score as low HALP and HALP high. Postoperative complication rates according to the Clavien Dindo classification (p: 0,298), anastomosis leakage rates (15% vs 11.3%, p: 0.692), and postoperative mortality rates (20% vs 8.1%, p: 0.142) were similar in the groups [41]. Similar to the literature, in our series, no statistical difference was found in terms of postoperative complication rates. The HALP score did not affect the reoperation rates (p: 0.596) and unplanned re-admission to the hospital (p: 0.183). In contrast, our 30-day mortality rate was higher in the low HALP group (7.1% vs 1.2%, p:0.012). The results of our study confirmed the prognostic significance of HALP. Preoperative low HALP score is associated with poor prognosis in CRC patients. However, we did not find any association with the risk of postoperative complications. The HALP score is an easy-to-access and inexpensive biomarker. The use of HALP levels as independent prognostic factors in CRC and determination of optimal cut-off values require further investigation. Prognostic tools are needed to create personalized cancer treatment programs.

The most important limitation of our study was its retrospective evaluation and Single-center study. However, our patient population was as large as those reported in the literature. We believe that our study provides comprehensive data on the relationship between HALP and postoperative complications and prognosis in colorectal concert and contributes to valuable reference data. Multicenter prospective studies are needed to confirm our findings.

Riassunto

Lo scopo di questo studio è stato quello di determinare la relazione tra il punteggio HALP e le complicanze postoperatorie (secondo la classificazione Clavien Dindo 3 e successive), in pazienti con carcinoma del colon-retto sottoposti a resezione chirurgica curativa e per determinare il suo valore clinico in prevedere la prognosi.

Sono stati inclusi nello studio 279 pazienti sottoposti a chirurgia curativa per carcinoma del colon-retto tra il 2015 e il 2018. Il valore HALP è stato calcolato dividendo il prodotto di emoglobina (g/L), albumina (g / L), linfociti (/ L) per il numero di piastrine (/ L). Al fine di generare un valore di cut off per HALP, sono state effettuate l'analisi ROC e la curva ROC. I pazienti sono stati divisi in due gruppi in base alla sopravvivenza e il valore di cut-off è stato trovato mediante analisi ROC. Sono stati creati due gruppi in base al valore cut-off di HALP: gruppo 1 (Low HALP) e gruppo 2 (High HALP). Sono stati confrontati tra i gruppi le caratteristiche demografiche, cliniche, i risultati intraoperatori, postoperatori e la sopravvivenza media.

Risultati - I pazienti sono stati divisi in due gruppi in base al valore di Cut-off di 15,73. Il gruppo 1 era composto da 113 pazienti; Il gruppo 2 era composto da 166 pazienti. L'età media era simile nei gruppi (62 vs 61, p: 0.480). I pazienti del gruppo 1 hanno ricevuto più terapia neoadiuvante (31% vs21%, p: 0,064). I livelli di CEA erano più alti nel Gruppo 1 (7.6vs4.3 p: 0.034). Il tipo istologico di adenocarcinoma mucinoso era più comune nel Gruppo 1 (24% vs13%, p: 0,040). Il grado patologico scarsamente differenziato era più comune nel Gruppo 1 (27% vs13%). I risultati postoperatori erano simili ai gruppi Abbiamo trovato il punteggio HALP come fattore di rischio per la sopravvivenza nell'analisi multivariata (HR = 0,8552 95% (CI: 0,6575-1,1125, p: 0,007). Se il valore HALP è inferiore a 15,73, si presume che la sopravvivenza media è di 28 mesi con una sensibilità del 45,4% e una specificità del 66,938%.

In conclusione i nostri risultati hanno mostrato che il punteggio HALP è strettamente correlato alle caratteristiche clinico-patologiche ed è un fattore prognostico indipendente per la sopravvivenza. Il suo valore nella stima della sopravvivenza media è limitato.

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