Research Article

Prognostic Value of Prognostic Nutritional Index in Colorectal Cancer Patients with Normal Serum CEA Levels

Ahmet Sencer Ergin[1*], Rıza Deryol[2], Ezgi Altinsoy[3] and Salim Demirci[2]

[1]Department of Surgical Oncology, Afyonkarahisar State Hospital, Afyonkarahisar, Turkey

[2]Department of Surgical Oncology, Ankara University of Medicine, Ankara, Turkey

[3]Department of General Surgery, Manisa City Hospital, Manisa, Turkey

Abstract

Background: The Prognostic Nutritional Index (PNI), a valuable parameter for predicting short-term and long-term postoperative outcomes in patients undergoing cancer surgery, is calculated based on serum albumin concentration and peripheral blood lymphocyte count. However, few studies have investigated the clinical significance of PNI in the surgical treatment of colorectal cancer. Therefore, we aimed to examine the relationship between PNI and short-term outcomes in patients with colorectal cancer.

Methods: This retrospective study included 328 patients who underwent surgery for colorectal cancer. The prognostic nutritional status was calculated based on admission data as follows: 10* serum albumin (g/dl)+0.005* total lymphocyte count (per mm3). Then we evaluated the relationship between PNI value and postoperative complications in colorectal cancer patients.

Results: Patients with low PNI (<35.3) had a significantly higher rate of postoperative complications (p<0.05) than those with a high PNI (≥35.3). In Univariate analysis low PNI (p=0.015), open surgical approach (p=0.010), tumor location (p=0.008), N stage ≥ 2 (p=0.037), serum albumin concentration (p=0.015) and CEA level ≥ 5 (p=0.017) were significantly associated with high complications rate. However, in multivariate analyses, low preoperative PNI was not identified as an independent factor for postoperative complications.

Conclusion: Preoperative PNI is a valuable marker for postoperative complications in patients with colorectal cancer.

Keywords: Colorectal cancer • Prognostic nutritional index • Postoperative complications • Chemotherapy

Introduction

Each year, over 1 million new cases of Colorectal Cancer (CRC) are diagnosed globally. CRC is the third most prevalent cancer worldwide and the fourth leading cause of cancer-related death. CRC remains the second leading cause of cancer-related death in the United States and other developed nations, despite prominent advances in diagnosis, surgery and chemotherapy [1].

The postoperative complication rate for colon cancer is approximately 29.7% and for rectal cancer, it is 40% [2]. The most prevalent of these postoperative complications are pneumonia (2.4%-6.2%), acute pulmonary edema (2.9%), acute renal failure (0.6%-2%), ischemic heart disease (0.5%) and acute cerebrovascular event (0.4%). The most significant surgical complications are surgical site infection (3.8%-14%), ileus paralysis (7.5%), and anastomotic leakage (8.5% for the colon and 15% for the rectum). During the subsequent thirty days following surgery, 6.7% of patients will perish [3-7].

In colorectal tumors, the tumor is infiltrated by various immune cells, including neutrophils, natural killer cells, mast cells, dendritic cells and tumor-associated macrophages, as is the case with many other solid malignant tumors [8]. Currently, data demonstrating a correlation between the survival rates and systemic immune response in varying types of malignancy are being published [9-11]. In addition, regardless of tumor markers, the systemic inflammatory response is an essential prognostic factor. Even though tumor markers are typically molecules derived from tumor cells, the systemic inflammatory response is a biochemical reaction chain against tumor cells. Hypercytokinemia induces inflammatory alterations associated with malignancy. Various scales can be used to indirectly determine these alterations and recent research has demonstrated a link between preoperative malnutrition, cancer-related inflammatory response and long-term surgical outcomes.

Currently, both the sensitivity and specificity of tumor markers for cancer diagnosis are extremely low, and their use is minimal. Normal tumor marker levels are common among patients diagnosed with advanced cancer. In addition to conventional tumor markers, it is therefore clinically essential to identify supportive prognostic parameters [12].

Several scores derived primarily from preoperative peripheral blood samples have been developed to identify new prognostic parameters in malignancy patients. One is the Prognostic Nutritional Index (PNI), created in 1984 by Onodera. PNI has been defined as a predictor for estimating the risk of post-gastrointestinal surgery complications and mortality. However, it has recently been shown to be an indicator of systemic inflammation related to cancer [13].

There are few studies and data about the nutritional status and postoperative outcomes of patients who have undergone curative CRC surgery. This study investigated the relationship between early postoperative mortality, complication rates and the prognostic nutritional index in colorectal cancer patients, who underwent curative surgery and had low preoperative serum Carcinoembryonic Antigen (CEA) levels.

Materials and Methods

Between January 2016 and December 2020, the medical records of 328 patients who underwent curative surgery with R0 resection for histologically verified colorectal adenocarcinoma were retrospectively reviewed, at the Ankara University Faculty of Medicine Surgical Oncology Clinic. The patients were found to be between the ages of 21 and 92, 175 of the patients were male and 153 were female. The depth of tumor invasion, lymph node metastasis and pathological tumor stage, were determined as grouping variables. Pathological microscopic surgical margins were used to identify patients who underwent R0 resection. All patients underwent laparoscopic or open colorectal surgery, depending on the abdominal surgical history of the patients. The retrospective design of this study was in compliance with the Declaration of Helsinki, and approval was obtained from the Ethics Committee of the Ankara University Faculty of Medicine.

The patients' clinical, laboratory, therapeutic and pathological information was extracted from their medical records. PNI=0.005* lymphocytes/mL+10* serum albumin [g/dL] is a simple mathematical formula used to assess nutritional and inflammatory status: higher values indicate that the patient's health is improving. This method was chosen as the nutritional assessment method.

The pathological stage of the primary tumor, the presence or absence of distant organ metastasis and lymph node metastases, were evaluated in accord with NCCN Guidelines for Colon Cancer, Version 2.2021 and Rectal Cancer, Version 1.2021.

Statistical analysis

The IBM SPSS V23 was used to analyze the data. Conformity to a normal distribution was evaluated with the Kolmogorov-Smirnov test and the Chi-square test was utilized to compare categorical variables between groups. A two-sample independent t-test was performed to evaluate normally distributed data between paired groups, whereas the Mann-Whitney U test was employed to evaluate non-normally distributed data. A ROC analysis was used to determine the cut-off value for the PNI value according to the presence of complications. Patients were divided into high or low preoperative PNI groups according to the cut-off value.

Binary logistic regression was used to examine the risk factors affecting morbidity. The analysis results for quantitative data were reported as mean standard deviation, median (minimum-maximum), and frequency (percent) for categorical data. The level of significance was set at $p=0.50$.

Results

The clinicopathological characteristics of all patients are shown in Tables 1 and 2. Quantitative data was described in Table 2. The mean PNI values for patients with normal (n=88) and high serum CEA levels (n=240) were 36.2 ± 6.8 and 34.1 ± 6.9, respectively. A significant correlation was found between PNI values and serum CEA levels when the Mann-Whitney U analysis was performed.

We found a statistically considerable relationship between PNI and these parameters, which is described in Tables 3-6 show the results of putting 88 patients with normal serum CEA levels before surgery into groups based on their PNI values. In univariate and multivariate logistic regression analysis, there were significant correlations between the summarized parameters in Table 7.

Table 1. Frequency distribution for categorical variables of all patients.

	Frequency (n)	Percent (%)
Gender		
Male	175	53.4
Female	153	46.6
Laparoscopy		
Yes	196	59.6
No	132	40.4
Tumor Location		
Right	78	23.8
Left	122	37.2
Rectum	128	39
CEA		
>5	88	26.9
≤ 5	240	73.1
PNI		
<35.3	106	32.3
≥ 35.3	222	67.7
Neoadjuvant Treatment		
Yes	125	38.1
No	203	61.9
Tumor Stage (AJCC 8th TNM stage)		
0	25	7.6
1	43	13.1
2	108	32.9
3	137	41.8
4	15	4.6
T stage		
T0 ve T1	40	12.2
T2	40	12.2
T3	181	55.2

T4	67	20.4
N stage		
N0	180	54.9
N1	108	32.9
N2	40	12.2
Complications Grade*		
0	215	65.5
1 ve 2	70	21.3
3 ve 4	43	13.1

Note: CEA: Carcinoembryonic Antigen; PNI: Prognostic Nutritional Index; *: Clavian-Dindo Classification

Table 2. Descriptive statistics for quantitative data.

	Mean	S. Error	Median	Minimum	Maximum
Age	62.2	12.5	63.0	21.0	92.0
CRP(mg/L)	21.5	34.0	7.3	0.2	282.3
Albumin (mg/dL)	37.4	6.2	38.5	15.4	48.1
Hemoglobin (g/dL)	12.1	2.0	12.1	6.5	17.0
Wbc	7.9	3.5	7.0	2.0	31.3
Count of lymphocyte	1.6	0.8	1.6	0.3	5.1
CEA (U/mL)	22.0	123.5	2.7	0.2	1957.0
CA 19-9 (U/mL)	160.8	1232.0	14.1	0.8	18890.0
PNI	37.4	6.2	38.5	15.4	48.1

Note: CRP: C-reactive protein; WBC: White Blood Cell; CEA: Carcinoembryonic Antigen; PNI: Prognostic Nutritional Index

Table 3. Comparison of categorical data according to PNI cut-off values

	Total patients				Propensity score matching			
	PNI cut-off		N	p1	PNI cut-off		N	p1
	<35,3 (n=106)	≥ 35,3 (n=222)			<35,3 (n=106)	≥ 35,3 (n=97)		
Gender								
Male	54 (50.9)	121 (54.5)	175 (53.4)	0.545	54 (50.9)	52 (53.6)	106 (52.2)	0.704
Female	52 (49.1)	101 (45.5)	153 (46.6)		52 (49.1)	45 (46.4)	97 (47.8)	
Laparoscopy								
Yes	51 (51)	141 (63.5)	192 (59.6)	0.034	51 (51)	48 (49.5)	99 (50.3)	0.832
No	49 (49)	81 (36.5)	130 (40.4)		49 (49)	49 (50.5)	98 (49.7)	
Tumor location								
Right	25 (23.6)	53 (23.9)	78 (23.8)	0.633	25 (23.6)	18 (18.6)	43 (21.2)	0.612
Left	36 (34)	86 (38.7)	122 (37.2)		36 (34)	38 (39.2)	74 (36.5)	
Rectum	45 (42.5)	83 (37.4)	128 (39)		45 (42.5)	41 (42.3)	86 (42.4)	
CEA level								
>5	35 (33.3)	53 (24.8)	88 (27.6)	0.108	35 (33.3)	29 (29.9)	64 (31.7)	0.600
≤ 5	70 (66.7)	161 (75.2)	231 (72.4)		70 (66.7)	68 (70.1)	138 (68.3)	
Neoadjuvant treatment								
Yes	40 (37.7)	85 (38.3)	125 (38.1)	0.923	40 (37.7)	34 (35.1)	74 (36.5)	0.691
No	66 (62.3)	137 (61.7)	203 (61.9)		66 (62.3)	63 (64.9)	129 (63.5)	
AJCC 8th TNM stage								
0	3 (2.8)	22 (9.9)	25 (7.6)	0.164	3 (2.8)	5 (5.2)	8 (3.9)	0.719
1	13 (12.3)	30 (13.5)	43 (13.1)		13 (12.3)	17 (17.5)	30 (14.8)	
2	36 (34)	72 (32.4)	108 (32.9)		36 (34)	31 (32)	67 (33)	
3	47 (44.3)	90 (40.5)	137 (41.8)		47 (44.3)	39 (40.2)	86 (42.4)	
4	7 (6.6)	8 (3.6)	15 (4.6)		7 (6.6)	5 (5.2)	12 (5.9)	
AJCC 8th T stage								
T0 ve T1	5 (4.7)	35 (15.8)	40 (12.2)	0.018	5 (4.7)	11 (11.3)	16 (7.9)	0.222
T2	14 (13.2)	26 (11.7)	40 (12.2)		14 (13.2)	15 (15.5)	29 (14.3)	
T3	59 (55.7)	122 (55)	181 (55.2)		59 (55.7)	53 (54.6)	112 (55.2)	
T4	28 (26.4)	39 (17.6)	67 (20.4)		28 (26.4)	18 (18.6)	46 (22.7)	

				AJCC 8th N stage				
N0	54 (50.9)	126 (56.8)	180 (54.9)	0.456	54 (50.9)	54 (55.7)	108 (53.2)	0.683
N1	36 (34)	72 (32.4)	108 (32.9)		36 (34)	32 (33)	68 (33.5)	
N2	16 (15.1)	24 (10.8)	40 (12.2)		16 (15.1)	11 (11.3)	27 (13.3)	
				Complication grade*				
0	49 (46.2)	166 (74.8)	215 (65.5)	<0.001	49 (46.2)	66 (68)	115 (56.7)	0.007
01-Feb	32 (30.2)	38 (17.1)	70 (21.3)		32 (30.2)	19 (19.6)	51 (25.1)	
03-Apr	25 (23.6)	18 (8.1)	43 (13.1)		25 (23.6)	12 (12.4)	37 (18.2)	
				Complications				
No	49 (46.2)	166 (74.8)	215 (65.5)	<0.001	49 (46.2)	66 (68)	115 (56.7)	0.002
Yes	57 (53.8)	56 (25.2)	113 (34.5)		57 (53.8)	31 (32)	88 (43.3)	

Note: 1Ki:square Test; CRP: C-Reactive Protein; CEA: Carcinoembryonic Antigen; PNI: Prognostic Nutritional Index; *: Clavian-Dindo Classification

Table 4. Comparison of categorical data by PNI cut-off value.

	Total patients			Propensity score matching		
	PNI cut-off		p	PNI cut-off		p
	<35,3 (n=106)	≥ 35,3 (n=222,0)		<35,3 (n=106)	≥ 35,3 (n=97,0)	
Age	65.1 ± 13.3 66.0 (21.0-92.0)	60.8 ± 11.9 61.0 (28.0-88.0)	0.004[1]	65.1 ± 13.3 66.0 (21.0 -92.0)	61.0 ± 12.9 61.0 (29.0-88.0)	0.029[1]
CRP(mg/L)	34.2 ± 46.7 16.0 (0.2-282.3)	15.3 ± 23.4 5.7 (0.2-174.3)	<0.001[2]	34.2 ± 46.7 16.0 (0.2-282.3)	17.2 ± 26.3 6.7 (0.2-174.3)	0.002[2]
Albumin(mg/dL)	30.1 ± 4.4 31.1 (15.4-35.2)	40.9 ± 3.1 41.1 (35.3-48.1)	<0.001[2]	30.1 ± 4.4 31.1 (15.4-35.2)	41.4 ± 3.2 42.0 (35.6-48.1)	<0.001[2]
Hemoglobin(g/dL)	11.1 ± 1.9 10.9 (6.5 - 16.3)	12.6 ± 1.9 12.7 (7.6-17.0)	<0.001[2]	11.1 ± 1.9 10.9 (6.5-16.3)	12.6 ± 1.6 12.4 (8.8-15.8)	<0.001[1]
Wbc	8.9 ± 4.4 7.9 (2.0-31.3)	7.5 ± 2.9 6.9 (2.3-21.5)	0.006[2]	8.9 ± 4.4 7.9 (2.0-31.3)	7.3 ± 2.8 6.7 (2.3-21.5)	0.006[2]
Count of Lymphocyte	1.4 ± 0.7 1.3 (0.3-3.8)	1.7 ± 0.8 1.6 (0.3-5.1)	0.003[1]	1.4 ± 0.7 1.3 (0.3-3.8)	1.6 ± 0.7 1.6 (0.3-5.1)	0.020[2]
CEA (U/mL)	33.7 ± 192.9 3.0 (0.4-1957.0)	16.2 ± 67.1 2.5 (0.2-664.5)	0.185[2]	33.7 ± 192.9 3.0 (0.4-1957.0)	28.2 ± 96.9 2.7 (0.2-664.5)	0.776[2]
CA 19-9 (U/mL)	296.2 ± 1887.1 15.8 (0.8-18890.0)	95.1 ± 723.4 13.9 (0.8-10438.0)	0.175[2]	296.2 ± 1887.1 15.8 (0.8-18890.0)	74.3 ± 216.2 14.6 (0.8-1366.8)	0.875[2]
PNI	30.1 ± 4.4 31.1 (15.4-35.2)	40.9 ± 3.1 41.1 (35.3-48.1)	<0.001[2]	30.1 ± 4.4 31.1 (15.4-35.2)	41.4 ± 3.2 42.0 (35.6-48.1)	<0.001[2]

Note: 1:Independent two-sample t-test; 2: Mann-Whitney U test ; CRP: C-Reactive Protein; WBC: White Blood Cell; CEA: Carcinoembryonic Antigen; PNI: Prognostic Nutritional Index

Table 5. Comparison of categorical data according to PNI cut-off value in patients with CEA ≤5.

	Total patients				Propensity score matching			
	PNI cut-off		N	p	PNI cut-off		N	P
	<35,3 (n=70)	≥ 35,3 (n=161)			<35,3 (n=70)	≥ 35,3 (n=68)		
				Gender				
Male	37 (52.9)	89 (55.3)	126 (54.5)	0.734	37 (52.9)	34 (50)	71 (51.4)	0.737
Female	33 (47.1)	72 (44.7)	105 (45.5)		33 (47.1)	34 (50)	67 (48.6)	
				Laparoscopy				
Yes	40 (61.5)	109 (67.7)	149 (65.9)	0.376	40 (61.5)	34 (50)	74 (55.6)	0.181
No	25 (38.5)	52 (32.3)	77 (34.1)		25 (38.5)	34 (50)	59 (44.4)	
				Tumor locations				
Right	14 (20)	40 (24.8)	54 (23.4)	0.552	14 (20)	12 (17.6)	26 (18.8)	0.705
Left	24 (34.3)	59 (36.6)	83 (35.9)		24 (34.3)	28 (41.2)	52 (37.7)	
Rectum	32 (45.7)	62 (38.5)	94 (40.7)		32 (45.7)	28 (41.2)	60 (43.5)	

				p				p
Neoadjuvant therapy								
Yes	25 (35.7)	47 (29.2)	72 (31.2)	0.325	25 (35.7)	16 (23.5)	41 (29.7)	0.117
No	45 (64.3)	114 (70.8)	159 (68.8)		45 (64.3)	52 (76.5)	97 (70.3)	
AJCC 8th TNM Stage								
0	3 (4.3)	20 (12.4)	23 (10)	0.098	3 (4.3)	5 (7.4)	8 (5.8)	0.440
1	11 (15.7)	28 (17.4)	39 (16.9)		11 (15.7)	17 (25)	28 (20.3)	
2	24 (34.3)	58 (36)	82 (35.5)		24 (34.3)	24 (35.3)	48 (34.8)	
3	28 (40)	53 (32.9)	81 (35.1)		28 (40)	20 (29.4)	48 (34.8)	
4	4 (5.7)	2 (1.2)	6 (2.6)		4 (5.7)	2 (2.9)	6 (4.3)	
AJCC 8th T stage								
T0/ T1	5 (7.1)	32 (19.9)	37 (16)	0.017	5 (7.1)	11 (16.2)	16 (11.6)	0.044
T2	12 (17.1)	24 (14.9)	36 (15.6)		12 (17.1)	15 (22.1)	27 (19.6)	
T3	39 (55.7)	91 (56.5)	130 (56.3)		39 (55.7)	38 (55.9)	77 (55.8)	
T4	14 (20)	14 (8.7)	28 (12.1)		14 (20)	4 (5.9)	18 (13)	
AJCC 8th N Stage								
N0	39 (55.7)	106 (65.8)	145 (62.8)	0.012	39 (55.7)	46 (67.6)	85 (61.6)	0.012
N1	20 (28.6)	48 (29.8)	68 (29.4)		20 (28.6)	21 (30.9)	41 (29.7)	
N2	11 (15.7)	7 (4.3)	18 (7.8)		11 (15.7)	1 (1.5)	12 (8.7)	
Complications grade*								
0	37 (52.9)	131 (81.4)	168 (72.7)	<0.001	37 (52.9)	55 (80.9)	92 (66.7)	0.002
01-Feb	19 (27.1)	24 (14.9)	43 (18.6)		19 (27.1)	9 (13.2)	28 (20.3)	
03-Apr	14 (20)	6 (3.7)	20 (8.7)		14 (20)	4 (5.9)	18 (13)	
Complications								
No	37 (52.9)	131 (81.4)	168 (72.7)	<0.001	37 (52.9)	55 (80.9)	92 (66.7)	<0.001
Yes	33 (47.1)	30 (18.6)	63 (27.3)		33 (47.1)	13 (19.1)	46 (33.3)	
Mortality								
Survival	64 (91.4)	159 (98.8)	223 (96.5)	0.005	64 (91.4)	67 (98.5)	131 (94.9)	0.057
Exitus	6 (8.6)	2 (1.2)	8 (3.5)		6 (8.6)	1 (1.5)	7 (5.1)	

Note: PNI: Prognostic Nutritional Index; *:Clavian-Dindo Classification

Table 6. Comparison of quantitative data according to PNI cut-off value in patients with CEA ≤ 5.

	Total patients			Propensity score matching		
	PNI cut-off		p	PNI cut-off		P
	<35,3 (n=70)	≥ 35,3 (n=161)		<35,3 (n=70)	≥ 35,3 (n=68)	
Age	66.0 ± 12.1	61.1 ± 11.8	0.005[1]	66.0 ± 12.1	60.4 ± 13.0	0.0101
	67.0 (41.0 - 92.0)	62.0 (29.0 - 88.0)		67.0 (41.0 - 92.0)	61.0 (29.0 - 88.0)	
CRP(mg/L)	27.6 ± 36.7	11.2 ± 19.4	<0.001[2]	27.6 ± 36.7	13.5 ± 25.1	0.0022
	14.7 (0.5 - 184.8)	4.7 (0.2 - 174.3)		14.7 (0.5 - 184.8)	4.8 (0.2 - 174.3)	
Albumin (mg/dL)	30.6 ± 4.2	41.2 ± 3.1	<0.001[2]	30.6 ± 4.2	41.9 ± 3.1	<0.0012
	32.0 (17.2 - 35.2)	41.6 (35.3 - 48.0)		32.0 (17.2 - 35.2)	43.0 (35.6 - 48.0)	
Hemoglobin (g/dL)	11.1 ± 1.9	12.8 ± 1.9	<0.001[2]	11.1 ± 1.9	12.7 ± 1.6	<0.0011
	10.9 (6.5 - 16.2)	13.0 (8.0 - 17.0)		10.9 (6.5 - 16.2)	12.6 (8.8 - 15.8)	
WBC	8.4 ± 3.5	7.3 ± 2.8	0.054[2]	8.4 ± 3.5	7.3 ± 3.1	0.0652
	7.3 (2.0 - 18.6)	6.8 (2.4 - 21.5)		7.3 (2.0 - 18.6)	6.7 (2.4 - 21.5)	
Count of lymphocytes	1.4 ± 0.8	1.7 ± 0.8	0.003[2]	1.4 ± 0.8	1.7 ± 0.8	0.0292
	1.2 (0.3 - 3.8)	1.7 (0.3 - 5.1)		1.2 (0.3 - 3.8)	1.6 (0.3 - 5.1)	
CEA(U/mL)	2.2 ± 1.2	2.2 ± 1.2	0.961[2]	2.2 ± 1.2	2.2 ± 1.2	0.9491
	1.9 (0.4 - 4.9)	2.0 (0.2 - 4.7)		1.9 (0.4 - 4.9)	2.1 (0.2 - 4.7)	
CA 19-9(U/mL)	45.7 ± 223.3	14.9 ± 13.5	0.428[2]	45.7 ± 223.3	13.7 ± 8.0	0.5802
	12.0 (0.8 - 1879.2)	11.9 (0.8 - 133.2)		12.0 (0.8 - 1879.2)	11.9 (0.8 - 40.8)	
PNI	30.6 ± 4.2	41.3 ± 3.1	<0.001[2]	30.6 ± 4.2	41.9 ± 3.1	<0.001
	32.0 (17.2 - 35.2)	41.6 (35.3 - 48.0)		32.0 (17.2 - 35.2)	43.0 (35.6 - 48.0)	

Note: 1:Independent two-sample t-test; 2:Mann-Whitney U test; CRP: C-Reactive Protein; WBC: White Blood Cell; CEA: Carcinoembryonic Antigen; PNI: Prognostic Nutritional Index

Table 7. Investigation of risk factors affecting complication rates after propensity score matching.

	Univariate		Multivariate	
	OR (%95 CI)	p	OR (%95 CI)	p
Gender	0.798 (0.295-2.159)	0.657		
Open Surgery	5.333 (1.482-19.199)	0.010	0.15 (0.038-0.593)	0.007
Tumor locations				
Right	5.426 (1.564-18.823)	0.008	6.42 (1.647-25.03)	0.007
Left	1.171 (0.283-4.857)	0.827	1.388 (0.309-6.242)	0.669
Not Receiving Neoadjuvant therapy	2.094 (0.771-5.687)	0.147	3.972 (1.205-13.096)	0.023
AJCC 8th N stage				
0-1	1.645 (0.508-5.326)	0.406	-	-
02-Mar	3.864 (1.082-13.801)	0.037	-	-
Age	1.011 (0.973-1.051)	0.570	1.044 (0.996 - 1.094)	0.073
CRP (mg/L)	1.005 (0.995-1.015)	0.327	-	-
Albumin (mg/dL)	0.914 (0.851-0.982)	0.015	-	-
Hemoglobin (g/dL)	0.888 (0.681-1.157)	0.378	-	-
WBC	1.053 (0.942-1.176)	0.364	-	-
Count of lymphocytes	1.05 (0.542-2.032)	0.886	-	-
CEA (U/mL)	1 (0.997-1.003)	0.980	-	-
CA 19-9 (U/mL)	1 (1-1)	0.846	-	-
PNI	0.914 (0.851-0.982)	0.015	-	-
CEA level (>5)	0.289 (0.104-0.797)	0.017	-	-

Discussion

This study examined the connections between PNI levels and clinicopathological characteristics in 328 colorectal malignancy patients who underwent curative surgery. Low preoperative PNI values were related to age, white and red cell levels, tumor stage, depth of invasion, lymph node involvement, an advanced pathological stage, low serum albumin levels and higher C-Reactive Protein (CRP) levels. However, no considerable correlation was found between preoperative serum CEA levels and PNI.

PNI was originally created to predict peri-operative problems, including anastomosis leaking, prolonged wound healing and postoperative long-term hospitalization [13]. Recent research indicates that preoperative PNI may be a positive prognostic factor and a more accurate method for assessing the condition of malignancy patients [14].

In this study, the mean PNI values for patients with normal (n=88) and high serum CEA levels (n=240) were 36.2 ± 6.8 and 34.1 ± 6.9, respectively. A significant correlation was found between PNI values and serum CEA levels. The optimal PNI lower critical value was determined as 35, 3 based on postoperative complication rates.

Patients with colorectal cancer are frequently malnourished. In addition to poor oral nutritional intake and protein loss from the disease, cancer cells secrete cytokines, such as tumor necrosis factor-alpha, which negatively impact catabolic metabolism [15].

The use of PNI values as a marker in cancer patients has not become widespread because the cut-off values for PNI in predicting postoperative survival remain controversial [15, 16]. In this study, optimal PNI cut-off value was established at 35.3. This value is lower than the average value of 45 reported by other studies for PNI [13] and the reason for this may be the advanced tumor stages of the patients included in the study.

The findings obtained in this study support the hypothesis that a low PNI indicates chronic inflammation and malnutrition in aggressive or advanced cancer patients. In an analysis of 328 patients using univariate logistic regression to determine the effect of preoperative PNI values on complications, a low PNI value was found to be associated with higher postoperative complication rates. In the multivariate analysis, however, a low PNI value could not be confirmed as an independent variable associated

with a higher postoperative complication rate. As patients with a low preoperative PNI have an elevated risk of postoperative complications, the preoperative PNI value may be indicative of both the short- and long-term postoperative outcomes. According to studies, the prognosis is typically worse for cancer patients who experience postoperative complications [17-19]. In the present study, we show that PNI was the most valuable predictor of the incidence of postoperative complications.

Albumin is one of the parameters in the PNI formula. Produced by hepatocytes, albumin is a commonly used nutritional biomarker. Serum albumin levels are controlled by proinflammatory cytokines such as interleukin-1 (IL-1), IL-6, and Tumor Necrosis Factor (TNF-α). These proinflammatory cytokines are produced by tumor cells and contribute to carcinogenesis, the progression of cancer and neoangiogenesis [20].

CEA is a glycoprotein expressed on the surface of enterocytes and fetal intestinal cells that plays a role in cell adhesion and programmed cell death [21]. The literature recommends using CEA levels to monitor postoperative patients for disease recurrence. However, even in advanced cases, elevated serum CEA levels may not always be detected in colorectal cancer patients. At the time of initial disease detection, however, it is not recommended to use CEA levels in patients with normal CEA levels for further follow-up [22]. Therefore, in our study, we looked at how well PNI could predict the risk of complications after surgery in colorectal cancer patients whose serum CEA levels were normal before surgery.

In order to translate our findings into clinical practice, perioperative nutritional intervention will be necessary. Preoperative enteral nutrition for malnourished surgical patients with digestive cancers improves postoperative outcomes by elevating albumin levels and lymphocyte counts significantly [15].

Our study has a few limitations that should be acknowledged. First, the study was conducted at a single center with a small sample size and was planned retrospectively. In addition, preoperative PNI values were accounted for in the study, but dynamic changes in PNI values over the course of disease progression were not evaluated. Larger prospective studies are required in order to investigate the molecular mechanisms linking low PNI with poor prognosis and high complication risk in patients with colorectal cancer. Despite these limitations, our study demonstrated that low preoperative PNI is a potential independent risk factor for poor

prognosis in patients with colorectal cancer with normal serum CEA levels. These findings could help clinicians make clinical decisions in colorectal malignancy patients with low PNI.

Conclusion

This research demonstrated that a low preoperative PNI score is a reliable biomarker of cancer-related inflammation. In addition, patients with normal serum CEA levels and low PNI values were associated with a high incidence of early postoperative complications. This study supports the hypothesis that the postoperative complication rates of malignancy patients are affected not only by tumor characteristics, but also by inflammation and malnutrition associated with the disease.

In this study, we demonstrated a correlation between preoperative PNI values and higher postoperative complications in colorectal cancer patients undergoing curative surgery. The PNI value can be used as a prognostic marker in colorectal cancer because it is a simple and inexpensive parameter. The study shows that an easy-to-find parameter like PNI can help clinicians make effective changes to treatment plans.

References