

# Impact of preoperative Prognostic Nutritional Index levels on morbidity in colorectal cancer surgery



Ann Ital Chir, 2022 93, 4: 422-426

pii: S0003469X22036235

Online ahead of print 2022 - Jan. 10

free reading: www.annitalchir.com

Aziz Serkan Senger\*, Mürşit Dincer\*\*, Orhan Uzun\*, Selcuk Gulmez\*, Deniz Avan\*\*\*, Cem B. Ofluoglu\*, Erdal Polat\*, Mustafa Duman\*

\*Department of Gastrointestinal Surgery, University of Health Sciences Turkey, Kartal Kosuyolu Higher Specialty Training and Research Hospital, Istanbul, Turkey

\*\*Department of Gastrointestinal Surgery, Firat University Faculty of Medicine, Elazığ

\*\*\*Department of Anesthesia and Reanimation Clinic, University of Health Sciences Turkey, Kartal Kosuyolu Higher Specialty Training and Research Hospital, Istanbul, Turkey

## Impact of preoperative Prognostic Nutritional Index levels on morbidity in colorectal cancer surgery

**AIM:** The Prognostic Nutritional Index (PNI) is a valuable parameter that indicates the immunonutritional status of patients with malignant tumors.

**MATERIAL AND METHODS:** Patients operated for colorectal cancer between January 2013 and December 2019 were analyzed retrospectively. The relationship between PNI and morbidity was investigated in the 314 patients included in the study. Based on previous studies, the PNI cutoff value was set at 45, and the patients were duly divided into two groups: PNI <45 and PNI ≥45. The demographic and clinicopathological characteristics, as well as postoperative complications in the two groups, were compared.

**RESULTS:** There was no statistical difference in gender, localization, T stage, N stage, perineural invasion, lymphovascular invasion, stage, Ca19-9 values, and body mass index(BMI) between the two groups. In contrast, there was a statistically significant difference in age, complications, and CEA values. ( $p=0.008$ ,  $p<0.001$ ,  $p=0.043$ , respectively). The median age was lower in patients with high PNI scores than in the low PNI group (61 vs. 64 years). When the patients were examined for complications, 36 (37.1%) patients were observed in the high PNI group, compared to 155 (71.4%) in the low PNI group. In terms of overall survival, the mean life expectancy was  $68.112\pm 2.646$  months for patients with low PNI group, compared to  $84.626\pm 2.701$  months in the high-PNI group, and the difference was statistically significant ( $p=0.001$ ).

**CONCLUSION:** This study's findings suggest that the preoperative Prognostic Nutritional Index may indicate postoperative complications and prognosis. The most significant benefit of this marker is that it can be improved preoperatively and practically.

**KEY WORDS:** Colorectal Neoplasms, Morbidity, Nutritional Status

## Introduction

Colorectal cancer (CRC) is a common and lethal disease and is the second most common cause of cancer-related death in the United States<sup>1</sup>. More than half of

all cases and deaths can be linked to modifiable risk factors such as smoking, unhealthy diet, high alcohol consumption, physical inactivity, and excess body weight, meaning that it can be described as a potentially preventable disease<sup>2</sup>. Mortality rates decrease with early diagnosis and treatment through radiological imaging methods. Currently, TNM staging is considered the primary prognostic indicator of colorectal cancer. However, this approach has certain limitations, as patients with the same stage may have different clinical outcomes<sup>3</sup>. As such, a new and more accurate prognostic indicator is needed for prognosis in patients with CRC.

Pervenuto in Redazione Giugno 2021. Accettato per la pubblicazione Luglio 2021

Correspondence to: Aziz Serkan Senger, Kartal Kosuyolu Higher Specialty Training and Research Hospital, Department of Gastrointestinal Surgery, Denizler cad. No:2. Kartal-Istanbul-Turkey (e-mail: serkansenger@yahoo.com)

Surgery is still an important factor in the treatment of colorectal cancer. Despite advances in surgery, adjuvant chemoradiotherapy, and targeted therapy, CRC patients' prognosis is still unsatisfactory<sup>4</sup>. Post-surgical morbidities can prolong hospital stays and can lead to work-force loss, reduced cost-effectiveness, and most importantly, mortality.

Malnutrition is one of the leading factors facilitating postoperative complications. The incidence of malnutrition among cancer patients is 40–80% and varies by the type, location, and tumor stage<sup>5</sup>. Malnutrition has been reported to be associated with an increased risk of infection, decreased compliance with anti-cancer treatment, reduced quality of life, and increased morbidity and mortality rates<sup>6,7</sup>.

The prognostic nutritional index (PNI) is a valuable parameter that shows the immuno-nutritional status of patients with malignant tumors and is calculated using the following formula: [serum albumin in g/dL × 10] + [0.005 × total lymphocyte count in cells/μL]. In some malignant diseases, low PNI levels have been reported to indicate postoperative complications and poor prognosis<sup>8,9</sup>. Lymphocytes play an essential role in host immune response and the elimination of tumors' formation and progression. Albumin is also a parameter that shows the nutritional status of the body. And hypoalbuminemia in cancer patients is seen as secondary to the presence of a systemic inflammatory response.

In hypoalbuminemia, liver function is impaired, and a continuous systemic inflammatory response develops either from the tumor itself or as a host reaction<sup>10</sup>. It is thought that this formula may affect prognosis in patients.

While the calculation system was more complex when it was first devised in 1980, it was later simplified and made more useful. Onodera et al.<sup>11</sup> have reported a low PNI score significantly associated with major postoperative complications and poor prognosis following gastrointestinal surgery. The present study investigates the relationship between PNI and morbidity in patients operated for colorectal cancer.

## Material and Method

A retrospective analysis was made of 314 patients operated for colorectal cancer at XXX Hospital between January 2013 and December 2019. Patients who underwent curative surgery were included in the study and those undergoing emergency surgery or palliative resection, and those without accessible records. The patients' demographic characteristics, ASA scores, body mass index (BMI), PNI values, leukocyte counts, CRP values, postoperative length of hospital stay, complications and location, size, and TNM tumor stage were recorded. The serum albumin (g/dl) and total lymphocyte counts (per mm<sup>3</sup>) measured from preoperatively collected serum sam-

ples were recorded. PNI was calculated using the formula: [serum albumin in g/dL × 10] + [0.005 × total lymphocyte count in cells/μL]. Based on previous studies, the cutoff value for PNI was set at 45, and the patients were duly divided into two groups: PNI <45 and PNI ≥45<sup>12</sup>. The effect of PNI levels on complications was investigated. The Clinical Research Ethics Committee approved our institution's study (Ethical Committee No. 2019 .7142-258).

IBM SPSS Statistics for Windows (Version 22.0. Armonk, NY: IBM Corp.) was used for the statistical analyses. The normality of the data was analyzed with a Kolmogorov-Smirnov test. Qualitative data were presented as frequency and percentages, and quantitative data as median (IQR) values. The association between the prognostic nutritional index and the categorical variables was analyzed with Chi-square and Fisher's exact tests. A Mann-Whitney U-test was used to establish any relationship between age and BMI. Univariate and multivariate analyses were performed using a Cox regression analysis to assess the prognostic factors for survival, including gender, age, CEA, CA 19-9, tumor localization, T stage, N stage, PNI status, and BMI.

## Results

A total of 314 patients who underwent curative surgery for colorectal cancer were compared for demographic and clinicopathological characteristics, as well as postoperative complications, according to the PNI value. There was no statistical difference in gender, localization, T stage, N stage, perineural invasion, lymphovascular invasion, stage, Ca19-9 values, or BMI between the two groups. In contrast, there was a statistically significant difference in age, complications, and CEA values ( $p=0.008$ ,  $p <0.001$ ,  $p=0.043$ , respectively). The median age was lower in patients with a high PNI than in the low PNI group (61 vs. 64 years). In addition, 29 (29.9%) of the high PNI patients had a high CEA val-

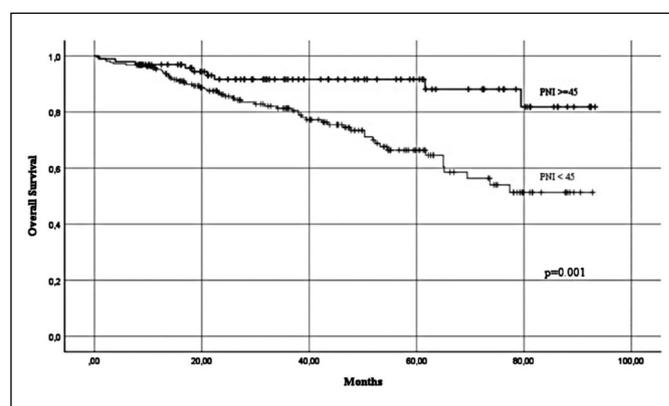


Fig. 1: Overall survival analysis with Kaplan-Meier test according to PNI status.

ue, while a high CEA value was identified in 91 (41.9%) of the other group. Complications were observed in 37.1% of the high PNI group, compared to 71.4% in the low PNI group.

An analysis involving a Kaplan-Meier test revealed a statistically significant difference in overall survival between the two groups ( $p=0.001$ ) (Fig. 1). The mean life expectancy was  $68.112 \pm 2.646$  months for patients with low PNI compared to  $84.626 \pm 2.701$  months in the high PNI group (Table II).

The prognostic factors for overall survival were evaluated by univariate and multivariate Cox regression analyses. The univariate and multivariate analyses revealed age, gender, CEA, CA 19-9, localization, N stage, and BMI to have no prognostic significance in survival. In contrast, the univariate analysis showed T stage and PNI to have prognostic value ( $p=0.049$ ,  $p=0.002$ , respectively), and the multivariate analysis identified only PNI as prognostically significant ( $p=0.002$ ).

## Discussion

Colorectal cancer is one of the leading causes of cancer-related death, although the morbidity and mortality asso-

ciated with colorectal cancer can be reduced through appropriate screening and follow-up planning<sup>1</sup>. The preoperative nutritional status of patients is also an influential factor for morbidity and mortality<sup>13</sup>. Establishing the nutritional status of patients preoperatively and administering nutritional support accordingly is one of the most effective approaches to reducing morbidity and mortality. The PNI was initially devised by Buzby et al.<sup>14</sup> to determine the operative risk of patients. After several modifications, it has become an objective and easily calculable parameter used to assess the patients' nutritional status based on albumin and lymphocyte values. In previous studies, a low PNI has been reported to be a predictor of both postoperative complications and poor prognosis in various types of malignancies<sup>8</sup>. Several studies in the literature have reported a low PNI associated significantly with major complications and poor prognosis following gastrointestinal surgery<sup>15,16</sup>. Gldođan et al.<sup>17</sup> retrospectively analyzed 180 patients who underwent curative surgery for colorectal cancer. They suggested that PNI can predict severe complications. In our study, 314 patients who underwent curative surgery were analyzed. The findings of the present study demonstrate that malnutrition negatively affects postoperative outcomes. The results were consistent with the literature.

TABLE I - Relationship of PNI status with demographic characteristics, clinicopathological factors and postoperative complications in patients undergoing surgery for CRC.

		PNI				p
		< 45		> = 45		
		n	%	n	%	
Gender	Male	128	59,0%	57	58,8%	0.970
	Female	89	41,0%	40	41,2%	
Localization	Colon	138	64,8%	63	65,6%	0.887
	Rectum	75	35,2%	33	34,4%	
pT stage	pT1	17	7,8%	7	7,2%	0.147
	pT2	22	10,1%	16	16,5%	
	pT3	140	64,5%	65	67,0%	
	pT4	38	17,5%	9	9,3%	
pN stage	pN0	120	55,3%	57	58,8%	0.540
	pN1	62	28,6%	29	29,9%	
	pN2	35	16,1%	11	11,3%	
TNM stage	Stage I	32	14,7%	18	18,6%	0.323
	Stage II	83	38,2%	39	40,2%	
	Stage III	71	32,7%	33	34,0%	
	Stage IV	31	14,3%	7	7,2%	
Lymphovascular invasion	Normal	142	65,4%	68	70,1%	0.417
	High	75	34,6%	29	29,9%	
Perineural invasion	Normal	157	72,4%	73	75,3%	0.591
	High	60	27,6%	24	24,7%	
Complications	No	62	28,6%	61	62,9%	<0.001
	Yes	155	71,4%	36	37,1%	
CEA, ng/mL	Normal	126	58,1%	68	70,1%	0.043
	High	91	41,9%	29	29,9%	
CA 19-9, U/mL	Normal	187	86,2%	90	92,8%	0.093
	High	30	13,8%	7	7,2%	
Age, years		Median	IQR	Median	IQR	0.008
BMI, kg/m <sup>2</sup>		27.5	23.7-32.4	27.5	23.7-31.6	0.949

TABLE II - Comparison of overall survival of patients according to PNI status

PNI	Mean( Month)	Overall Survival		
		±SE	95% CI	p
<45	68.112	2.646	62.927-73.298	0.001
≥45	84.626	2.701	79.332-89.920	
Overall	73.334	2.101	69.215-77.452	

TABLE III - Univariate and multivariate analyses for overall survival in patients with CRC undergoing primary tumor resection.

	Univariate Analysis			Multivariate Analysis		
	OR	95.0% CI	p	OR	95.0% CI	p
Gender	1.348	0.826-2.200	0.233	1.409	0.831-2.390	0.204
Age	1.009	0.988-1.030	0.394	1.005	0.984-1.027	0.636
CEA	1.024	0.614-1.708	0.928	0.815	0.463-1.434	0.477
CA19-9	1.349	0.642-2.836	0.430	1.267	0.562-2.857	0.568
Localization	1.549	0.948-2.532	0.081	1.505	0.894-2.533	0.124
T Stage			0.049			0.193
T1						
T2	2.423	0.523-11.218	0.258	2.563	0.534-12.299	0.240
T3	1.913	0.461-7.949	0.372	1.991	0.464-8.543	0.354
T4	4.018	0.927-17.407	0.063	3.661	0.769-17.427	0.103
N Stage			0.149			0.598
N0						
N1	1.494	0.855-2.610	0.936	1.300	0.712-2.374	0.393
N2	1.795	3.445	0.078	1.388	0.660-2.919	0.387
PNI	0.322	0.159-0.652	0.002	0.319	0.154-0.659	0.002
BMI	1.021	0.972-1.073	0.405	1.004	0.951-1.060	0.890

Patients can be assessed preoperatively based on their PNI value, being an easily calculable parameter, and interventions can be made to improve nutritional status in those with low values. It may further become a significant parameter in improving outcomes in patients scheduled for colorectal surgery.

Despite the positive aspects of PNI, its reliability decreases in some instances. In a study, antiviral therapy was reported to be associated with high PNI. In addition, nutritional supplementation with branched-chain amino acid granules has been shown to improve hypoalbuminemia, preserve the hepatic functional reserve, and prevent perioperative complications<sup>18</sup>. Therefore, the use of PNI to aid in the prognosis of patients undergoing antiviral therapy or nutritional supplementation with branched-chain amino acid granules may encounter some limitations. The present study included no patients receiving antiviral therapy or nutritional supplements with branched-chain amino acid granules.

This study's limitations include its retrospective design, the low number of cases, and the uncertainty of follow-up duration and adjuvant therapy processes.

In conclusion, the present study has shown preoperative

PNI to predict postoperative morbidity among patients undergoing colorectal cancer surgery effectively. PNI should be calculated in cases scheduled for surgery for colorectal cancer, and patients should be evaluated in terms of enteral or parenteral nutritional support in cases with low PNI. Randomized and controlled studies are needed to confirm the findings of this study and aid in planning nutritional support in such patient groups.

### References

1. Siegel RL, Miller KD, Jemal A: *Cancer statistics, 2020*. CA Cancer J Clin, 2020; 70(1):7-30.
2. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al.: *Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States*. CA Cancer J Clin, 2018; 68(1):31-54.
3. Liu Q, Luo D, Cai S, Li Q, Li X: *P-TNM staging system for colon cancer: Combination of P-stage and AJCC TNM staging system for improving prognostic prediction and clinical management*. Cancer Manag Res, 2018; 10:2303-14.

4. Yang Y, Gao P, Chen X, Song Y, Shi J, Zhao J, et al.: *Prognostic significance of preoperative prognostic nutritional index in colorectal cancer: Results from a retrospective cohort study and a meta-analysis*. *Oncotarget*, 2016; 7(36):58543–52.
5. Tsujinaka T, Sasako M, Yamamoto S, Sano T, Kurokawa Y, Nashimoto A, et al.: *Influence of overweight on surgical complications for gastric cancer: Results from a randomized control trial comparing D2 and extended para-aortic D3 lymphadenectomy (JCOG9501)*. *Ann Surg Oncol*, 2007; 14(2):355–61.
6. Feng F, Zheng G, Guo X, Liu Z, Xu G, Wang F, et al.: *Impact of body mass index on surgical outcomes of gastric cancer*. *BMC Cancer*, 2018; 18(1):1–8.
7. Kamachi K, Ozawa S, Hayashi T, Kazuno A, Ito E, Makuuchi H: *Impact of body mass index on postoperative complications and long-term survival in patients with esophageal squamous cell cancer*. *Dis Esophagus*, 2016; 29(3):229–35.
8. Okada S, Shimada J, Kato D, Tsunozuka H, Teramukai S, Inoue M: *Clinical significance of prognostic nutritional index after surgical treatment in lung cancer*. *Ann Thorac Surg* [Internet]. 2017; 104(1):296–302. Available from: <http://dx.doi.org/10.1016/j.athoracsur.2017.01.085>
9. Li C, Oh SJ, Kim S, Hyung WJ, Yan M, Zhu ZG, et al.: *Risk factors of survival and surgical treatment for advanced gastric cancer with large tumor size*. *J Gastrointest Surg*, 2009; 13(5):881–85.
10. Al-Shaiba R, McMillan DC, Angerson WJ, Leen E, McArdle CS, Horgan P: *The relationship between hypoalbuminaemia, tumour volume and the systemic inflammatory response in patients with colorectal liver metastases*. *Br J Cancer*, 2004; 91(2):205–07.
11. Onodera T, Goseki N, Kosaki G: *Nihon Geka Gakkai zasshi*. 1984; 85(9), 1001–05.
12. Wang J, Yu B, Ye Y, Shen J, Ding N, Tang H, et al.: *Predictive value of nutritional risk screening 2002 and prognostic nutritional index for esophageal cancer patients undergoing definitive radiochemotherapy*. *Nutr Cancer* [Internet]. 2018; 70(6):879–85. Available from: <https://doi.org/10.1080/01635581.2018.1470656>
13. Miao Y, Li S, Yan Q, Li B, Feng Y: *Prognostic significance of preoperative prognostic nutritional index in epithelial ovarian cancer patients treated with platinum-based chemotherapy*. *Oncol Res Treat*, 2016; 39(11):712–19.
14. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF: *Prognostic nutritional index in gastrointestinal surgery*. *Am J Surg*, 1980; 139(1):160–67.
15. Jiang N, Deng JY, Ding XW, Zhang L, Liu HG, Liang YX, et al.: *Effect of complication grade on survival following curative gastrectomy for carcinoma*. *World J Gastroenterol*, 2014; 20(25):8244–52.
16. Zhao LY, Zhang WH, Chen XZ, Yang K, Chen XL, Liu K, et al.: *Prognostic significance of tumor size in 2405 patients with gastric cancer a retrospective cohort study*. *Med (United States)*. 2015; 94(50):1–10.
17. Emir Güldogan C, Çetinkaya E, Akgül Ö, Tez M: *Does the preoperative prognostic nutritional index predict postoperative complications in patients with colorectal cancer who underwent curative resection?* *Ann Ital Chir*, 2017; 88:43–7.
18. Takaguchi K, Moriwaki H, Doyama H, Iida M, Yagura M, Shimada N, et al.: *Effects of branched-chain amino acid granules on serum albumin level and prognosis are dependent on treatment adherence in patients with liver cirrhosis*. *Hepatol Res*, 2013; 43(5):459–66.