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WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc*.

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ORIGINAL ARTICLE

Retrospective Study

Prognostic value of combined systemic inflammation response index and prognostic nutritional index in colorectal cancer patients

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Abstract

BACKGROUND

The prognosis of colorectal cancer (CRC) patients is notably influenced by both inflammation and nutritional status. The prognostic nutritional index (PNI) and systemic inflammatory response index (SIRI) have been reported in prognostic studies of various tumors. However, the efficacy of the combination of the two in predicting the prognosis of CRC patients has not been studied.

AIM

To evaluate the effectiveness of PNI and SIRI in predicting the prognosis of patients with CRC.

METHODS

We retrospectively gathered data from 470 CRC patients who underwent feasible radical surgery at Xinjiang Cancer Hospital. The optimal cut-off values for SIRI and PNI, along with their predictive power for survival, were determined through area under the receiver operating characteristic curve using time-dependent receiver operating characteristic analysis. The Kaplan-Meier method and log-rank test were applied to assess prognostic impact, and a multifactorial Cox proportional hazards model was employed for analysis. Additionally, a new model, PSIRI, was developed and assessed for its survival prediction capability.

RESULTS

The optimal cutoff values for PNI and SIRI were determined to be 47.80 and 1.38, respectively. Based on these values, patients were categorized into high PNI and low PNI groups, as well as high SIRI and low SIRI groups. Significant differences in age, T stage, neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte

ratio (MLR), and platelet-to-lymphocyte ratio (PLR) subgroups were observed between the PNI groups in the baseline profile. In the SIRI group, notable differences were found in gender, T stage, nerve invasion, intravascular tumor emboli, NLR, MLR, and PLR subgroups. Both low PNI and high SIRI were identified as independent risk factors for poor prognosis in CRC patients. When combined into the PSIRI model, it was shown that patients with a PSIRI ≤ 1 had a higher risk of death compared to those with a PSIRI of 2.

CONCLUSION

We assessed the impact of PNI and SIRI on the prognostic survival of CRC patients and developed a new model, PSIRI. This model demonstrated superior predictive accuracy, with a concordance index of 0.767.

Key Words: Colorectal cancer; Prognostic nutritional index; Systemic inflammatory response index; Prognosis

Core Tip: In this study, we analyzed the impact of the systemic inflammation response index and prognostic nutritional index on colorectal cancer (CRC) patients. For the first time, we combined these two indices to create a new prognostic index and evaluated its effectiveness. Our results demonstrate that the new index offers superior prognostic accuracy. This new index serves as a more reliable predictor of survival in CRC patients, thereby enhancing prognosis and facilitating the development of more personalized and targeted treatment strategies.

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INTRODUCTION

Colorectal cancer (CRC) ranks as the third most frequently diagnosed malignancy and has the second highest mortality rate among cancer-related deaths worldwide[1]. By 2040, the global incidence of CRC is projected to reach 3.2 million new cases annually[2]. The prognosis of patients with CRC has not substantially improved over the past decades, despite improvements in surgical techniques, adjuvant radiotherapy, targeted therapies, and other technologies. The integration of validated biomarkers into treatment strategies is clinically vital for identifying patients who are most likely to benefit from aggressive therapies such as radiotherapy, chemotherapy, and extended surgery[3]. A number of prognostic and predictive markers, including microsatellite instability, various gene mutations, and TNM staging, have been developed and have been used to provide insight into the management of patients with CRC[4-6]. However, these markers are obtained for invasive experiments and require specific laboratory equipment. Therefore, there is a pressing demand for non-invasive, easily accessible, and cost-effective prognostic indicators in the clinic to forecast the outcome of CRC patients and to evaluate therapeutic results.

Research has shown that outcome of CRC patients is not only related to the characteristics of the tumor, but also influenced by the inflammatory response and nutritional status[7]. Inflammatory responses play a role throughout tumor formation and progression. Inflammation resulting from non-hereditary cancers could facilitate local tumor progression and distant metastasis, generally manifested by elevated concentrations of inflammatory cells and pro-inflammatory agents[8-10]. Simultaneously, tumor-produced inflammation-promoting cytokines disrupt systemic carbohydrate, fat and protein metabolism, exacerbating catabolism and leading to muscle breakdown[11,12]. Systemic inflammation response index (SIRI), calculated from circulating neutrophil count multiplied by the monocyte count and then divided by the lymphocyte count, has recently been introduced and used as a novel nonspecific indicator of inflammation and immunity [13]. Up to now, the prognostic value of SIRI has been reported in merely a limited number of studies. Malnutrition is a prevalent characteristic of CRC, and malnutrition in patients with cancer leads to generalized debilitation, weakens the body's defensive immunity, and affects the prolongation of the recovery period[14]. There is also a negative impact on well-being and therapy-associated toxicity, and it is projected between 10% and 20% of cancer patients succumb to complications of malnutrition instead of the tumor itself[15]. The prognostic nutritional index (PNI), defined as albumin (g/L) + 5 × absolute lymphocyte count (10^9/L)[16], is extensively utilized to evaluate the nutritional condition and postoperative complications in patients with digestive malignancies of the gastrointestinal tract.

Most research has concentrated on examining the individual impact of SIRI or PNI on various diseases. However, a single index may not precisely predict the outcome in cancer patients. At present, the prognostic significance of combining SIRI with PNI for CRC patients remains unexplored. Therefore, in this study, we analyzed the relationship between preoperative SIRI combined with PNI and the pathological characteristics of CRC to assess the prognostic value of this combination in CRC patients.

MATERIALS AND METHODS

Study populations

This study retrospectively selected 470 CRC individuals who underwent radical surgery in Xinjiang Medical University Cancer Hospital from 2016 to 2018. Inclusion criteria: (1) Individuals aged over 18 years; (2) Postoperative pathology confirmed primary CRC; (3) Blood laboratory indicators were available within one week before surgery; and (4) Comprehensive clinical and follow-up data of patients. Exclusion criteria: (1) Non-primary CRC; (2) Distant metastasis of the lesion that cannot be resected; (3) Suffering from hematologic diseases or autoimmune diseases; (4) Patients receiving enteral nutrition therapy before surgery; and (5) The patient has severe hepatic or renal dysfunction or diseases that cause malnutrition. Outcome data was retrieved from medical records or family contacts throughout the follow-up period, which was concluded at the time of the patient's death, loss to follow-up, or in March 2023. The primary endpoint was overall survival (OS). The study obtained informed consents from all patients and was approved by the Ethics Committee of the Affiliated Cancer Hospital of Xinjiang Medical University (K-2024056).

Data collection

Baseline information includes basic information (height, age, weight, sex, drinking and smoking history), hematological parameters [platelets, lymphocytes, neutrophils, monocytes, serum albumin, hemoglobin, and carcinoembryonic antigen (CEA)] in the 1 week before surgery, postoperative pathology (degree of differentiation of the tumor, vascular embolus, neuro invasion, histological type, and TNM stage) and follow-up information (survival outcome and survival time). Nutritional and immunization indicators: Neutrophil to lymphocyte ratio (NLR) = neutrophil/lymphocyte; SIRI = neutrophil × monocyte/lymphocyte; platelet-to-lymphocyte ratio (PLR) = platelet/lymphocyte; PNI = albumin + 5 × mphocyte; monocyte to lymphocyte ratio (MLR) = monocyte/lymphocyte.

Statistical analysis

SPSS 26.0 was applied to analyze the data statistically. For baseline clinical data, normally distributed data were expressed as mean ± SD for continuous variables, median (interquartile spacing, IQR) for unconditional variables, and counts (percentage, %) for categorical variables, using the χ^2 test or Fisher's exact test for qualitative data, *t*-test or analysis of variance (ANOVA) for quantitative data, and Wilcoxon test for hierarchical data, the general clinical data and pathological characteristics of each group were comparatively analyzed. The predictive ability of SIRI and PNI for survival was assessed using time-dependent receiver operating characteristic (ROC) curves and area under the curve (AUC). The thresholds for PNI and SIRI were determined using standardized log-rank statistics with the best cut-off values set at 47.80 and 1.38, respectively. The nonlinear association between PNI, SIRI, and CRC mortality risk was captured by restrictive cubic spline (RCS). Based on the cut-off values PNI ≥ 47.80 was scored as 1, PNI < 47.80 was scored as 0, SIRI ≥ 1.38 was scored as 0, and SIRI < 1.38 was scored as 1. Survival was plotted by Kaplan-Meier (KM) and compared by Log-Rank test. Variables calculated to have an effect on OS were incorporated in a multivariate Cox proportional risk model. Subsequently, a new evaluation index PSIRI was established and assessed in a survival prognostic model.

RESULTS

Patients' characteristics

The present study retrospectively analyzed 470 patients with CRC, of whom the median age was 61 years old, 279 (59.4%) were male, and 20.0%, 40.4%, and 39.6% were classified as TNM stages I, II, and III, respectively. The degree of differentiation was mainly in 385 cases (81.9%) with moderate differentiation, 73 cases (15.5%) with high differentiation, and 12 cases (2.6%) with low differentiation. Other baseline information such as smoking, drink and body mass index (BMI) can be seen in Table 1.

Associations of PNI and SIRI with clinicopathological parameters

Based on the time-dependent ROC curve, we assessed the accuracy of PNI and SIRI in predicting patients' prognosis, yielding AUCs of 0.746 and 0.689, respectively, as shown in Figure 1. Patients were categorized into 2 groups including high PNI and low PNI according to the cutoff value, the differences between which were statistically significant with respect to age, T stage, NLR, MLR, or PLR ($P < 0.05$). Meanwhile, patients were classified as high SIRI and low SIRI categories as well, the differences between which were statistically significant in terms of gender, nerve invasion, intravascular tumor emboli, T stage, NLR, MLR, and PLR ($P < 0.05$).

Prognostic value of PNI and SIRI in CRC

We employed RCS in order to assess the association between PNI, SIRI, and hazard ratio (HR), and results showed that HR gradually increased with decreasing PNI and increasing SIRI, suggesting that PNI is a protective factor against CRC mortality while SIRI is a risk factor (Supplementary Figure 1). KM curves were employed in order to show the low PNI group of CRC patients was correlated with shorter OS ($P < 0.001$), and by including PNI and other clinicopathological parameters in a multifactorial cox regression analysis, the results revealed that low PNI was an independent risk factor for poor prognosis [HR: 2.96, 95% confidence interval (95%CI): 1.79-4.92]. In subgroup analyses, we found that an increased risk of death was independently associated with low PNI compared with the high PNI group. We then

Table 1 Relationship between preoperative prognostic nutritional index and systemic inflammation response index levels and clinicopathologic characteristics of colorectal cancer patients, *n* (%)

Characteristics	Overall patients, *n* = 470	High PNI (≥ 47.8), *n* = 315	Low PNI (< 47.8), *n* = 155	*P* value	High SIRI (≥ 1.38), *n* =112	Low SIRI (< 1.38), *n* = 358	*P* value
Age				0.031			0.794
≥ 60	261 (55.5)	164 (52.1)	97 (62.6)		61 (54.5)	200 (55.9)	
< 60	209 (44.5)	151 (47.9)	58 (37.4)		51 (45.5)	158 (44.1)	
Gender				0.317			0.011
Male	279 (59.4)	192 (61.0)	87 (56.1)		78 (69.6)	201 (56.1)	
Female	191 (40.6)	123 (39.0)	68 (43.9)		34 (30.4)	157 (43.9)	
BMI				0.278			0.688
< 18.5	14 (3.0)	9 (2.9)	5 (3.2)		5 (4.5)	9 (2.5)	
18.5-24.0	203 (43.2)	129 (41.0)	74 (47.7)		48 (42.9)	155 (43.3)	
24.0-28.0	189 (40.2)	135 (42.9)	54 (34.8)		44 (39.3)	145 (40.5)	
≥ 28.0	64 (13.6)	42 (13.3)	22 (14.2)		15 (13.4)	49 (13.7)	
Smoking				0.465			0.323
Yes	150 (31.9)	104 (33.0)	46 (29.7)		40 (35.7)	110 (30.7)	
No	320 (68.1)	211 (67.0)	109 (70.3)		72 (64.3)	248 (69.3)	
Drink				0.180			0.827
Yes	89 (18.9)	65 (20.6)	24 (15.5)		22 (19.6)	67 (18.7)	
No	381 (81.1)	250 (79.4)	131 (84.5)		90 (80.4)	291 (81.3)	
T stage				< 0.001			0.002
T1	33 (7.0)	29 (9.2)	4 (2.6)		2 (1.8)	31 (8.7)	
T2	71 (15.1)	55 (17.5)	16 (10.3)		12 (10.7)	59 (16.5)	
T3	335 (71.3)	218 (69.2)	117 (75.5)		87 (77.7)	248 (69.3)	
T4	31 (6.6)	13 (4.1)	18 (11.6)		11 (9.8)	20 (5.6)	
N stage				0.267			0.411
N0	282 (60.0)	193 (61.3)	89 (57.4)		64 (57.1)	218 (60.9)	
N1	112 (23.8)	77 (24.4)	35 (22.6)		27 (24.1)	85 (23.7)	
N2	76 (16.2)	45 (14.3)	31 (20.0)		21 (18.8)	55 (15.4)	
Tumor stage				0.109			0.063
I	94 (20.0)	74 (23.5)	20 (12.9)		12 (10.7)	82 (22.9)	
II	190 (40.4)	119 (37.8)	71 (45.3)		52 (46.4)	138 (38.5)	
III	186 (39.6)	122 (38.7)	64 (41.3)		48 (42.9)	138 (38.5)	
Differentiated degree				0.495			0.071
Poorly	73 (15.5)	47 (14.9)	26 (16.8)		25 (22.3)	48 (13.4)	
Moderately	385 (81.9)	256 (82.2)	126 (81.3)		83 (74.1)	302 (84.4)	
Well	12 (2.6)	9 (2.9)	3 (1.9)		4 (3.6)	8 (2.2)	
Nerve invasion				0.141			< 0.001
Positive	84 (17.9)	50 (15.9)	34 (21.9)		87 (77.7)	59 (16.5)	
Negative	386 (82.1)	265 (84.1)	121 (78.1)		25 (22.3)	299 (83.5)	
Intravascular tumor emboli				0.497			< 0.001

Positive	87 (18.5)	61 (19.4)	26 (16.8)		88 (78.6)	63 (17.6)	
Negative	383 (81.5)	254 (80.6)	129 (83.2)		24 (21.4)	295 (82.4)	
CEA				0.462			0.103
High	171 (36.4)	111 (35.2)	60 (38.7)		48 (42.9)	123 (34.4)	
Normal	299 (63.6)	204 (64.8)	95 (61.3)		64 (57.1)	235 (65.6)	
NLR, median (IQR)	2 (1.50-2.69)	1.88 (1.43-2.52)	2.33 (1.69-3.04)	< 0.001	3.12 (2.61-3.83)	1.78 (1.40-2.20)	< 0.001
MLR, median (IQR)	0.24 (0.19-0.33)	0.23 (0.18-0.29)	0.30 (0.23-0.40)	< 0.001	0.40 (0.33-0.48)	0.22 (0.18-0.27)	< 0.001
PLR, median (IQR)	131.23 (101.07-173.58)	117.24 (95.14-151.97)	163.11 (122.92-223.84)	< 0.001	162 (120.46-211.60)	122.61 (96.34-161.73)	< 0.001

PNI: Prognostic nutritional index; SIRI: Systemic inflammation response index; BMI: Body mass index; CEA: Carcinoembryonic antigen; NLR: Neutrophil to lymphocyte ratio; MLR: Monocyte to lymphocyte ratio; IQR: Interquartile range.

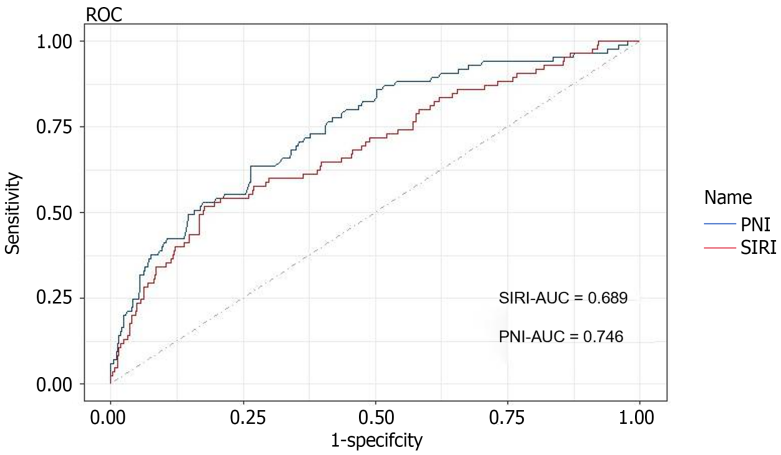

Figure 1 Area under the receiver operating characteristic curve of prognostic nutritional index and systemic inflammation response index. PNI: Prognostic nutritional index; SIRI: Systemic inflammation response index; ROC: Receiver operating characteristic; AUC: Area under receiver operating characteristic curve.

conducted an evaluation of SIRI in relation to OS of CRC patients and the results demonstrated that SIRI ≥ 1.38 served as an independent predictor of poor prognosis (HR: 2.27, 95%CI: 1.26-4.11). Subgroup analyses likewise demonstrated a correlation between SIRI and mortality in CRC, as shown in Table 2, Figure 2, and Supplementary Figure 2.

Prognostic and predictive value of PSIRI in CRC

We incorporated PNI and SIRI to construct a novel model called PSIRI, as presented in Table 3, and based on the time-ROC curve, we evaluated the PSIRI's effect on CRC patients' prognostic accuracy, which was higher compared to PNI and SIRI (AUC: 0.767) (Figure 3). We then defined PSIRI as 0 for patients with PNI < 47.82 and SIRI ≥ 1.38, 2 for patients with PNI ≥ 47.82 and SIRI < 1.38, and 1 for all other patients. Patients with PSIRI 0 and 1 had an increased mortality compared with patients with PSIRI 2, with HRs of 3.56 and 9.53, and the HR (95%CI) for all-cause mortality in PSIRI ≤ 1 subgroups was 3.77 (2.03-6.98). KM curves showed that compared with subgroups PSIRI ≤ 1, subgroup PSIRI 2 exhibited a longer OS (P < 0.001) with the median OS reaching up to 60 months. Stratified analyses were used to explore possible influences on the association of PSIRI with CRC. No significant interaction was found after stratification by gender, age, BMI, smoke, drink, CEA, differentiated degree, tumor stage, nerve invasion, and intravascular tumor emboli, as shown in Figure 4, Figure 5, and Table 4.

DISCUSSION

Inflammation refers to the body's response to tissue injury caused by trauma, infection, toxin exposure, or other forms of damage. The inflammatory response triggers cellular changes and immune reactions, leading to tissue repair and cell proliferation at the site of injury[17]. However, when the cause of inflammation persists or regulatory mechanisms that terminate the inflammatory process fail, the inflammation can become chronic. Chronic inflammation often leads to cellular mutations and abnormal growth, creating a conducive environment for cancer development[18,19]. Chronic

Table 2 Univariate and multivariate analysis on the overall survival of prognostic nutritional index and systemic inflammation response index

Variables	Model 1		Model 2		Model 3		Model 4	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value
PNI								
≥ 47.82	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
< 47.82	3.93 (2.53-6.10)	< 0.001	3.33 (2.08-5.33)	< 0.001	3.33 (2.08-5.33)	< 0.001	2.96 (1.79-4.92)	< 0.001
SIRI								
< 1.38	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
≥ 1.38	4.00 (2.61-6.12)	< 0.001	3.78 (2.42-5.92)	< 0.001	3.78 (2.42-5.92)	< 0.001	2.27 (1.26-4.11)	0.007

Model 1: Crude; Model 2: Adjusted with age and gender; Model 3: Adjusted with Model 2 + body mass index, smoke, and drink; Model 4: Adjusted with Model 3 + T stage, N stage, differentiated degree, nerve invasion, intravascular tumor emboli, carcinoembryonic antigen, neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, and platelet-to-lymphocyte ratio. HR: Hazard ratio; 95%CI: 95% confidence interval; PNI: Prognostic nutritional index; SIRI: Systemic inflammation response index.

Table 3 Development of PSIRI

PSIRI	PNI	SIRI	Number
0	< 47.82	≥ 1.38	46
1	PNI ≥ 47.82 or SIRI < 1.38		175
2	≥ 47.82	< 1.38	249

PNI: Prognostic nutritional index; SIRI: Systemic inflammation response index.

Table 4 Cox regression analysis of PSIRI and overall survival

Variables	Model 1		Model 2		Model 3		Model 4	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value	HR (95%CI)	*P* value
PSIRI								
2	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
1	4.00 (2.24-7.13)	< 0.001	3.92 (2.13-7.21)	< 0.001	3.92 (2.13-7.21)	< 0.001	3.56 (1.89-6.71)	0.018
0	13.61 (7.35-25.19)	< 0.001	13.26 (6.76-26.00)	< 0.001	13.26 (6.76-26.00)	< 0.001	9.53 (4.08-22.26)	< .001
PSIRI								
2	1.00 (reference)		1.00 (reference)		1.00 (reference)		1.00 (reference)	
≤ 1	5.60 (3.25-9.64)	< 0.001	5.30 (2.97-9.45)	< 0.001	5.30 (2.97-9.45)	< 0.001	3.77 (2.03-6.98)	< 0.001

Model 1: Crude; Model 2: Adjusted with age and gender; Model 3: Adjusted with Model 2 + body mass index, smoke, and drink; Model 4: Adjusted with Model 3 + T stage, N stage, differentiated degree, nerve invasion, intravascular tumor emboli, carcinoembryonic antigen, neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, and platelet-to-lymphocyte ratio. HR: Hazard ratio; 95%CI: 95% confidence interval.

inflammation is characterized by ongoing tissue damage, cell proliferation triggered by injury, and tissue repair. In these cases, cell proliferation is commonly associated with metaplasia, which refers to the reversible change in cell type. "Dysplasia" is a disorderly proliferation of cells that results in atypical cells and is considered a precursor to cancer, as it often occurs near tumor sites[17]. Chronic inflammation is linked to various stages of tumorigenesis, including cellular transformation, promotion, survival, proliferation, invasion, angiogenesis, and metastasis[20].

Common systemic inflammatory response markers include circulating white blood cells and acute phase proteins. Studies have shown that white blood cell counts and levels of acute phase proteins, such as C-reactive protein, hold prognostic significance across various types of cancer[21-24]. The SIRI, which is calculated using neutrophils, lymphocytes, and monocytes, was initially applied to predict outcomes in patients with pancreatic cancer[12]. In this study, we identified SIRI as a potential predictor for CRC prognosis. Existing evidence suggests that neutrophils contribute to

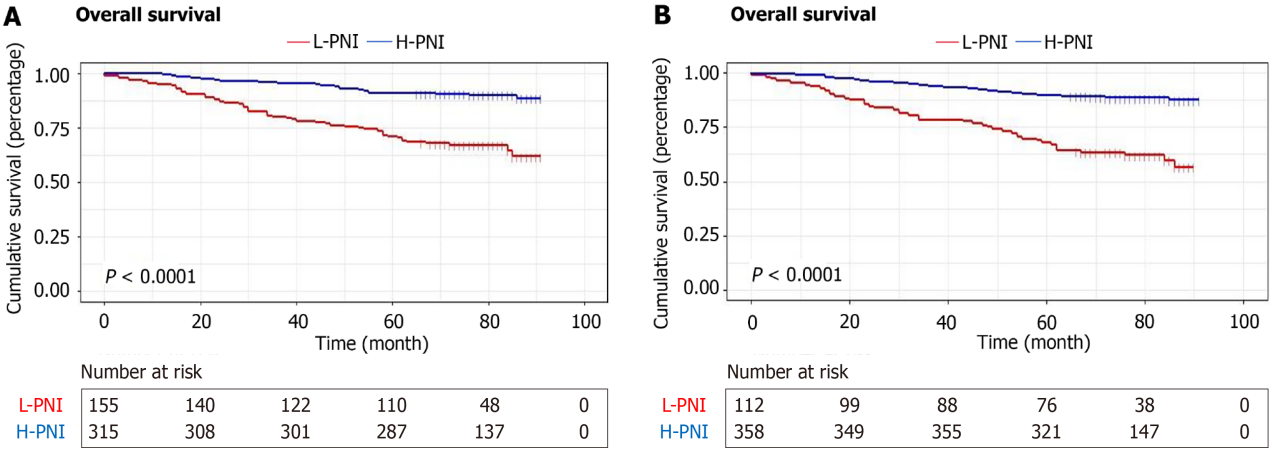

Figure 2 Cox regression analysis of prognostic nutritional index and systemic inflammation response index associated with overall survival. A: Prognostic nutritional index; B: Systemic inflammation response index. L-PNI: Low-prognostic nutritional index; H-PNI: High-prognostic nutritional index; SIRI: Systemic inflammation response index.

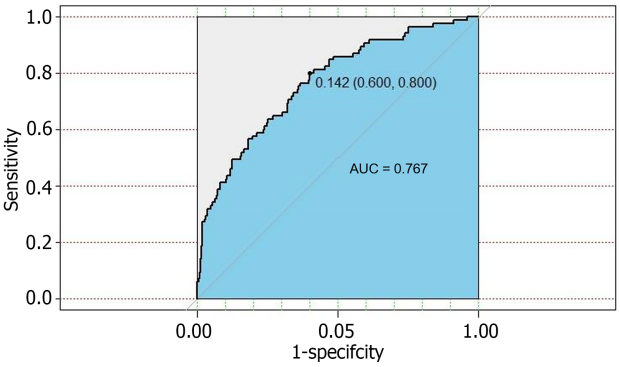

Figure 3 Area under the receiver operating characteristic curve of PSIRI and optimal cutoff values. AUC: Area under receiver operating characteristic curve.

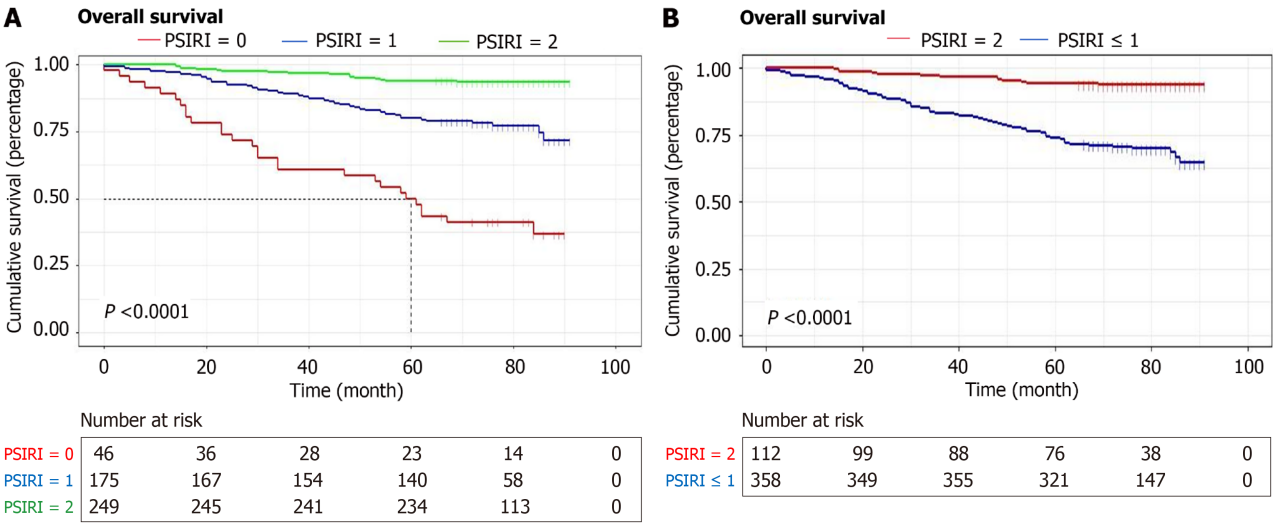

Figure 4 Kaplan–Meier curves for overall survival of PSIRI. A: Categorized by PSIRI = 0, 1, 2; B: Categorized by PSIRI = 1, 2.

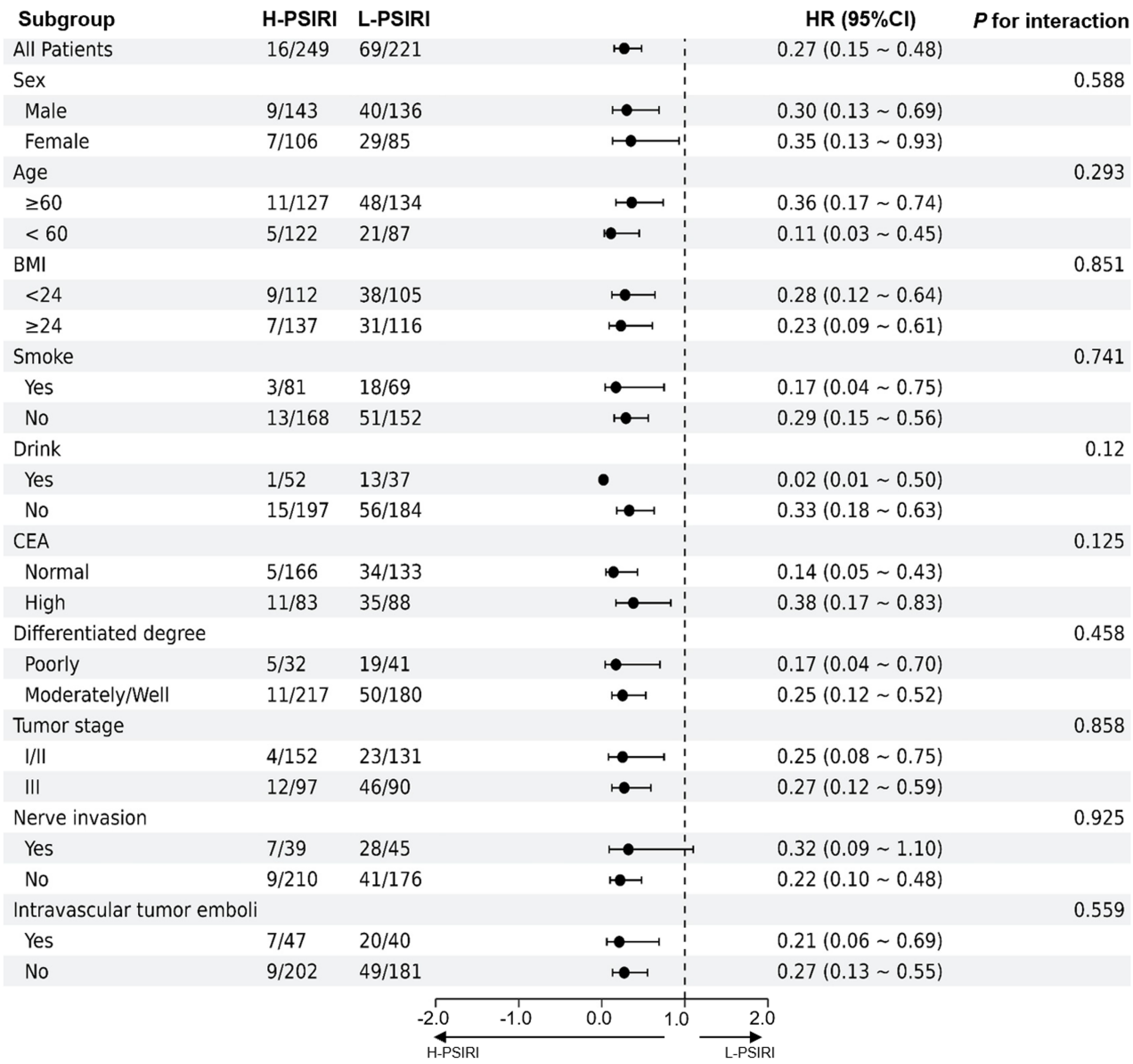

Figure 5 Stratification analysis of PSIRI in colorectal cancer. Adjusted for age, gender, BMI, smoke, drink, T stage, N stage, tumor stage, differentiated degree, nerve invasion, intravascular tumor emboli, carcinoembryonic antigen, neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, and platelet-to-lymphocyte ratio. SIRI: Systemic inflammation response index; BMI: Body mass index; CEA: Carcinoembryonic antigen; 95%CI: 95% confidence interval; HR: Hazard ratio.

oxidative DNA damage in the lungs by releasing reactive oxygen species[25,26]. In inflamed colonic tissue, neutrophils induce DNA double-strand breaks in epithelial cells by releasing pro-inflammatory microRNA particles, leading to impaired tissue healing in this inflammatory environment[27,28]. Neutrophils also support tumor cell proliferation through paracrine signaling pathways[29]. Peripheral lymphocytes play a crucial role in the host's cytotoxic immune response to tumors and are indicative of patient health[30-32]. Previous studies have demonstrated that lower pre-operative lymphocyte counts are important predictors of poor outcomes in patients with pancreatic ductal adenocarcinoma[33,34]. During the inflammatory response, neutrophils suppress the immune system by inhibiting lymphocytes and the cytolytic activity of T-cells and natural killer cells. A lower lymphocyte count is associated with weaker immune function[35,36]. Research found that lymphopenia is an independent prognostic factor for both overall and progression-free survival in various cancers[37,38]. Monocytes are recruited throughout the entire tumor progression process, from early tumor growth to the establishment of distant metastases[39-43]. They contribute to tumorigenesis and angiogenesis and can suppress the body's anti-tumor immune response. Moreover, monocytes can differentiate into tumor-associated macrophages (TAMs) within the tumor microenvironment[44]. TAMs promote tumor angiogenesis and growth by secreting tumor necrosis factor-alpha and vascular endothelial growth factor[45]. They also facilitate tumor invasion and migration by degrading the extracellular matrix through the secretion of proteases and protease activators[46]. By including three inflammatory markers, SIRI offers a more comprehensive reflection of the link between inflammation and prognosis. In our study, elevated SIRI was identified as an independent risk factor for poor prognosis in CRC patients (HR: 2.27, 95%CI: 1.26-4.11).

In cancer patients, a combination of factors, such as reduced nutrient absorption, changes in appetite, taste, and dietary intake, metabolism altered by hormones, and immune activation due to cancer-related cytokine release, can lead to disease progression and muscle wasting[47]. A prospective observational study reported that 51.1% of cancer patients experienced malnutrition, and 64.0% had weight loss six months after diagnosis[48,49]. Malnutrition has been linked to prolonged hospital stays, higher readmission rates, delayed wound healing, immune system deterioration, and cancer-related mortality[50]. The association between malnutrition and disease progression is well established, beyond a simple cause-and-effect relationship. A multicenter study investigating malnutrition prevalence in patients undergoing cancer treatment found that age, hospital stay duration, and metastasis were all related to malnutrition. Additionally, malnutrition was associated with increased infection rates and longer hospitalizations[51,52].

PNI is a nutritional assessment index based on albumin and lymphocytes. Serum albumin is a crucial indicator of the nutritional status of cancer patients and is closely linked to cancer prognosis. Albumin plays several anti-cancer roles, including regulating cell growth and DNA replication, maintaining hormone balance, and providing antioxidant defense against carcinogens such as aflatoxins[53]. Additionally, albumin is important in anti-tumor therapies. It enhances tumor specificity, reduces drug-induced cytotoxicity, and helps sustain the concentration of therapeutic agents, such as drugs, peptides, proteins, and genes, over a longer duration[54-56]. A recent prospective study found an inverse linear relationship between pre-diagnostic serum albumin levels and cancer risk, particularly in lung, colorectal, and liver cancer patients[57,58]. Moreover, albumin acts as a carrier for delivering anti-cancer drugs and food components. A decrease in albumin levels directly affects treatment outcomes and prognosis in cancer patients. The role of recombinant albumin and albumin-based nanocarriers in drug delivery and cancer treatment is currently under extensive investigation[59,60].

Our study identified low PNI as an independent risk factor for poor prognosis in CRC patients (HR: 2.96, 95%CI: 1.79-4.92). In this study, we collected baseline blood parameters and clinical information from 470 CRC patients, adhering to inclusion and exclusion criteria. Initially, we analyzed the relationship between PNI, SIRI, and clinical outcomes. Survival analysis revealed significantly poorer prognoses for patients in the low PNI group and high SIRI group. We then combined PNI and SIRI to create the PSIRI scoring system, which proved to be an accurate and practical tool for assessing clinical prognosis in CRC patients. PSIRI is defined as follows: Patients with PNI < 47.82 and SIRI ≥ 1.38 are scored 0; patients with PNI ≥ 47.82 and SIRI < 1.38 are scored 2; all other patients are scored 1. This scoring system encompasses all patients. For those with scores below 1, timely nutritional interventions and anti-inflammatory treatments can be provided. This lays the foundation for early identification of high-risk patients and personalized treatment strategies.

However, our study has several limitations. First, it is a single-center retrospective study with a relatively small sample size. Second, the patients were exclusively from our institution, and external validation was not performed. Third, we excluded frail patients, limiting the generalizability of our findings to broader populations. Therefore, future research should be conducted as large-scale, multicenter prospective studies with external validation to strengthen the reliability and scientific robustness of the findings. Despite these limitations, our study confirms that PSIRI can serve as an independent prognostic factor for CRC patients, aiding in the development of personalized treatment and follow-up strategies.

CONCLUSION

In conclusion, our retrospective analysis revealed that preoperative PNI and SIRI were independent risk factors for the prognosis of CRC patients. In addition, we constructed and validated the new index PSIRI. which was then found to have a high-test efficacy by analysis. Therefore, PSIRI may be a practical biomarker for prognosis prediction in CRC patients.

FOOTNOTES

Author contributions: Li KJ wrote the original draft; Li KJ and Zhang ZY contributed to the data analysis; Zhao ZL led the quality assessments; Subinur S, Shu Y, Wang K, Saibihutula A, and Zeng XY collected the data; and all authors have agreed on the manuscript to be submitted.

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