ASTR

ORIGINAL ARTICLE
pISSN 2288-6575 • eISSN 2288-6796
https://doi.org/10.4174/astr.2024.106.3.169
Annals of Surgical Treatment and Research

Effect of preoperative pan-immune-inflammation value on clinical and oncologic outcomes after colorectal cancer surgery: a retrospective study

Yun Ju Seo[1,*], Kyeong Eui Kim[2,*], Woon Kyung Jeong[2], Seong Kyu Baek[2], Sung Uk Bae[2]

[1]Department of Medicine, Keimyung University School of Medicine, Daegu, Korea
[2]Department of Surgery, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Korea

Purpose: Surgical resection, the primary treatment for colorectal cancer (CRC), is often linked with postoperative complications that adversely affect the overall survival rates (OS). The pan-immune-inflammation value (PIV), a novel biomarker, is promising in evaluating cancer prognoses. We aimed to explore the impact of preoperative immune inflammation status on postoperative and long-term oncological outcomes in patients with CRC.
Methods: A retrospective analysis of 203 patients with CRC who underwent surgery (January 2016–June 2020) was conducted. The preoperative PIV was calculated as [(neutrophil count + platelet count + monocyte count) / lymphocyte counts]. The PIV optimal cutoff value was determined based on the OS using the Contal and O'Quigley methods.
Results: A PIV value ≥155.90 was defined as high. Patients were categorized into low-PIV (n = 85) and high-PIV (n = 118) groups. Perioperative clinical outcomes (total operation time, time to gas out, sips of water, soft diet, and hospital stay) were not significantly different between the groups. The high-PIV group exhibited more postoperative complications (P = 0.024), and larger tumor size compared with the low-PIV group. Multivariate analysis identified that American Society of Anesthesiologists grade III (P = 0.046) and high-PIV (P = 0.049) were significantly associated with postoperative complications. The low-PIV group demonstrated higher OS (P = 0.001) and disease-free survival rates (DFS) (P = 0.021) compared with the high-PIV group. Advanced N stage (P = 0.005) and high-PIV levels (P = 0.047) were the identified independent prognostic factors for OS, whereas advanced N stage (P = 0.045) was an independent prognostic factor for DFS.
Conclusion: Elevated preoperative PIV was associated with an increased incidence of postoperative complications and served as an independent prognostic factor for OS.
[Ann Surg Treat Res 2024;106(3):169-177]

Key Words: Colorectal neoplasms, Inflammation, Immune system, Postoperative complication, Survival

INTRODUCTION

Inflammation is a complex biological response triggered by infection or tissue injury, involving immune cell activation, release of inflammatory mediators, and immune cell recruitment to the affected site [1,2]. Chronic inflammation is a prolonged pathological condition characterized by mononuclear immune cell infiltration, sustained tissue damage, damage-induced cellular proliferation, and tissue repair [3,4]. Some solid cancers originate from sites of chronic inflammation, and solid

Received September 18, 2023, **Revised** December 12, 2023, **Accepted** December 12, 2023

Corresponding Author: Sung Uk Bae
Department of Surgery, Keimyung University Dongsan Medical Center, Keimyung University School of Medicine, 1035 Dalgubeol-daero, Dalseo-gu, Daegu 42601, Korea
Tel/Fax: +82-53-250-7322
E-mail: sabiston0000@hanmail.net
ORCID: https://orcid.org/0000-0002-7876-4196

*Yun Ju Seo and Kyeong Eui Kim contributed equally to this study as co-first authors.

tumors can also induce an inflammatory microenvironment [5]. The association between chronic inflammation and cancer development and progression is well-established, encompassing cellular transformation, promotion, survival, proliferation, invasion, angiogenesis, and metastasis [4,6]. Notably, elevated circulating levels of CRP, indicative of inflammatory status, have been linked to poor prognoses in various cancers, including endometrial, liver, cervical, colorectal, breast, and non-small cell lung cancer [7-9].

Recent studies have identified several blood-based immune-inflammatory biomarkers that hold predictive value for the prognosis of colorectal cancer (CRC) [10-12]. For instance, a high neutrophil-to-lymphocyte ratio, high platelet-to-lymphocyte ratio, and low lymphocyte-to-monocyte ratio have been associated with unfavorable oncological outcomes in patients with CRC [13,14]. However, these biomarkers only assess 2 immune-inflammatory cell types, prompting the need for a novel biomarker encompassing all inflammatory cellular components from the peripheral blood.

Bioelectrical impedance analysis (BIA) is a well-known noninvasive anthropometric measurement including body composition, fat index, muscle index, obesity index, and phase angle [15]. And skeletal muscle index (SMI) was calculated to diagnose sarcopenia [16]. Recently, some studies showed the relationship between body composition and a patient's immune-inflammatory status [17-19].

The pan-immune-inflammation value (PIV) is a recently developed biomarker that considers neutrophil, platelet, monocyte, and lymphocyte counts [20]. Emerging studies have reported associations between PIV and oncological outcomes in various solid tumors, such as breast cancer, lung cancer, and melanoma [21,22]. However, the relationship between preoperative PIV and surgical outcomes in CRC, including postoperative complications and oncological results, remains unclear. As a result, our study aimed to investigate the impact of preoperative PIV on postoperative and oncological following CRC surgery.

METHODS

Ethical considerations

The study protocol received approval from the Institutional Review Board of Keimyung University Dongsan Medical Center (No. DSMC 2022-12-040). Data acquisition and analysis were carried out with ethical considerations, ensuring the patients' right to privacy. Informed consent requirements were waived due to the retrospective nature of the study.

Patients and data collection

This retrospective study comprised 210 patients who underwent curative resection for stage I–IV CRC between January 2016 and June 2020. Exclusion criteria encompassed synchronous or prior malignancies, malignancies other than adenocarcinoma, familial adenomatous polyposis, hereditary non-polyposis CRC, and incomplete blood cell count information (Fig. 1).

Data collection and definitions

Various variables were collected from prospectively maintained databases and electronic medical records. These included patient demographics such as age, sex, preoperative CEA level, preoperative CRP level, American Society of Anesthesiologists (ASA) physical status (PS) grade, body mass index, sarcopenia, phase angle, visceral fat area (VFA), tumor location, perioperative clinical outcomes (e.g., operation time, time to gas out, sips of water, time to soft diet, and length of stay), morbidity within 30 days after surgery, Clavien-Dindo (CD) classification, and postoperative pathologic outcomes (e.g., T stage, N stage, M stage, histology, and number examined lymph nodes). The PIV data were retrospectively collected from electronic medical records 2 days before the surgery. PIV was calculated as follows: neutrophil count ($\times 10^3/mm^3$) × platelet count ($\times 10^3/mm^3$) × monocyte count ($\times 10^3/mm^3$) / lymphocyte count ($\times 10^3/mm^3$).

The CD classification, a widely used grading system for surgical adverse events, was applied [23]. The TNM stage of

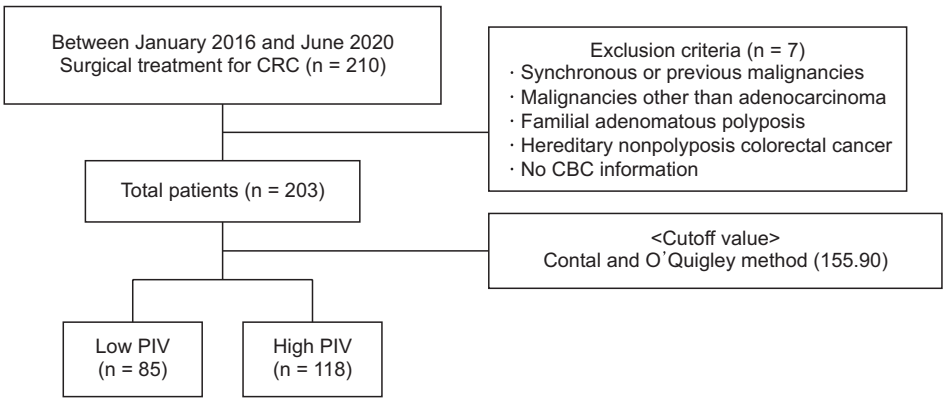

Fig. 1. Flow chart of the exclusion criteria. CRC, colorectal cancer; CBC, complete blood count; PIV, pan-immune-inflammation index.

each CRC patient was classified according to the 8th edition of the American Joint Committee on Cancer classification system. Overall survival (OS) was defined as the interval between the date of surgery and the most recent follow-up visit or the date of death from any cause. Disease-free survival (DFS) was defined as the interval between the date of surgery and the date of recurrence, with recurrence defined as the radiologically or histologically confirmed presence of a tumor. Local recurrence referred to the recurrence in the surgical field, while local recurrence with concurrent systemic recurrence was considered systemic recurrence.

BIA using the InBody 770 (Biospace) was conducted to evaluate body composition, VFA, appendicular skeletal muscle mass, and phase angle. SMI was calculated by appendicular skeletal muscle mass (kg) divided by the square of height (m^2), and sarcopenia was defined as SMI <7.0 kg/m^2 in male and <5.7 kg/m^2 in female [16]. VFA, the measurement of visceral fat in the abdominal region, was defined as high if >70.2 cm^2 in male and >82.4 cm^2 in female, based on the median value.

Statistical analysis

We determined the optimal cutoff value for PIV in our study using the Contal and O'Quigley method. In survival analysis, the Contal and O'Quigley approach is employed to identify cutoff points in continuous variables [17]. The process involves computing all log-rank statistics and selecting the optimal cut point based on the maximum value of the log-rank statistic. This method was applied to every possible cutoff, and the one with the highest Q statistic was selected for further investigation. Mortality events were considered in the Contal and O'Quigley equations. The optimal cutoff value of PIV for stratifying patients into the low-PIV group and high-PIV group was determined based on OS using the Contal and O'Quigley method, with PIV defined as high if ≥155.90. Continuous outcomes were presented as means with standard deviations, and categorical outcomes as frequencies with percentages. The t-test and Mann-Whitney U-test were employed to analyze the association between PIV and continuous variables, while the Fisher exact test and chi-square test were used for categorical variables. Complications were analyzed using a logistic regression model, and the effects of individual variables on complications were reported as odds ratios (OR) with 95% confidence intervals (CIs). And the variables with univariate regression P-value of <0.1 were included in multivariate regression analysis. Survival analysis was conducted using the Kaplan-Meier method to examine OS and DFS curves, and Cox proportional hazard regression models were used to report the effects of individual variables on patient survival with hazard ratios (HR) and CIs. Statistical significance was set at $P < 0.05$. Statistical analyses were performed using IBM SPSS Statistics ver. 26 (IBM Corp.).

Table 1. Patient and tumor characteristics

Characteristic	Low-PIV group	High-PIV group	P-value
No. of patients	85	118	
Age (yr)	65.6 ± 9.6	66.1 ± 10.2	0.712
Sex			0.002
Male	48 (56.5)	91 (77.1)	
Female	37 (43.5)	21 (22.9)	
Preoperative CEA (ng/mL)	5.1 ± 19.8	6.7 ± 16.8	0.561
Preoperative CRP (mg/dL)	0.4 ± 1.2	0.6 ± 1.2	0.439
ASA PS grade			0.067
I	31 (36.5)	28 (23.7)	
II	42 (49.4)	75 (63.6)	
III	12 (14.1)	15 (12.7)	
Body mass index (kg/m^2)	23.4 ± 2.7	23.4 ± 3.0	0.958
Sarcopenia			0.430
Yes	23 (27.1)	38 (32.2)	
No	62 (72.9)	80 (67.8)	
Phase angle	5.07 ± 0.6	5.04 ± 0.6	0.768
Visceral fat area	78.5 ± 28.2	79.2 ± 33.2	0.222
Location of tumor			0.067
Right	15 (17.6)	34 (16.7)	
Left	70 (82.4)	84 (71.2)	

Values are presented as number only, mean ± standard deviation, or number (%).
PIV, pan-immune-inflammation index; ASA, American Society of Anesthesiologists; PS, physical status.

RESULTS

Baseline characteristics of patients

A total of 203 patients were included in the study. Based on the optimal cutoff value, 85 patients (41.8%) had low PIV, and 118 patients (58.2%) had high PIV (Table 1). The high-PIV group had a significantly higher proportion of males compared to the low-PIV group (77.1% *vs.* 56.5%, P = 0.002). However, there were no significant differences in age, preoperative CEA, preoperative CRP, ASA PS grade, body mass index, or tumor location. Additionally, there were no significant differences in the preoperative body composition, including sarcopenia, phase angle, and VFA.

Perioperative clinical outcomes

Table 2 presents the perioperative clinical outcomes of the low- and high-PIV groups. There was no significant difference in overall perioperative outcomes, including total operation time, time to gas out, sips of water, time to soft diet, hospital stay, and CD classification of >3a between the 2 groups. However, the high-PIV group exhibited a higher incidence of postoperative complications than the low-PIV group (39.8% *vs.* 24.7%, P = 0.024).

Postoperative pathologic outcomes

Table 3 displays the postoperative pathological outcomes of the low- and high-PIV groups. High PIV was significantly associated with larger tumor size than low PIV (3.9 ± 2.3 *vs.* 3.3 ± 1.8, P = 0.044). However, there were no differences between low and high PIV in T stage, N stage, M stage, histology, number of retrieved lymph nodes, proportion of patients with >12 acquired lymph nodes, number of positive lymph nodes, and lymphovascular or perineural invasions.

Univariate and multivariate regression analysis of factors associated with postoperative complications

Univariate analysis identified the male sex, ASA PS grade III, advanced M stage, and high PIV as factors significantly associated with postoperative complications including all events that occurred after surgery (P < 0.1) (Table 4). In the multivariate regression analysis, ASA PS grade III (OR, 2.701; 95% CI, 1.018–7.166; P = 0.046) and high PIV (OR, 1.923; 95% CI, 1.003–3.686; P = 0.049) remained significantly associated with postoperative complications.

Oncologic outcomes

The median follow-up period was 40.8 months in the high-PIV group and 36.1 months in the low-PIV group (P = 0.057) (Supplementary Table 1). The low-PIV group exhibited higher 5-year OS rates (81.8% *vs.* 98.8%, P = 0.001) and 5-year DFS rates (78.3% *vs.* 90.1%, P = 0.021) compared with the high-PIV group (Fig. 2). Among the patients, 17 experienced recurrences within the follow-up period, with no significant difference in the recurrence pattern between the 2 groups. The low-PIV group had 5 cases of recurrence (4 systemic and 1 local recurrence), while the high-PIV group had 12 cases of recurrence (9 systemic and 3 local recurrences).

Table 2. Perioperative clinical outcomes

Variable	Low-PIV group (n = 85)	High-PIV group (n = 118)	P-value
Operation time (min)	200.7 ± 104.3	210.3 ± 92.9	0.493
Gas out (day)	2.9 ± 1.5	3.0 ± 2.1	0.639
Sips of water (day)	3.6 ± 2.4	4.2 ± 5.0	0.331
Time to soft diet (day)	6.0 ± 2.5	6.7 ± 5.3	0.215
Length of stay (day)	9.5 ± 3.6	10.8 ± 7.5	0.113
Morbidity within 30 days after surgery	21 (24.7)	47 (39.8)	0.024
Ileus	3 (3.5)	12 (10.2)	0.074
Anastomosis leakage	5 (5.9)	6 (5.1)	0.804
Dysuria	2 (2.4)	8 (6.8)	0.150
Chyle leakage	5 (5.9)	3 (2.5)	0.228
Bleeding (hematochezia)	3 (3.5)	5 (4.2)	0.798
Surgical site infection	2 (2.4)	5 (4.2)	0.468
Cardiac complication	0 (0)	2 (1.7)	0.228
Pseudomembranous colitis	0 (0)	2 (1.7)	0.228
Respiratory complication	1 (1.2)	1 (0.8)	0.815
Intraabdominal abscess	0 (0)	2 (1.7)	0.228
Colitis	0 (0)	1 (0.8)	0.395
Clavien-Dindo classifications >3a	3 (3.5)	7 (6.0)	0.427

Values are presented as mean ± standard deviation or number (%).
PIV, pan-immune-inflammation index.

Table 3. Postoperative pathologic outcomes

Variable	Low-PIV group (n = 85)	High-PIV group (n = 118)	P-value
Tumor stage			0.128
T0–T2	43 (50.6)	47 (39.8)	
T3, T4	42 (49.4)	71 (60.2)	
Nodal stage			0.197
N0	60 (70.6)	73 (61.9)	
N1, N2	25 (29.4)	45 (38.1)	
M stage			0.798
M0	82 (96.5)	113 (95.8)	
>M1	3 (3.5)	5 (3.9)	
Histology			0.365
Well-differentiated	4 (4.8)	8 (6.9)	
Moderately differentiated	77 (91.7)	99 (85.3)	
Poorly differentiated	3 (3.6)	9 (7.8)	
No. of retreived LNs	17.6 ± 8.7	19.4 ± 9.6	0.175
>12	73 (85.9)	102 (86.4)	0.909
Positive LNs	1.0 ± 2.4	0.9 ± 1.7	0.831
Tumor size (cm)	3.3 ± 1.8	3.9 ± 2.3	0.044
Lymphovascular invasion	26 (31.3)	28 (24.1)	0.261
Perineural invasion	16 (20.0)	25 (21.9)	0.746

Values are presented as number (%) or mean ± standard deviation.
PIV, pan-immune-inflammation index; LN, lymph node.

Table 4. Univariate and multivariate regression analysis of factors associated with postoperative complications

Variable	Univariate		Multivariate	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age (yr), < 65 *vs*. ≥ 65	1.178 (0.653–2.124)	0.587		
Sex, male *vs*. female	0.558 (0.288–1.081)	0.084	0.689 (0.345–1.376)	0.291
Preoperative CEA (ng/mL), <5 *vs*. ≥5	1.668 (0.830–3.353)	0.151		
Preoperative CRP (mg/L), < 0.21 *vs*. ≥ 0.21	1.214 (0.608–2.425)	0.583		
ASA PS grade				
I		0.098		0.093
II	1.143 (0.576–2.267)	0.703	1.087 (0.531–2.227)	0.819
III	2.661 (1.037–6.825)	0.042	2.701 (1.018–7.166)	0.046
Sideness, right *vs*. left	0.828 (0.423–1.621)	0.582		
Operation time (min), <180 *vs*. ≥180	1.249 (0.694–2.247)	0.458		
T stage, T0–T2 *vs*. T3, T4	1.329 (0.735–2.401)	0.347		
N stage, N0 *vs*. N1, N2	0.784 (0.421–1.462)	0.444		
M stage, M0 *vs*. ≥M1	3.492 (0.809–15.074)	0.094	3.515 (0.766–16.135)	0.106
Tumor size (cm), <3.4 *vs*. ≥3.4	1.407 (0.782–2.532)	0.254		
Phase angle, low *vs*. high	0.685 (0.376–1.245)	0.214		
Sarcopenia, no *vs*. yes	1.445 (0.773–2.699)	0.248		
VFA, low *vs*. high	1.093 (0.609–1.959)	0.766		
PIV, <155.90 *vs*. ≥155.90	2.017 (1.090–3.733)	0.025	1.923 (1.003–3.686)	0.049

OR, odds ratio; CI, confidence interval; VFA, visceral fat area; PIV, pan-immune-inflammation index.

Univariate and multivariate regression analysis for prognostic factors of oncologic outcomes

Supplementary Table 2 presents the prognostic factors associated with 5-year survival. Univariate analysis showed that male sex, high preoperative CRP levels, N and M stages, complications within 30 days after surgery, and high PIV levels were associated with a worse 5-year OS ($P < 0.1$). Similarly, male sex; higher preoperative CEA levels; longer operation times; advanced T, N, and M stages; and higher VFA and PIV levels were associated with better 5-year DFS ($P < 0.1$). In

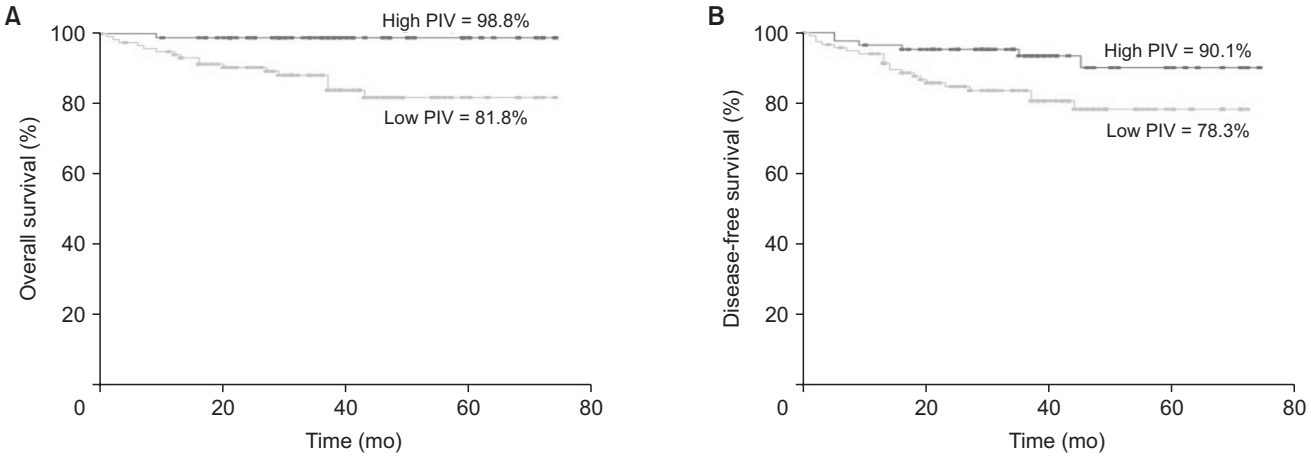

Fig. 2. The Kaplan-Meier survival curve for the overall survival and disease-free survival. PIV, pan-immune-inflammation index.

Table 5. Prognostic factors of overall survival and disease-free survival in multivariate analysis

Variable	Reference category	Overall Survival		Disease-free survival	
		HR (95% CI)	P-value	HR (95% CI)	P-value
Female sex	Male sex	0.940 (0.174–5.071)	0.943	0.251 (0.031–2.043)	0.196
Preoperative CEA, ≥5 ng/mL	<5	1.017 (0.278–3.729)	0.979	0.926 (0.258–3.323)	0.906
CRP, ≥0.21 mg/L	<0.21	2.000 (0.540–7.408)	0.300	0.839 (0.287–2.455)	0.748
T stage, T3 & T4	T1, T2	0.571 (0.096–3.391)	0.538	1.701 (0.437–6.627)	0.444
N stage, N1 & N2	N0	9.411 (1.976–44.814)	0.005	3.250 (1.027–10.281)	0.045
M stage, ≥M1	M0	0.774 (0.125–4.798)	0.783	0.833 (0.136–5.114)	0.843
Morbidity within 30 days, yes	No	2.542 (0.747–8.657)	0.136	2.627 (0.945–7.300)	0.064
VFA, high	Low	1.108 (0.366–3.350)	0.856	1.711 (0.608–4.813)	0.309
PIV, high	Low	8.363 (1.028–68.016)	0.047	2.215 (0.596–8.235)	0.235
Operation time, ≥180 min	<180	1.352 (0.446–4.094)	0.594	1.951 (0.682–5.581)	0.213

HR, hazard ratio; CI, confidence interval; VFA, visceral fat area; PIV, pan-immune-inflammation index.

the multivariate analysis, a high preoperative PIV level was identified as an independent prognostic factor for the OS (HR, 1.108; 95% CI, 0.366–3.350; P = 0.047), whereas the nodal stage was an independent prognostic factor for both the OS (HR, 9.411; 95% CI, 1.976–44.814; P = 0.005) and DFS (HR, 3.250; 95% CI, 1.027–10.281; P = 0.045) (Table 5).

DISCUSSION

This study aimed to analyze the impact of preoperative PIV on clinical and oncologic outcomes after surgery in patients with CRC, including stage 4 cases treated with curative intent. Our results revealed significantly higher OS and DFS rates in the low-PIV group than in the high-PIV group. In the multivariate analysis of postoperative complications, ASA PS grade III and high preoperative PIV were identified as independent risk factors. For oncological outcomes, the advanced N stage and high preoperative PIV levels were independent prognostic factors for the OS, while only the advanced N stage was an independent prognostic factor for the DFS.

Numerous factors can influence the postoperative complications in CRC surgery. A meta-analysis by van Kooten et al. [24] highlighted several risk factors for major postoperative complications, including older age, frailty, male sex, high ASA PS grade, elevated preoperative inflammatory biomarkers (e.g., WBC count, CRP), malnutrition, preoperative weight loss, sarcopenia, overweight, and advanced tumor stage. Some studies have specifically investigated immunoinflammatory markers in predicting complications after CRC surgery. For example, Kamonvarapitak et al. [25] found that the preoperative lymphocyte-to-monocyte ratio could predict postoperative infectious complications, whereas Feng et al. [26] demonstrated that the systemic inflammation index is a useful predictor for postoperative infectious complications. Similarly, Sato et al. [27] and Sato et al. [28] reported associations between PIV and postoperative complications in CRC patients. Postoperative complications are reportedly associated with inflammatory response and malnutrition. Past reports have also shown

that low albumin and low total lymphocyte count are closely related to the development of an inflammatory response in patients with malignancy. Our study's findings align with these previous works, as high preoperative PIV was significantly associated with postoperative complications in patients with CRC.

Recent studies have explored the relationship between body composition, sarcopenia, VFA, phase angle, and CRC prognosis [29,30]. Body composition can reflect the nutritional status and may have associations with a patient's immune-inflammatory status [17,18]. Song et al. [30] reported that body composition indices, including fat and muscle indices, were related to platelet and lymphocyte ratios in CRC, particularly in male patients. Previous research has indicated that preoperative VFA measured using the BIA could serve as an independent prognostic factor for DFS [15,31]. However, in our study, no significant associations were observed between sarcopenia, VFA, phase angle, and PIV. Furthermore, these body composition markers did not exhibit significant correlations with oncologic outcomes. Future research is warranted to further explore the association between body composition and blood-based inflammatory markers, such as PIV, and their impact on oncological outcomes.

Several studies have demonstrated that a high preoperative PIV has prognostic implications for the OS and DFS and for other immune-inflammatory markers like the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, and prognostic nutritional index in patients with CRC [13,32]. High PIV has also been linked to poor oncological outcomes in breast and lung cancer [21,22]. However, the association between elevated PIV and oncological outcomes in CRC has shown slightly varying results in previous studies. Fuca et al. [20] reported that high PIV had the most significant impact on the OS and progression-free survival among immune-inflammatory biomarkers in metastatic CRC. In contrast, Sato et al. [28] found that high preoperative PIV was associated with poor survival in patients with CRC and a stent-inserted in obstructive tumors due to potential tumor cell apoptosis triggered by platelet-derived microparticles infiltrating the solid tumor. The progression of tumors involves the activation of myeloid-derived suppressor cells by neutrophils and monocytes. Monocytes can also transform into tumor-associated macrophages, promoting tumor growth and metastasis. A diminished lymphocyte count indicates a weakened antitumor response, as cytotoxic T-cell infiltration predicts the survival and response of CRC patients to immune therapy [27]. PIV includes these blood components, which interact with other blood components. Therefore, high preoperative PIV, reflecting a compromised immune-inflammatory status, significantly correlated with poorer OS, indicating the need for further investigation.

Our study has a few limitations. It was a retrospective analysis, and certain relevant factors related to the patients' immune-inflammatory status may not have been included. Additionally, being a single-center study, the median duration of follow-up for the patients was relatively short, limiting our ability to analyze long-term oncological outcomes. Further research is needed to overcome these limitations and provide a more comprehensive understanding of the associations between PIV, immune-inflammatory status, and CRC outcomes.

In conclusion, a high preoperative PIV was associated with more postoperative complications and independently predicted worse OS in CRC patients. PIV shows promise as a comprehensive biomarker with potential applications in risk assessment and decision-making for treatment. Further research is needed to explore its underlying mechanisms and validate its predictive value in larger patient cohorts.

SUPPLEMENTARY MATERIALS

Supplementary Tables 1 and 2 can be found via https://doi.org/10.4174/astr.2024.106.3.169.

ACKNOWLEDGEMENTS

Fund/Grant Support

This work was supported by the National Research Foundation of Korea (NRF) Grant by the Korea Government (MSIP) (No. 2021R1F1A1064310).

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

ORCID iD

Yun Ju Seo: https://orcid.org/0009-0003-7625-1041
Kyeong Eui Kim: https://orcid.org/0000-0001-9984-9976
Woon Kyung Jeong: https://orcid.org/0000-0001-8421-218X
Seong Kyu Baek: https://orcid.org/0000-0001-6427-8675
Sung Uk Bae: https://orcid.org/0000-0002-7876-4196

Author Contribution

Conceptualization, Formal analysis, Methodology: YJS, KEK, SUB
Writing – Original Draft: YJS, SUB
Writing – Review & Editing: KEK, WKJ, SKB

REFERENCES

1. Medzhitov R. Origin and physiological roles of inflammation. Nature 2008;454:428-35.
2. Serhan CN, Levy BD. Resolvins in inflammation: emergence of the pro-resolving superfamily of mediators. J Clin Invest 2018;128:2657-69.
3. Khansari N, Shakiba Y, Mahmoudi M. Chronic inflammation and oxidative stress as a major cause of age-related diseases and cancer. Recent Pat Inflamm Allergy Drug Discov 2009;3:73-80.
4. Singh N, Baby D, Rajguru JP, Patil PB, Thakkannavar SS, Pujari VB. Inflammation and cancer. Ann Afr Med 2019;18:121-6.
5. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? Lancet 2001;357:539-45.
6. Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 2008;454:436-44.
7. Allin KH, Nordestgaard BG. Elevated C-reactive protein in the diagnosis, prognosis, and cause of cancer. Crit Rev Clin Lab Sci 2011;48:155-70.
8. Numata K, Ono Y, Ju M, Onuma S, Tanaka A, Kawabe T, et al. Evaluating prognostic significance of preoperative C-reactive protein to albumin ratio in older patients with pathological stage II/III colorectal cancer. Ann Coloproctol 2022 Oct 11 [Epub]. https://doi.org/10.3393/ac.2022.00367.0052
9. Utsumi M, Inagaki M, Kitada K, Tokunaga N, Kondo M, Sakurai Y, et al. Preoperative lymphocyte-to-C-reactive protein ratio predicts hepatocellular carcinoma recurrence after surgery. Ann Surg Treat Res 2022;103:72-80.
10. Yamamoto T, Kawada K, Obama K. Inflammation-related biomarkers for the prediction of prognosis in colorectal cancer patients. Int J Mol Sci 2021;22:8002.
11. Kang Y, Zhu X, Lin Z, Zeng M, Shi P, Cao Y, et al. Compare the diagnostic and prognostic value of MLR, NLR and PLR in CRC patients. Clin Lab 2021;67:10.7754/Clin.Lab.2021.201130..
12. Feng Y, Luo J, Liu P, Liu L, Zhu Y, Cheng G, et al. Glasgow prognostic score and combined positive score for locally advanced rectal cancer. Ann Surg Treat Res 2022;102:153-8.
13. Huang XZ, Chen WJ, Zhang X, Wu CC, Zhang CY, Sun SS, et al. An elevated platelet-to-lymphocyte ratio predicts poor prognosis and clinicopathological characteristics in patients with colorectal cancer: a meta-analysis. Dis Markers 2017;2017:1053125.
14. An SH, Kim IY. Can pretreatment platelet-to-lymphocyte and neutrophil-to-lymphocyte ratios predict long-term oncologic outcomes after preoperative chemoradiation followed by surgery for locally advanced rectal cancer? Ann Coloproctol 2022;38:253-61.
15. Kim KE, Bae SU, Jeong WK, Baek SK. Impact of preoperative visceral fat area measured by bioelectrical impedance analysis on clinical and oncologic outcomes of colorectal cancer. Nutrients 2022;14:3971.
16. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. J Am Med Dir Assoc 2020;21:300-7.
17. Fleming CA, O'Connell EP, Kavanagh RG, O'Leary DP, Twomey M, Corrigan MA, et al. Body composition, inflammation, and 5-year outcomes in colon cancer. JAMA Netw Open 2021;4:e2115274.
18. Wu H, Ding P, Wu J, Yang P, Tian Y, Zhao Q. Phase angle derived from bioelectrical impedance analysis as a marker for predicting sarcopenia. Front Nutr 2022;9:1060224.
19. Lim M, Kim JM, Yang J, Kwon J, Kim KD, Jeong ES, et al. Upper thigh skeletal muscle index predicts outcomes in liver transplant recipients. Ann Surg Treat Res 2023;105:219-27.
20. Fucà G, Guarini V, Antoniotti C, Morano F, Moretto R, Corallo S, et al. The pan-immune-inflammation value is a new prognostic biomarker in metastatic colorectal cancer: results from a pooled-analysis of the Valentino and TRIBE first-line trials. Br J Cancer 2020;123:403-9.
21. Ligorio F, Fucà G, Zattarin E, Lobefaro R, Zambelli L, Leporati R, et al. The pan-immune-inflammation-value predicts the survival of patients with human epidermal growth factor receptor 2 (HER2)-positive advanced breast cancer treated with first-line taxane-trastuzumab-pertuzumab. Cancers (Basel) 2021;13:1964.
22. Fucà G, Beninato T, Bini M, Mazzeo L, Di Guardo L, Cimminiello C, et al. The pan-immune-inflammation value in patients with metastatic melanoma receiving first-line therapy. Target Oncol 2021;16:529-36.
23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
24. van Kooten RT, Bahadoer RR, Peeters KC, Hoeksema JH, Steyerberg EW, Hartgrink HH, et al. Preoperative risk factors for major postoperative complications after complex gastrointestinal cancer surgery: a systematic review. Eur J Surg Oncol 2021;47:3049-58.
25. Kamonvarapitak T, Matsuda A, Matsumoto S, Jamjittrong S, Sakurazawa N, Kawano Y, et al. Preoperative lymphocyte-to-monocyte ratio predicts postoperative infectious complications after laparoscopic colorectal cancer surgery. Int J Clin Oncol 2020;25:633-40.
26. Feng L, Xu R, Lin L, Liao X. Effect of the systemic immune-inflammation index on postoperative complications and the long-term prognosis of patients with colorectal cancer: a retrospective cohort study. J Gastrointest Oncol 2022;13:2333-9.
27. Sato S, Shimizu T, Ishizuka M, Suda K, Shibuya N, Hachiya H, et al. The

preoperative pan-immune-inflammation value is a novel prognostic predictor for with stage I-III colorectal cancer patients undergoing surgery. Surg Today 2022;52:1160-9.
28. Sato R, Oikawa M, Kakita T, Okada T, Abe T, Tsuchiya H, et al. A decreased preoperative platelet-to-lymphocyte ratio, systemic immune-inflammation index, and pan-immune-inflammation value are associated with the poorer survival of patients with a stent inserted as a bridge to curative surgery for obstructive colorectal cancer. Surg Today 2023;53:409-19.
29. Takenami T, Tsujinaka S, Miyakura Y, Kakizawa N, Maemoto R, Machida E, et al. Impact of sarcopenia on surgical and oncologic outcomes of laparoscopic surgery for colorectal cancer. Asian J Surg 2022;45:2686-90.
30. Song WJ, Kim KE, Bae SU, Jeong WK, Baek SK. Association between body composition measured by bioelectrical impedance analysis and platelet-to-lymphocyte ratio in colorectal cancer. Korean J Clin Oncol 2019;15:7-14.
31. Trejo-Avila M, Bozada-Gutiérrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis 2021;36:1077-96.
32. Wu Q, Hu T, Zheng E, Deng X, Wang Z. Prognostic role of the lymphocyte-to-monocyte ratio in colorectal cancer: an up-to-date meta-analysis. Medicine (Baltimore) 2017;96:e7051.