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Original Article

Expression of serum inflammatory markers in colorectal cancer and their relationship with clinical pathological characteristics

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Abstract: Objective: This retrospective study primarily aimed to measure serum inflammatory markers in colorectal cancer and examine their relationship with clinical pathological characteristics. Methods: A total of 147 CRC patients (assigned to the training group (103 cases) or the validation group (44 cases) at a 7:3 ratio) and 100 control participants were enrolled. Interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) levels in serum were compared between the training and control groups. The diagnostic value of these markers for CRC and their relationship with the clinical pathological characteristics of CRC patients were evaluated. The correlations among inflammatory markers and their correlations with tumor markers were analyzed. Finally, the clinical data of the training and validation groups were compared, and the diagnostic value of each inflammatory marker was verified in the validation group. Results: Inflammatory markers were notably elevated in the CRC group and showed significant correlations with Tumor-Node-Metastasis (TNM) staging, lymph node metastasis (LNM), and tumor diameter. Additionally, all these three markers showed positive correlations with each other and with tumor markers. Each inflammatory marker demonstrated certain diagnostic efficacy for clinical pathological characteristics. Specifically, IL-6 exhibited outstanding efficacy for LNM (area under the curve (AUC) = 0.798), and CRP performed best in differentiating tumor diameter (AUC = 0.730). Moreover, the AUC values in the validation group were comparable to those in the training group. Results: IL-6, TNF-α, and CRP may serve as potential tools to assist in the assessment of disease progression and metastatic potential in colorectal cancer.

Keywords: Colorectal cancer, interleukin-6, tumor necrosis factor-α, C-reactive protein, clinical pathological characteristics

Introduction

Colorectal cancer (CRC), a common gastrointestinal tumor worldwide, poses a high risk of incidence and mortality [1]. Factors such as processed foods, sugary beverages, obesity, alcohol consumption, and smoking all increase the risk of the disease, and the risk is also influenced by the complex interplay of multiple genetic and environmental factors [2]. Data from the Global Cancer Observatory (GLOBOCAN) indicates that in 2020, there were nearly 2 million new cases of CRC and 940,000 deaths in the world, with the highest incidence (52%) in Asia [3]. Diagnostic delays still exist among CRC patients, so that they are diagnosed at an advanced stage and miss the optimal treatment timing, resulting in poor prognosis [4]. This study aims to explore effective and reliable auxiliary diagnostic tools based on serum inflammatory markers to optimize CRC management, which has significant clinical value for the effective prevention and treatment of CRC.

Interleukin-6 (IL-6), as a multifunctional cytokine, mediates immune regulation, promotes the formation of an inflammatory tumor microenvironment (TME), and is associated with multiple cancers, including CRC [5]. It activates the Janus kinase 2/signal transducer and activator of transcription 3 signaling pathway to promote epithelial-mesenchymal transition (EMT), thereby participating in malignant tumor invasion and metastasis [6]. Yamamoto T et al. [7] reported that abnormally elevated IL-6

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Table 1. General data

Data	n	Training group (n = 103)	Control group (n = 100)	$Z/t/\chi^2$ value	*P* value
Gender				0.370	0.543
Male	116	61 (59.22)	55 (55.00)		
Female	87	42 (40.78)	45 (45.00)		
Age (years)	203	64.83±7.08	63.95±7.04	0.888	0.376
BMI (kg/m^2)	203	23.00 (22.00, 24.00)	23.00 (21.00, 24.00)	1.494	0.137
Smoking history	43	25 (24.27)	18 (18.00)	1.195	0.274
Alcohol abuse history	48	28 (27.18)	20 (20.00)	1.451	0.228
Concomitant diabetes mellitus	51	31 (30.10)	20 (20.00)	2.750	0.097
Concomitant hypertension	25	15 (14.56)	10 (10.00)	0.978	0.323

Note: BMI, Body Mass Index.

levels in tumor-infiltrating immune cells were closely related to the accumulation of immunosuppressive cells in TME and reflected the poor prognosis of patients with CRC. In addition to IL-6, tumor necrosis factor-α (TNF-α) also reflects the inflammatory burden in CRC and helps predict survival outcomes in patients with stage III CRC [8]. As a macrophage-derived cytokine, TNF-α is notably upregulated in sodium dextran sulfate-induced colitis-associated cancers; it contributes to CRC development by enhancing the stemness of Doublecortin-like kinase 1 (Dclk1)-positive cluster cells [9]. The levels of C-reactive protein (CRP), along with IL-6 and TNF-α, are considered serum markers reflecting CRC progression, such as advanced tumor and poor histological differentiation, suggesting that the three may function as supplementary serum indicators for evaluating CRC clinical pathological characteristics [10].

At present, there are few studies on the expression of serum IL-6, TNF-α, and CRP in CRC and their relationship with clinical pathological characteristics. Continued exploration in this area may help elucidate the potential clinical value of these markers, providing more useful references for effective clinical management of CRC patients.

Materials and methods

General data

From January 2023 to June 2025, 103 CRC patients admitted to the Affiliated Hospital of Zunyi Medical University were included as study subjects and assigned to the CRC group. Besides, 100 healthy individuals were selected and enrolled in the control group. No statistically significant intergroup differences were observed in general data (P > 0.05), indicating clinical comparability. This retrospective study has obtained approval from the Ethics Committee of the Affiliated Hospital of Zunyi Medical University.

Inclusion and exclusion criteria

Inclusion criteria: Patients aged 18-80 years; patients with pathologically confirmed diagnosis of primary CRC [11]; Patients with no concomitant malignant tumors; treatment-naive patients; Patients with complete medical records.

Exclusion criteria: Patients complicated with acute or chronic infections, autoimmune diseases, recent trauma or surgical history (not related to CRC), or other conditions prone to significantly affect inflammatory marker levels; Patients complicated with diseases causing abnormal liver function (e.g., viral hepatitis, drug-induced hepatitis, alcoholic hepatitis); Patients complicated with blood-borne or infectious diseases; Patients complicated with other inflammatory-related conditions (e.g., colitis); Patients complicated with serious hepatic, renal, cardiac, or pulmonary insufficiency; Patients with expected survival < 3 months; Patients complicated with serious concomitant systemic diseases; pregnant or lactating women.

Measurement methods

Fasting venous blood (about 5 mL) was collected from CRC patients within 8 hours after admission and from healthy individuals on the day of physical examination, respectively. Both

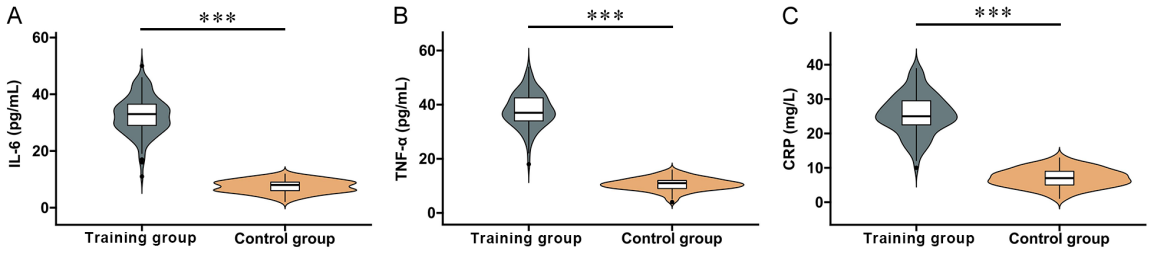

Figure 1. Serum inflammatory marker levels in the two groups. A. IL-6 in the CRC and control groups. B. TNF-α in the CRC and control groups. C. CRP in the CRC and control groups. Note: ***P < 0.001. CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein.

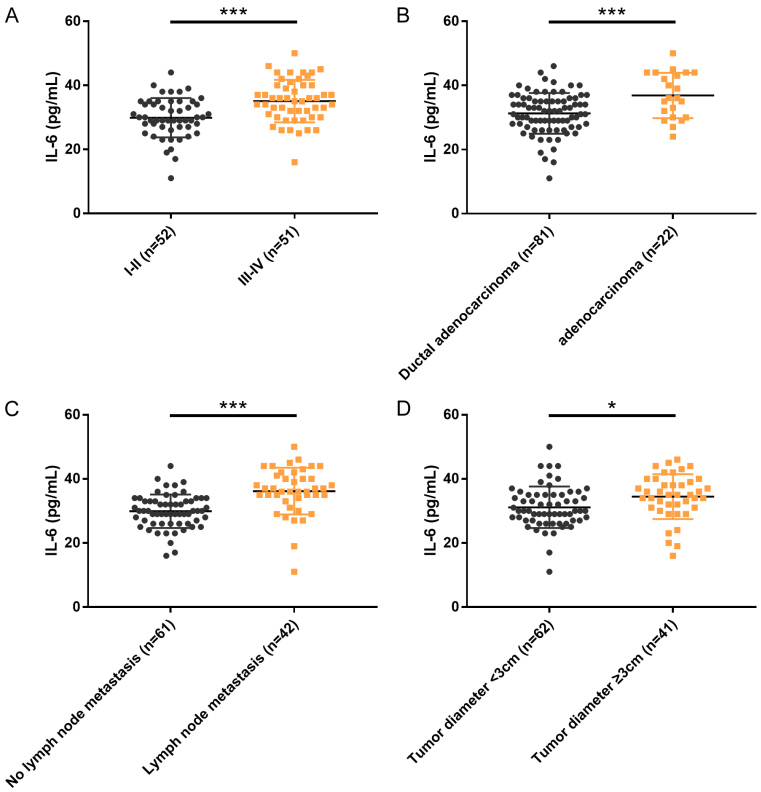

Figure 2. Relationship between IL-6 and clinical pathological characteristics of CRC. A. Association between IL-6 and TNM staging in CRC patients. B. Association between IL-6 and histological classification in CRC patients. C. Association between IL-6 and lymph node metastasis in CRC patients. D. Association between IL-6 and tumor diameter in CRC patients. Note: ***P < 0.001, *P < 0.05. CRC, Colorectal cancer; IL-6, Interleukin-6; TNM, Tumor-Node-Metastasis.

tubes were left to clot naturally and then centrifuged to obtain serum. Enzyme-linked immunosorbent assay (ELISA) was applied for the measurement of IL-6, TNF-α, CRP, carbohydrate antigen 125 (CA125), carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP) in serum, with specific procedures strictly adhering to the kit instructions (Shanghai Zhong Qiao Xin Zhou Biotechnology Co., Ltd., EKH207-P, EKH002-P, EKH159-P; Shanghai EK-Bioscience Biotechnology Co., Ltd., AB6653, AB5302, EKH11000). The normal reference ranges for the various inflammatory markers were as follows [12]: IL-6 < 7.0 pg/mL, TNF-α < 8.1 pg/mL, and CRP < 10.0 mg/L; a marker was deemed abnormal if its measured value exceeded the upper limit of the normal reference range.

Indicators

Via the electronic medical record system, general and clinical pathological data of study subjects were collected. General data included gender, age, body mass index (BMI), smoking history, alcohol abuse history, concomitant diabetes mellitus, and concomitant hypertension. Clinical pathological data encompassed Tumor-Node-Metastasis (TNM) staging, histological classification, lymph node metastasis (LNM), and tumor diameter. The histological classification of colorectal cancer in this study strictly adheres to the WHO 2020 edition of the *Classification of Tumors of the Digestive System* (5th Edition) [13]. Tubular adenocarcinoma: ≥ 50% of the tumor tissue consists of differentiated glandular structures, with tumor cells arranged in tubular, papillary, or sieve-like patterns,

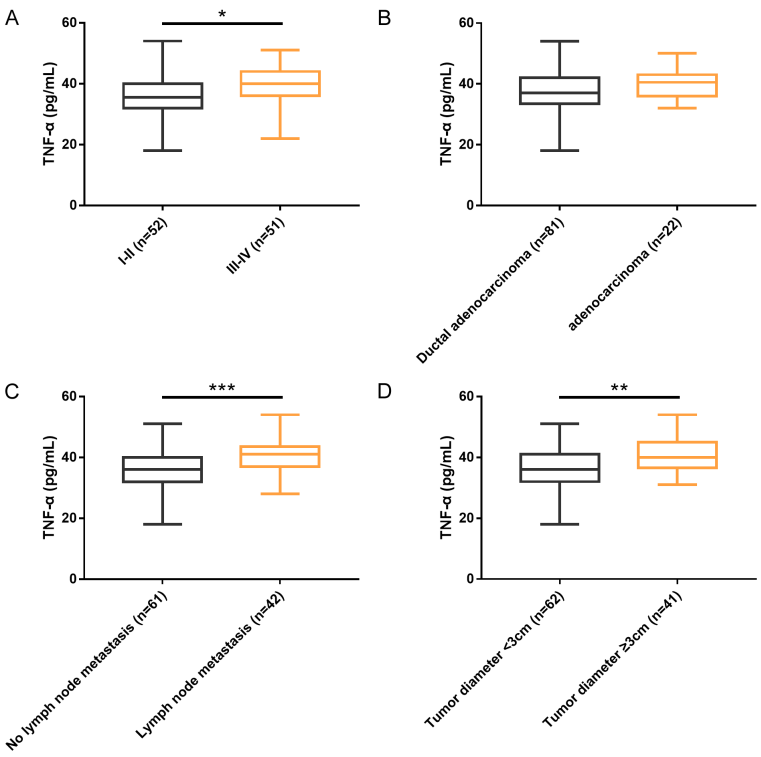

Figure 3. Relationship between TNF-α and clinical pathological characteristics of CRC. A. Association between TNF-α and TNM staging in CRC patients. B. Association between TNF-α and histological classification in CRC patients. C. Association between TNF-α and lymph node metastasis in CRC patients. D. Association between TNF-α and tumor diameter in CRC patients. Note: ***P < 0.001, **P < 0.01, *P < 0.05. CRC, Colorectal cancer; TNF-α, Tumor necrosis factor-alpha; TNM, Tumor-Node-Metastasis.

exhibiting moderate to high cellular atypia. Mucinous adenocarcinoma: ≥ 50% mucinous components (extracellular mucin pools, signet-ring cells with intracellular mucin accumulation) in tumor tissue, with diffuse or focal mucin distribution. Tumor diameter: The maximum tumor diameter was measured from postoperative pathological specimens. All specimens were fixed in 10% formalin, sectioned along the tumor's largest plane, and measured with a ruler to obtain the maximum diameter (recorded as the tumor diameter, in cm).

Statistical analysis

Measurement data and enumeration data in this study were imported into the SPSS 20.0 software package for statistical analysis. Enumeration data were presented as number/percentages (n/%), while measurement data were described as mean ± standard deviation (SD) or median (interquartile range) [M (Q1, Q3)]. The χ^2 test was used for comparisons of enumeration data, and the independent samples t-test for intergroup comparisons of measurement data. The correlations among serum inflammatory markers and the correlations between these markers and tumor markers were determined using the Pearson correlation coefficient, where r = 0.1 to 0.3 indicates weak correlation, r = 0.3 to 0.5 indicates moderate correlation, and r > 0.5 indicates strong correlation. The relationship between serum inflammatory markers and clinical pathological characteristics of CRC patients was evaluated using the receiver operating characteristic (ROC) curves. The difference was statistically significant when P < 0.05.

Results

General data

Table 1 presents no significant intergroup differences in general characteristics such as gender, age, BMI, smoking history, alcohol abuse history, concomitant diabetes mellitus, and concomitant hypertension (P > 0.05).

Serum inflammatory marker levels in the two groups

Figure 1 demonstrated that IL-6, TNF-α, and CRP levels were remarkably elevated in the CRC group relative to the control group, and the abnormality rate of all three indicators was 100% (all P < 0.001).

Relationship between serum inflammatory markers and clinical pathological characteristics of CRC

Through **Figures 2-4**, IL-6 was significantly associated with TNM staging, histological classification, LNM, and tumor diameter in CRC patients (all P < 0.05); TNF-α was significantly associated with TNM staging, LNM, and tumor

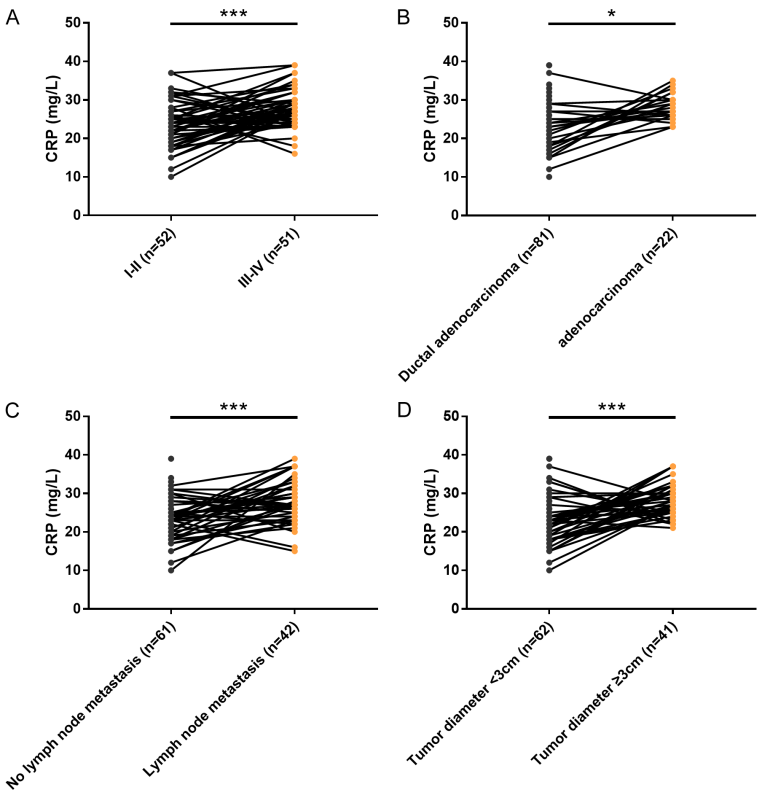

Figure 4. Relationship between CRP and clinical pathological characteristics of CRC. A. Association between CRP and TNM staging in CRC patients. B. Association between CRP and histological classification in CRC patients. C. Association between CRP and lymph node metastasis in CRC patients. D. Association between CRP and tumor diameter in CRC patients. Note: ***P < 0.001, *P < 0.05. CRC, Colorectal cancer; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis.

Table 2. Correlation among serum inflammatory markers in CRC patients

Indicator	r value	*P* value
IL-6 (pg/mL) vs. TNF-α (pg/mL)	0.339	< 0.001
IL-6 (pg/mL) vs. CRP (mg/L)	0.376	< 0.001
TNF-α (pg/mL) vs. CRP (mg/L)	0.303	0.002

Note: CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein.

diameter in CRC patients (all P < 0.05), but not significantly associated with histological classification (P > 0.05); CRP was significantly associated with TNM staging, histological classification, LNM, and tumor diameter in CRC patients (all P < 0.05).

Correlation among serum inflammatory markers in CRC patients

Table 2 revealed a remarkable positive association between IL-6 and TNF-α (r = 0.339, P < 0.001); a remarkable positive association between IL-6 and CRP (r = 0.376, P < 0.001); and a remarkable positive association between IL-6 and TNF-α (r = 0.303, P = 0.002).

Correlation between serum inflammatory markers and tumor markers

There was a notable positive correlation of IL-6 with CA-125 (r = 0.296, P = 0.002), CEA (r = 0.264, P = 0.007), and AFP (r = 0.494, P < 0.001); a notable positive correlation of TNF-α with CA125 (r = 0.301, P = 0.002), CEA (r = 0.322, P < 0.001), and AFP (r = 0.387, P < 0.001); a notable positive correlation of CRP with CA125 (r = 0.451, P < 0.001), CEA (r = 0.339, P < 0.001), and AFP (r = 0.293, P = 0.003) (**Table 3**).

Diagnostic efficacy of serum inflammatory markers in evaluating clinical pathological characteristics of CRC

Figure 5 and **Table 4** present the diagnostic efficacy of serum inflammatory markers for different CRC clinical pathological characteristics. The AUC values of IL-6, TNF-α, and CRP were respectively 0.721, 0.672, and 0.719 for TNM staging (stages I-II vs. stages III-IV); respectively 0.711, 0.633, and 0.688 for the differentiation of histological classification (ductal adenocarcinoma vs. mucinous adenocarcinoma); respectively 0.798, 0.726, and 0.692 for predicting LNM; and respectively 0.673, 0.689, and 0.730 for tumor diameter (< 3 cm vs. ≥ 3 cm).

Comparison of clinical data

The comparison of clinical data between the training and validation groups is shown in **Table 5**, demonstrating no considerable difference in gender, age, BMI, smoking/alcoholism history, diabetes, hypertension, TNM staging, histological classification, LNM, tumor diameter, IL-6, TNF-α, and CRP (P > 0.05).

Table 3. Correlation between serum inflammatory markers and tumor markers

Indicator	r value	*P* value
IL-6 (pg/mL) vs. CA125 (U/mL)	0.296	0.002
IL-6 (pg/mL) vs. CEA (ng/mL)	0.264	0.007
IL-6 (pg/mL) vs. AFP (μg/L)	0.494	< 0.001
TNF-α (pg/mL) vs. CA125 (U/mL)	0.301	0.002
TNF-α (pg/mL) vs. CEA (ng/mL)	0.322	< 0.001
TNF-α (pg/mL) vs. AFP (μg/L)	0.387	< 0.001
CRP (mg/L) vs. CA125 (U/mL)	0.451	< 0.001
CRP (mg/L) vs. CEA (ng/mL)	0.339	< 0.001
CRP (mg/L) vs. AFP (μg/L)	0.293	0.003

Note: IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; CA125, Carbohydrate antigen 125; CEA, Carcinoembryonic antigen; AFP, Alpha-fetoprotein.

Diagnostic efficacy of serum inflammatory markers in evaluating the clinicopathological features of CRC patients in the validation set

The diagnostic efficacy assessment results of serum inflammatory markers for CRC patients with different clinicopathological features in the validation set are shown in **Figure 6** and **Table 6**. The AUC values of IL-6, TNF-α, and CRP were 0.713, 0.669, and 0.714 for differentiating TNM staging (I-II vs. III-IV), and 0.707, 0.651, and 0.668 for distinguishing histological classification (tubular adenocarcinoma vs. mucinous adenocarcinoma), respectively. In predicting LNM, IL-6 showed an AUC of 0.783, TNF-α exhibited a value of 0.722, and CRP had an AUC of 0.687. For tumor diameter differentiation (< 3 cm vs. ≥ 3 cm), the AUC was 0.653 (IL-6), 0.707 (TNF-α), and 0.747 (CRP).

Discussion

Previous studies have focused on investigating the diagnostic value of serum markers in evaluating tumor clinical pathological characteristics. For instance, Zhang Z et al. [14] demonstrated that serum expression levels of pituitary tumor-transforming gene (PTG) correlate closely with clinical pathological characteristics (LNM, TNM staging, and differentiation degree) and prognosis in laryngeal cancer patients. Namikawa T et al. [15] suggested that serum zinc levels were deficient in 66.3% of gastric cancer patients and were highly correlated with serum albumin. In this study, IL-6, TNF-α, and CRP were notably upregulated in CRC patients compared to healthy individuals, consistent with the findings of Maryam S et al. [16]. These results suggest that the above markers may mediate the malignant process of CRC and may be helpful to evaluate the clinical pathological characteristics of CRC. Besides, IL-6 and CRP were closely related to TNM staging, histological classification, LNM, and tumor diameter of CRC patients, while TNF-α was only closely related to TNM staging, LNM, and tumor diameter. These suggest that IL-6 and CRP may broadly participate in pathological processes such as tumor proliferation, differentiation, and invasion, whereas TNF-α is prone to reflect tumor growth and diffusion, with potentially lower involvement in tumor glandular differentiation types. TNF-α mediates CRC tumor cell proliferation and metastasis via activating the nuclear factor (NF)-κB signaling pathway, partially explaining its strong association with LNM and tumor diameter in CRC patients [17]. Zheng J et al. [18] reported that IL-6 and TNF-α were closely related to LNM and TNM staging of CRC patients, similar with the results of this study. In contrast, Waniczek D et al. [19] revealed that elevated serum TNF-α levels correlated with higher tumor grades in CRC patients, but showed no significant association with distant metastasis and/or regional LNM, nor with tumor location, differing from the findings of the present study. As a member of the interleukin family, IL-6 promotes tumor cell proliferation, metastasis, mitosis, migration, and angiogenesis in CRC, which may partially explain its high clinical screening potential [16]. In the study of Yarmohammadi R et al. [20], IL-6 and CRP were notably correlated with advanced disease stage and poor prognosis of gastrointestinal cancer patients, complementing the findings of this study. There is also supporting evidence showing that higher CRP levels reflect metastasis (T1-4N+M+), tumor size > 3 cm, higher World Health Organization (WHO) grade, and tumor localization (proximal colon) in CRC patients [21]. In the report by Bagheri A et al. [22], IL-6, TNF-α, and CRP levels also reflected the efficacy of Mediterranean diet intervention in cachectic CRC patients. Furthermore, Hjortborg M et al. [23] indicated that systemic inflammatory responses reflected by elevated CRP levels correlate with impaired mismatch repair and survival capacity in CRC.

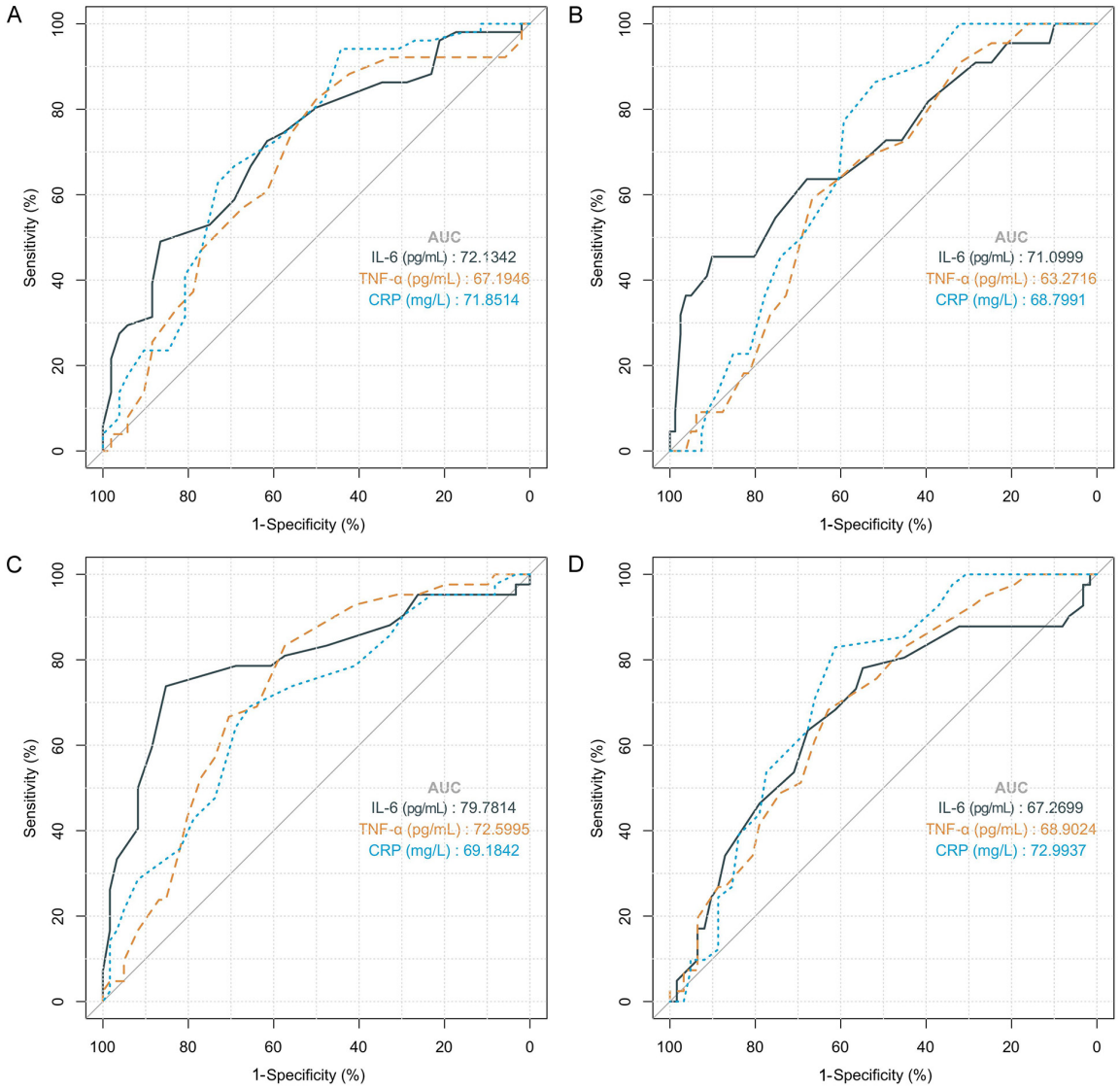

Figure 5. ROC of diagnostic efficacy of serum inflammatory markers for clinical pathological characteristics of CRC. A. Diagnostic efficacy of markers for TNM staging in CRC patients. B. Diagnostic efficacy of markers for histological classification in CRC patients. C. Diagnostic efficacy of markers for lymph node metastasis in CRC patients. D. Diagnostic efficacy of markers for tumor diameter in CRC patients. Note: ROC, Receiver Operating Characteristic; CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis; AUC, area under the curve.

In correlation analysis, significant positive correlations were observed between IL-6, TNF-α, and CRP in pairwise comparisons, though all correlations were weak. Hence, these serum inflammatory markers may be independently regulated in CRC patients and may exhibit synergistic effects on disease progression. IL-6 and TNF-α are involved in tumor cell proliferation, angiogenesis, and metastasis of CRC, and they may have synergistic effects on CRC [24]. We further evaluated correlations between serum inflammatory markers and tumor markers. All serum inflammatory markers showed at least weak positive correlations with tumor markers, with moderate positive correlations observed only between IL-6 and AFP, and between CRP and CA125, demonstrating a potential association between the inflammatory microenvironment of CRC and tumor burden. As shown by ROC curve analysis, in CRC, IL-6 showed the optimal diagnostic performance for TNM staging (AUC: 0.721), histological classifi-

Table 4. Diagnostic efficacy of serum inflammatory markers in evaluating clinical pathological characteristics of CRC

Item		AUC	95% CI	Optimal cut-off value	Sensitivity	Specificity
TNM staging (I-II vs. III-IV)	IL-6 (pg/mL)	0.721	0.623-0.819	35.5	49.02%	86.54%
	TNF-α (pg/mL)	0.672	0.566-0.778	35.5	82.35%	50.00%
	CRP (mg/L)	0.719	0.619-0.818	22.5	94.12%	44.23%
Histological classification (ductal adenocarcinoma vs. mucinous adenocarcinoma)	IL-6 (pg/mL)	0.711	0.582-0.840	38.5	45.45%	90.12%
	TNF-α (pg/mL)	0.633	0.517-0.749	39.5	59.09%	66.67%
	CRP (mg/L)	0.688	0.585-0.791	24.5	86.36%	51.85%
Lymph node metastasis (no vs. yes)	IL-6 (pg/mL)	0.798	0.703-0.892	34.5	73.81%	85.25%
	TNF-α (pg/mL)	0.726	0.628-0.824	36.5	83.33%	57.38
	CRP (mg/L)	0.692	0.588-0.796	25.5	69.05%	65.57%
Tumor diameter (< 3 cm vs. ≥ 3 cm)	IL-6 (pg/mL)	0.673	0.563-0.782	30.5	78.05%	54.84%
	TNF-α (pg/mL)	0.689	0.588-0.790	37.5	68.29%	62.90%
	CRP (mg/L)	0.730	0.634-0.826	24.5	82.93%	61.29%

Note: CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis; AUC, area under the curve; 95% CI, 95% confidence interval.

Table 5. Clinical data of the two groups

Data	Training group (n = 103)	Validation group (n = 44)	$Z/t/\chi^2$ value	*P* value
Sex			0.580	0.446
Male	61 (59.22)	29 (65.91)		
Female	42 (40.78)	15 (34.09)		
Age (years)	64.83±7.08	66.68±6.33	1.496	0.137
Body mass index (kg/m^2)	23.00 (22.00, 24.00)	23.00 (21.25, 24.00)	-0.060	0.952
Smoking history	25 (24.27)	12 (27.27)	0.147	0.701
Alcoholism history	28 (27.18)	13 (29.55)	0.085	0.770
Diabetes	31 (30.10)	11 (25.00)	0.392	0.531
Hypertension	15 (14.56)	8 (18.18)	0.306	0.580
TNM staging			0.204	0.652
I-II	52 (50.49)	24 (54.55)		
III-IV	51 (49.51)	20 (45.45)		
Histological typing			0.034	0.854
Ductal adenocarcinoma	81 (78.64)	34 (77.27)		
Mucinous adenocarcinoma	22 (21.36)	10 (22.73)		
Lymph node metastasis			0.580	0.446
No	61 (59.22)	29 (65.91)		
Yes	42 (40.78)	15 (34.09)		
Tumor diameter			0.018	0.894
< 3 cm	62 (60.19)	27 (61.36)		
≥ 3 cm	41 (39.81)	17 (38.64)		
IL-6 (pg/mL)	32.47±6.86	32.89±5.88	0.354	0.724
TNF-α (pg/mL)	38.03±6.36	37.57±7.07	0.388	0.698
CRP (mg/L)	25.62±5.92	24.57±6.96	0.933	0.352

Note: IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis.

cation (AUC: 0.711), and LNM (AUC: 0.798); CRP showed the optimal diagnostic performance for tumor diameter (AUC: 0.730); and TNF-α showed the optimal sensitivity for LNM

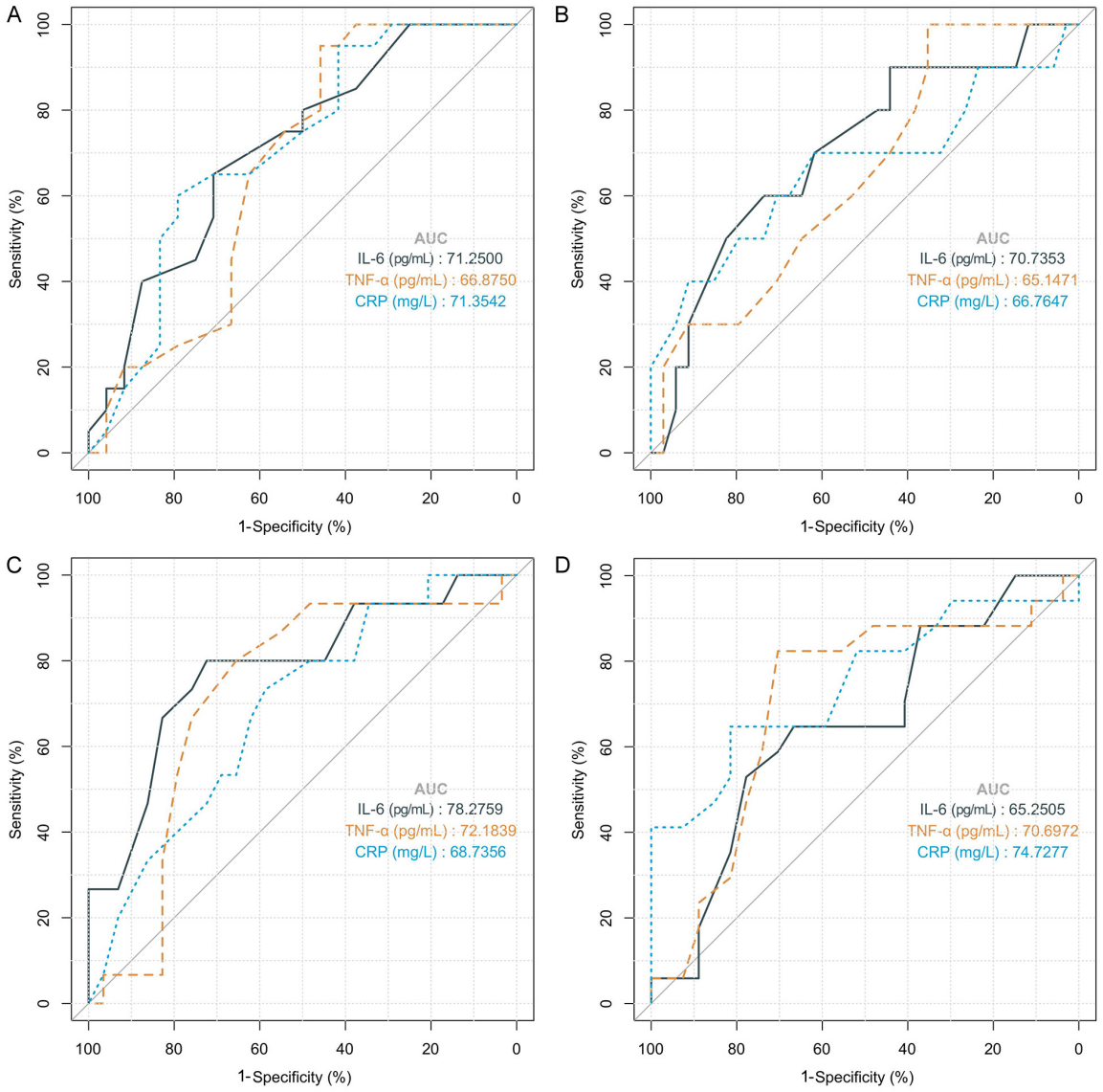

Figure 6. ROC analysis of the diagnostic efficacy of various inflammatory markers for the clinicopathological features of CRC patients in the validation set. A. Diagnostic efficacy of markers for TNM staging. B. Diagnostic efficacy of markers for histological subtyping. C. Diagnostic efficacy of markers for lymph node metastasis. D. Diagnostic efficacy of markers for tumor diameter. Note: ROC, Receiver Operating Characteristic; CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis; AUC, area under the curve.

(83.33%) and specificity for tumor diameter (62.90%) in CRC. All the above suggest that IL-6 can serve as a reliable auxiliary serum marker for CRC tumor staging, malignant degree, and LNM, with the highest clinical decision-making value for LNM; CRP has the greatest advantage in evaluating CRC tumor burden, and TNF-α may be used as a supplementary marker for CRC LNM and tumor burden. Xiao J et al. [25] reported that IL-6 combined with CEA increased the diagnostic efficacy to 0.583 for LNM. In contrast, IL-6 in this study demonstrated higher diagnostic efficacy for predicting LNM in CRC. Rauduvytė K et al. [26] reported that preoperative TNF-α levels predicted stable postoperative outcomes in patients undergoing colorectal cancer surgery (AUC = 0.722), offering new directions for the clinical application of TNF-α herein. Park BS et al. [27] further indicated that CRP levels on postoperative day 2 aid in predicting postoperative infection complications following laparo-

Table 6. Diagnostic efficacy of serum inflammatory markers in evaluating clinicopathological features of CRC

Categories		AUC	95% CI	Optimal cutoff	Sensitivity	Specificity
TNM staging (I-II vs. III-IV)	IL-6 (pg/mL)	0.713	0.561-0.864	33.50	65.00%	70.83%
	TNF-α (pg/mL)	0.669	0.507-0.831	34.50	95.00%	45.83%
	CRP (mg/L)	0.714	0.560-0.867	26.50	60.00%	79.17%
Histological classification (ductal adenocarcinoma vs. mucinous adenocarcinoma)	IL-6 (pg/mL)	0.707	0.523-0.891	30.50	90.00%	44.12%
	TNF-α (pg/mL)	0.651	0.470-0.833	34.50	100.00%	35.29%
	CRP (mg/L)	0.668	0.448-0.887	25.00	70.00%	61.76%
Lymph node metastasis (no vs. yes)	IL-6 (pg/mL)	0.783	0.634-0.932	33.50	80.00	72.41
	TNF-α (pg/mL)	0.722	0.561-0.883	38.50	80.00	65.52
	CRP (mg/L)	0.687	0.527-0.848	23.50	73.33	58.62
Tumor diameter (< 3 cm vs. ≥ 3 cm)	IL-6 (pg/mL)	0.653	0.486-0.819	33.50	64.71	66.67
	TNF-α (pg/mL)	0.707	0.542-0.872	38.50	82.35	70.37
	CRP (mg/L)	0.747	0.589-0.906	27.50	64.71	81.48

Note: CRC, Colorectal cancer; IL-6, Interleukin-6; TNF-α, Tumor necrosis factor-alpha; CRP, C-reactive protein; TNM, Tumor-Node-Metastasis; AUC, area under the curve; 95% CI, 95% confidence interval.

scopic colorectal surgery, which provides fresh insights for the clinical application of CRP herein. Finally, we found that IL-6, TNF-α, and CRP showed robust and consistent diagnostic efficacy across the training and validation sets. On the one hand, it strongly confirmed the potential of systemic inflammatory reaction as a reliable auxiliary diagnostic index in CRC progression, and on the other, it strengthened the high potential of IL-6 in predicting CRC LNM (AUC > 0.78).

In conclusion, IL-6, TNF-α, and CRP were abnormally elevated in CRC. These three markers can be used for auxiliary screening of clinical pathological characteristics in CRC, providing more useful references for clinical management and decision-making.

Disclosure of conflict of interest

None.

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