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The Predictive Value of the Preoperative Fibrinogen-to-Prealbumin Ratio for Overall Survival in Patients with Resectable Stage I - III Colorectal Cancer

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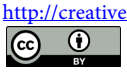

Abstract

Objective: This paper aims to evaluate the prognostic value of the preoperative fibrinogen-to-prealbumin ratio (FPR) for 5-year overall survival (OS) in patients with resectable stage I - III colorectal cancer (CRC). **Methods:** This retrospective cohort included 159 patients with stage I - III CRC who underwent R0 resection at Jingzhou Central Hospital between January and December 2020. Clinicopathological characteristics, preoperative laboratory indices, and follow-up data were collected. X-tile 3.6.1 was used to determine optimal cut-off values. Receiver operating characteristic (ROC) analysis, Kaplan-Meier survival analysis with the log-rank test, and univariable and multivariable Cox proportional hazards models were performed. **Results:** The optimal FPR cut-off for 5-year OS was 30.7342, yielding 119 patients in the low-FPR group and 40 in the high-FPR group. Patients with high FPR were older and more frequently had stage III disease, elevated CA19-9, and perineural invasion (all $P < 0.05$). The AUC of FPR for predicting 5-year OS was 0.717 (95% CI, 0.639 - 0.795). Five-year OS rates were 62.2% and 22.5% in the low- and high-FPR groups, respectively (log-rank $\chi^2 = 48.564$, $P < 0.001$). FPR significantly stratified survival among patients with stage III disease ($\chi^2 = 18.256$, $P < 0.001$), but not among those with stage I or II disease. Multivariable Cox analysis showed that high FPR (HR = 2.544, 95% CI, 1.550 - 4.170, $P < 0.001$), CEA, and CA19-9 were independently associated with poorer OS. **Conclusion:** Preoperative FPR is associated with long-term survival after curative resection for stage I - III CRC and may serve as a simple adjunct for postoperative risk stratification, particularly in stage III disease.

Keywords

Colorectal Cancer, Fibrinogen, Prealbumin, Fibrinogen-to-Prealbumin

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Ratio, Overall Survival, Prognosis

1. Introduction

Colorectal cancer is one of the most common malignant tumors of the digestive system. With advancements in standardized radical surgical procedures, perioperative management, and adjuvant therapies, long-term survival rates have improved for some patients; however, significant variations in disease outcomes can still be observed among patients with identical pathological stages. Current clinical risk assessment primarily relies on TNM staging, histological differentiation, vascular or neural invasion, as well as biomarkers such as CEA and CA19-9. These markers predominantly reflect the anatomical or biological characteristics of the tumor itself and do not fully capture the impact of host inflammatory responses, immune status, and nutritional reserves on prognosis. Therefore, identifying auxiliary prognostic indicators that are stable in origin, cost-effective, and readily obtainable preoperatively holds practical significance for further identification of high-risk populations.

Systemic inflammation and nutritional imbalance are increasingly recognized as important factors in tumor development, disease progression, and treatment response. Inflammatory cells and cytokines can influence tumor cell proliferation, angiogenesis, invasion, and metastasis, while also reshaping the immune microenvironment. Persistent inflammation may, in turn, promote protein catabolism and nutrient depletion, thereby creating a host environment that is less favorable for effective antitumor immunity. Previous studies have shown that several inflammation- and nutrition-related biomarkers derived from routine blood tests, including the neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), and prognostic nutritional index (PNI), are associated with prognosis in colorectal cancer [1].

Fibrinogen (FIB) is a crucial acute-phase reactant; elevated levels can reflect systemic inflammation or may participate in tumor cell adhesion, angiogenesis, and tumor-associated coagulation processes. Prealbumin (PAB) has a relatively short half-life and is highly sensitive to recent changes in protein synthesis and nutritional status. The fibrinogen-to-prealbumin ratio (FPR), derived from these two biomarkers, integrates both inflammatory and nutritional dimensions into a single clinical indicator. Previous cohort studies involving colorectal cancer patients across stages I - III or II - III have demonstrated that elevated preoperative FPR is associated with poorer survival outcomes and may possess independent prognostic value [2]-[6].

Based on this premise, this study conducted a retrospective analysis of patients with stage I - III colorectal cancer who underwent radical resection, aiming to evaluate the relationship between preoperative FPR and 5-year overall survival (OS), compare it with other inflammatory nutritional markers, and investigate its prognostic stratification value using stratified survival analysis and Cox regres-

sion, with the goal of providing a simple auxiliary indicator for postoperative prognosis assessment in colorectal cancer.

2. Materials and Methods

2.1. Study Subjects

This study is a single-center retrospective cohort study. Patients with colorectal cancer who underwent radical surgery at Jingzhou Central Hospital between January 1, 2020, and December 31, 2020, and whose cases were confirmed by postoperative pathological examination, were enrolled in this study.

Inclusion criteria: 1) Postoperative pathological diagnosis of colorectal adenocarcinoma, including histological subtypes such as mucinous adenocarcinoma and signet-ring cell carcinoma; 2) Receipt of R0 radical resection with negative surgical margins; 3) Staging according to the 8th edition of the American Joint Committee on Cancer (AJCC) staging system as stage I - III; 4) No prior antitumor therapy (e.g., radiotherapy, chemotherapy, or targeted therapy) administered before surgery; 5) Complete availability of clinicopathological data, preoperative laboratory tests, and follow-up records.

Exclusion criteria: 1) Concomitant presence of other malignant tumors; 2) Concomitant severe dysfunction of vital organs such as the heart, liver, or kidneys; 3) Presence of active infection, autoimmune disease, or any other significant inflammatory disorder; 4) Preoperative evidence of significant coagulation abnormalities; 5) Missing critical clinical data or follow-up information (Figure 1). After applying the inclusion and exclusion criteria and excluding cases with missing key data, a total of 159 patients were ultimately enrolled in this study, comprising 95 males (59.7%) and 64 females (40.3%).

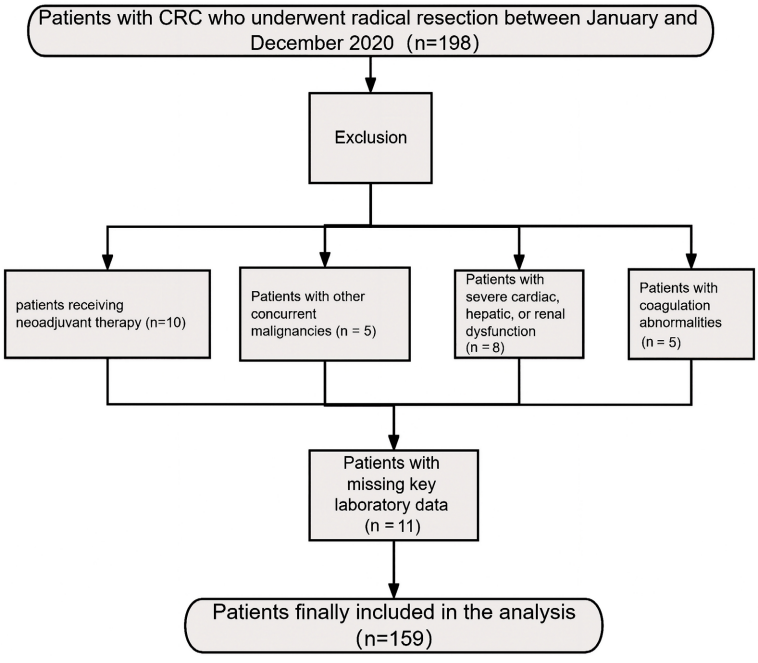

Figure 1. The participant selection flow chart of this study.

2.2. Clinical Data and Laboratory Parameters

Clinical and pathological data, including patient age, gender, primary site of tumor, pathological TNM stage, histological differentiation grade, nerve invasion, and vascular invasion, were collected via the hospital's electronic medical record system.

Collect laboratory test results completed within one week prior to surgery, including FIB, albumin (ALB), PAB, neutrophil count, lymphocyte count, monocyte count, platelet count, as well as CEA and CA19-9. For all parameters, the most recent preoperative test results obtained after excluding potential interfering factors such as overt acute infections shall be used.

2.3. Calculation of Inflammatory Nutritional Markers

FPR = FIB (mg/L)/PAB (mg/L); if the laboratory reports FIB in g/L, the value should be converted to mg/L before calculation. The fibrinogen-to-albumin ratio (FAR) = FIB (g/L)/ALB (g/L).

NLR = Neutrophil count/Lymphocyte count; LMR = Lymphocyte count/Monocyte count; PNI = ALB (g/L) + 5 × Lymphocyte count ($\times 10^9$/L); SII = Platelet count × Neutrophil count/Lymphocyte count.

2.4. Follow-Up and Study Endpoints

Patient postoperative survival status was obtained by combining electronic medical record queries with telephone follow-up; follow-up continued until January 2026. Overall survival (OS) was defined as the interval from the date of radical surgery to death from any cause or the date of the last follow-up visit. This study used 5-year OS as the primary endpoint.

2.5. Statistical Analysis

Using X-tile 3.6.1 software, optimal cutoff values for FPR and other inflammatory and nutritional indicators were determined based on survival outcomes, and patients were subsequently grouped accordingly. Statistical analyses were performed using SPSS 26.0 software.

Continuous variables conforming to a normal distribution are expressed as mean ± standard deviation; intergroup comparisons were performed using the independent samples t-test. Continuous variables that do not conform to a normal distribution are expressed as median (interquartile range); intergroup comparisons were conducted using the Mann-Whitney U test. Categorical variables are presented as number of cases (percentage); depending on the characteristics of the data, the χ^2 test or Fisher's exact test was employed for analysis.

The Time-dependent receiver operating characteristic (ROC) curves were used to assess the ability of inflammatory and nutritional markers to predict 5-year overall survival (OS). The area under the curve (AUC) and its 95% confidence interval (CI) were calculated for each marker. Patients who had not completed 5 years of follow-up were considered censored in the survival analysis. Kaplan-

Meier curves were generated to estimate survival, and differences between groups were examined using the log-rank test. Variables associated with OS were first evaluated by univariate Cox regression analysis. Those showing statistical significance were then entered into the multivariate Cox regression model. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient Baseline Characteristics and FPR Grouping

A total of 159 patients were included in the analysis, comprising 95 men (59.7%) and 64 women (40.3%). The median age was 62 years (range, 54 - 69 years). Of the study population, 32 patients (20.1%) had stage I disease, 56 (35.2%) had stage II disease, and 71 (44.7%) had stage III disease. The primary tumor was located in the colon in 75 cases (47.2%) and in the rectum in 84 cases (52.8%). During the follow-up period, 76 deaths occurred.

Using X-tile software, the optimal cutoff value of preoperative FPR for 5-year overall survival (OS) was determined to be 30.7342. Patients were subsequently divided into a low-FPR group (FPR < 30.7342, n = 119) and a high-FPR group (FPR ≥ 30.7342, n = 40). Compared with the low-FPR group, the high-FPR group exhibited older age [66 (57 - 73) years vs. 61 (53 - 69) years, P = 0.031], a higher proportion of TNM stage III patients (62.5% vs. 38.7%, P = 0.015), a higher incidence of elevated CA19-9 levels (87.5% vs. 68.1%, P = 0.029), and a significantly higher rate of nerve invasion (47.5% vs. 26.9%, P = 0.026). No statistically significant differences were observed between the two groups regarding gender, tumor location, histological differentiation grade, or vascular invasion (all P > 0.05) (Table 1).

Table 1. Comparison of clinicopathological characteristics among patients at different FPR levels.

variable	classify	Overall (n = 159)	Low FPR group (n = 119)	High FPR group (n = 40)	P price
Age (years)	Median (IQR)	62 (54 - 69)	61 (53 - 69)	66 (57 - 73)	0.031
sex	Man	95 (59.7)	68 (57.1)	27 (67.5)	0.332
	Woman	64 (40.3)	51 (42.9)	13 (32.5)	
TNM by stages	I designated time	32 (20.1)	27 (22.7)	5 (12.5)	0.245
	II designated time	56 (35.2)	46 (38.7)	10 (25.0)	0.170
	III designated time	71 (44.7)	46 (38.7)	25 (62.5)	0.015
Differentiation degree	well-differentiated	25 (15.7)	20 (16.8)	5 (12.5)	0.692
	Moderately differentiated	114 (71.7)	85 (71.4)	29 (72.5)	1.000
	Poorly differentiated	20 (12.6)	14 (11.8)	6 (15.0)	-

Continued

Tumor location	Colon	75 (47.2)	59 (49.6)	16 (40.0)	0.386
	Rectum	84 (52.8)	60 (50.4)	24 (60.0)	
Elevated CA19-9 levels	>37 U/mL	116 (73.0)	81 (68.1)	35 (87.5)	0.029
Neural invasion	Have	51 (32.1)	32 (26.9)	19 (47.5)	0.026
Vascular invasion	Have	54 (34.0)	39 (32.8)	15 (37.5)	0.724

Note: Count data are expressed as n (%); IQR denotes the interquartile range; FPR refers to the fibrinogen-to-prealbumin ratio.

3.2. ROC Analysis of Inflammatory Nutritional Markers

The ROC analysis demonstrated that all indicators exhibited varying degrees of discriminative ability for 5-year overall survival (OS). Among these, SII showed the highest AUC value at 0.925 (95% CI: 0.884 - 0.962); the AUC values for NLR, LMR, and PNI were 0.841, 0.830, and 0.825, respectively. The AUC for FPR was 0.717 (95% CI: 0.639 - 0.795), which was higher than that of FAR (0.630; 95% CI: 0.538 - 0.712). These results indicate that although FPR did not demonstrate the highest discriminative ability among the indicators in this study, it could simultaneously reflect both inflammatory status and nutritional status, thereby possessing distinct clinical interpretative value compared to purely immunoinflammatory markers (Table 2, Figure 2).

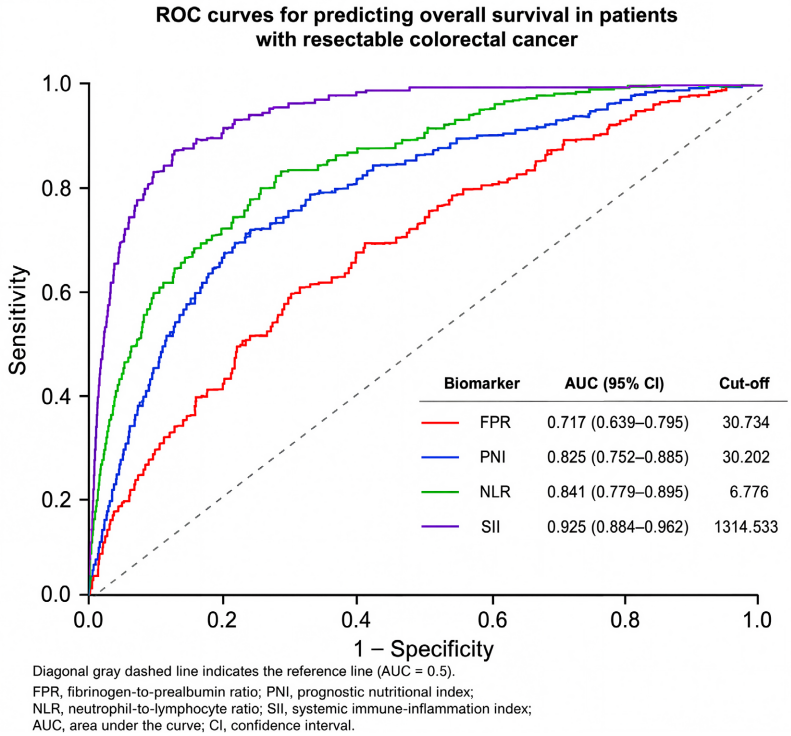

Figure 2. ROC curve for predicting 5-year overall survival (OS) using inflammatory and nutritional biomarkers.

Table 2. ROC analysis of various inflammatory nutritional markers for predicting 5-year overall survival (OS).

metric	Cut-off	AUC	95% CI
FPR	30.7342	0.717	0.639 - 0.795
FAR	0.1443	0.630	0.538 - 0.712
PNI	30.202	0.825	0.752 - 0.885
LMR	2.3971	0.830	0.764 - 0.890
NLR	6.7755	0.841	0.779 - 0.895
SII	1314.5325	0.925	0.884 - 0.962

Note: AUC refers to the area under the ROC curve; CI refers to the confidence interval.

Figure 2 shows the ROC curves for FPR, PNI, NLR, and SII; the AUC values for other indicators are presented in Table 2.

3.3. Kaplan-Meier Survival Analysis and TNM Staging Subgroup Analysis

The Kaplan-Meier survival analysis demonstrated that the overall survival (OS) rate in the high FPR group was significantly worse than that in the low FPR group, with the two survival curves gradually diverging during the early follow-up period. The 5-year OS rates were 62.2% in the low FPR group versus 22.5% in the high FPR group; the Log-rank test confirmed that this difference was statistically significant ($\chi^2 = 48.564$, $P < 0.001$) (Figure 3).

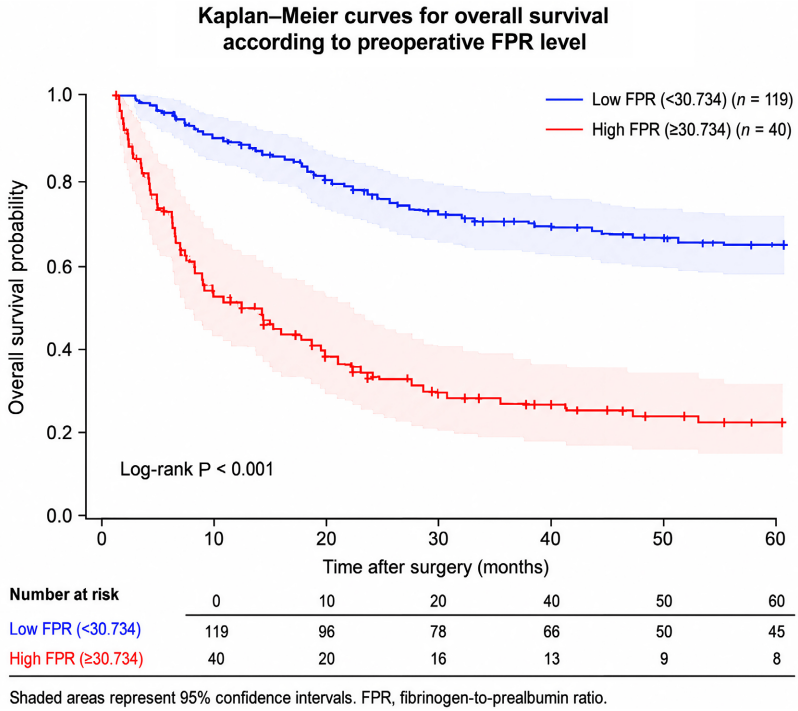

Figure 3. Kaplan-Meier curves depicting overall postoperative survival in patients at dif-

ferent FPR levels.

Further subgroup analyses were conducted based on the TNM staging system. Among patients with stage III disease, a significant difference in overall survival (OS) was observed between the high FPR group and the low FPR group (Log-rank χ^2 = 18.256, P < 0.001); however, among patients with stage I (χ^2 = 1.025, P = 0.311) and stage II (χ^2 = 2.158, P = 0.142), no statistically significant differences in OS were detected across different FPR levels. These findings indicate that the prognostic stratification effect of FPR in this study cohort is primarily evident in patients with stage III disease.

3.4. Cox Proportional Hazards Regression Analysis

Univariate Cox regression analysis demonstrated that FPR, CEA, and CA19-9 were significantly associated with overall survival (OS) in patients (all P < 0.05), whereas age, gender, TNM stage, nerve invasion, and vascular invasion did not reach statistical significance in the univariate analysis. When FPR, CEA, and CA19-9 were included in the multivariate Cox model, elevated FPR remained independently associated with a higher mortality risk (HR = 2.544, 95% CI: 1.550 - 4.170, P < 0.001); CEA (HR = 1.005, 95% CI: 1.001 - 1.009, P = 0.017) and CA19-9 (HR = 1.010, 95% CI: 1.004 - 1.016, P = 0.001) were also independently associated with OS (Table 3).

Table 3. Univariate and multivariate Cox regression analyses of factors influencing 5-year overall survival (OS) in patients with colorectal cancer after surgery.

variable	Single-factor HR	95%CI	P price	multiple factor HR	95%CI	P price
FPR (High vs. Low)	2.419	1.520 - 3.850	<0.001	2.544	1.550 - 4.170	<0.001
age	1.009	0.990 - 1.028	0.391	1.002	0.982 - 1.022	0.841
sex	0.751	0.456 - 1.237	0.228	0.765	0.471 - 1.243	0.285
TNM by stages	1.220	0.910 - 1.635	0.190	0.771	0.552 - 1.077	0.143
CEA	1.006	1.002 - 1.010	0.002	1.005	1.001 - 1.009	0.017
CA19-9	1.009	1.004 - 1.014	0.001	1.010	1.004 - 1.016	0.001
Neural invasion	1.544	0.976 - 2.441	0.064	1.364	0.850 - 2.188	0.205
Vascular invasion	1.376	0.895 - 2.116	0.174	1.270	0.780 - 2.608	0.341

Note: HR denotes the hazard ratio; 95% CI refers to the 95% confidence interval. In the multivariate model, variables with P < 0.05 from the univariate analysis were included.

4. Discussion

This study examined the relationship between the preoperative fibrinogen-to-prealbumin ratio (FPR) and overall survival in patients with resectable stage I - III colorectal cancer. ROC analysis identified 30.7342 as the optimal cutoff value. Patients with an FPR above this threshold had a markedly lower 5-year overall sur-

vival rate, and FPR remained an independent adverse prognostic factor after multivariable adjustment. Overall, these results are in line with previous reports on preoperative FPR in stage I - III colorectal cancer [2]-[6] and support its potential use in postoperative prognostic assessment.

One potential advantage of FPR is that it reflects both systemic inflammation and nutritional status rather than a single biological process. Fibrinogen (FIB), as an acute-phase protein, usually increases in response to systemic inflammation. In patients with cancer, persistent inflammatory activity may promote tumor progression by creating conditions that favor tumor growth, invasion, and metastasis. Prealbumin (PAB) provides information from a different perspective. As a negative acute-phase protein, its concentration may decrease during inflammation and is also commonly used to assess nutritional status. Thus, a low PAB level may indicate poor nutritional reserve, an increased inflammatory burden, or both. An elevated FPR may therefore represent a state in which systemic inflammation and nutritional impairment occur simultaneously. Both inflammatory responses and malnutrition are common in colorectal cancer and have been associated with poorer clinical outcomes [7]-[10].

We also found that a high FPR was significantly associated with more advanced TNM stage. Patients with elevated FPR values may therefore tend to have a greater disease burden and, potentially, more aggressive clinicopathological characteristics. Similar relationships between nutritional status, systemic inflammatory markers, tumor characteristics, and survival have been described in previous studies [8]-[13]. This association should nevertheless be interpreted cautiously. Because the present study was retrospective, it cannot establish that an elevated FPR has a direct role in driving tumor progression. It is more likely that FPR acts as a surrogate measure of the patient's inflammatory and nutritional condition, which changes in parallel with increasing disease severity.

An interesting finding from the ROC analysis was that FPR did not have the highest AUC among the six inflammation- and nutrition-related markers examined. SII, NLR, LMR, and PNI all showed higher AUC values, whereas FPR performed better than FAR. This result is important when considering how FPR should be positioned clinically. Its value may not come from being the strongest single discriminator. Rather, it provides a different type of information. NLR and LMR are mainly derived from circulating immune cell counts and reflect systemic inflammation and immune status, while SII is intended to capture the balance among inflammatory and immune components. FPR is based on fibrinogen and prealbumin and therefore incorporates information related to both inflammation/coagulation and nutritional status. In this sense, it may complement, rather than replace, blood cell-based inflammatory indices. Another practical point is that FPR can be calculated directly when FIB and PAB are already included in routine preoperative blood testing. No additional assay is required, which makes repeated assessment relatively straightforward in clinical practice. Previous studies have likewise explored the use of FPR in colorectal cancer diagnosis and risk

stratification [4] [14] [15].

The stage-stratified analysis yielded another finding of potential clinical interest. FPR clearly separated survival outcomes among patients with stage III colorectal cancer, whereas no statistically significant difference was observed in stage I or stage II disease. Several explanations are possible. Stage III tumors are generally associated with a higher tumor burden and regional lymph-node involvement, conditions that may be accompanied by a stronger systemic inflammatory response and greater nutritional disturbance. FPR may therefore be more sensitive to differences in host status in this setting. At the same time, the stage I and II subgroups contained relatively few patients and survival events. Limited statistical power could have obscured a genuine prognostic difference. For this reason, the stronger discriminatory ability observed in stage III disease should be considered exploratory. The current data are not sufficient to conclude that the prognostic relevance of FPR is confined to patients with stage III colorectal cancer.

CEA and CA19-9 were also identified as independent predictors of overall survival in the multivariable analysis. These markers and FPR may describe different dimensions of risk. CEA and CA19-9 are more closely related to tumor burden and biological behavior, whereas FPR primarily reflects the host response, particularly systemic inflammation and nutritional depletion. Their prognostic information is therefore unlikely to be entirely redundant. In practice, evaluating FPR together with TNM stage, CEA, CA19-9, and established high-risk pathological features may help identify patients who warrant closer postoperative surveillance or more individualized follow-up. However, such an approach remains hypothetical in the present study. We did not construct or validate a combined prediction model, and there is no evidence from our data that changing treatment on the basis of FPR would improve long-term survival. At present, FPR should therefore be regarded as an adjunctive risk-stratification marker rather than an alternative to TNM staging or established treatment decision-making systems.

A further advantage of FPR is its simplicity. Both fibrinogen and prealbumin can be obtained from routine preoperative blood tests, without the need for expensive molecular assays or specialized platforms. Similar composite indices combining inflammatory and nutritional variables have shown prognostic potential in gastric cancer, hepatocellular carcinoma, and other malignancies [16] [17]. Direct comparison across studies, however, remains difficult. Differences in laboratory procedures, baseline patient characteristics, treatment strategies, and methods used to select cutoff values can all affect the reported results. The cutoff of 30.7342 derived from our cohort should therefore not be assumed to apply to other institutions or populations. External validation in an independent cohort is needed before a fixed threshold can be recommended for broader clinical use.

Several limitations need to be considered when interpreting these findings. First, this was a retrospective study conducted at a single center, and selection bias could not be completely avoided. Some potentially relevant confounding variables were also unavailable or were not included in the analysis. Second, only 159 pa-

tients were enrolled. The number of survival events became even smaller after stratification by TNM stage, which limits the robustness of the subgroup findings and makes validation in a larger cohort particularly important. Third, FPR was assessed only once before surgery. We were unable to examine whether postoperative changes in FPR, or fluctuations during adjuvant treatment, were associated with recurrence or treatment response. Finally, overall survival was the main endpoint. Disease-free survival, recurrence patterns, and molecular subtypes of colorectal cancer were not evaluated in the current analysis.

Further studies are needed to confirm these findings in larger, multicenter prospective cohorts. In addition, changes in FPR over time may be more informative than a single preoperative measurement. Serial assessment before surgery, after surgery, and during adjuvant therapy could help clarify whether dynamic changes in FPR are related to disease progression or long-term outcome. Future studies could also incorporate FPR into prognostic models together with established clinicopathological factors and molecular characteristics. The extent to which FPR adds prognostic value beyond currently available models requires further investigation.

5. Conclusion

Preoperative FPR was significantly associated with postoperative survival in patients with stage I - III colorectal cancer undergoing curative-intent resection. Patients with a high FPR had poorer 5-year OS, and an elevated FPR remained independently associated with an increased risk of death after adjustment for other prognostic factors. As a composite inflammation- and nutrition-related marker derived from routinely available preoperative laboratory tests, FPR may provide complementary prognostic information in addition to conventional clinicopathological factors. In the present cohort, its ability to stratify survival appeared more evident among patients with stage III disease, although this subgroup finding requires confirmation in larger independent cohorts. Multicenter prospective studies are needed to validate an appropriate cutoff value and to determine whether incorporating FPR into established clinical models can improve prognostic assessment and risk stratification in colorectal cancer.

Ethical Statement

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Jingzhou Central Hospital (Approval No.: 2025-177-01; Date: 2025-07-29). The requirement for informed consent was waived because the study used anonymized retrospective clinical data. All procedures complied with the principles of the Helsinki Declaration.

Author Contributions

Conceptualization, Tianlong Zhou and Zilong Zhang; methodology, Tianlong

Zhou and Zilong Zhang; software, Tianlong Zhou; validation, Tianlong Zhou and Zilong Zhang; formal analysis, Tianlong Zhou; investigation, Tianlong Zhou and Fangyan Lu; resources, Tianlong Zhou; data curation, Tianlong Zhou and Fangyan Lu; writing—original draft preparation, Tianlong Zhou; writing—review and editing, Tianlong Zhou and Zilong Zhang; visualization, Tianlong Zhou; supervision, Zilong Zhang; project administration, Zilong Zhang. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All authors declare that there are no conflicts of interest related to this article.

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