RESEARCH REPORT

Prognostic significance of preoperative fibrinogen in patients with colon cancer

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Abstract

AIM: To investigate the prognostic significance of preoperative fibrinogen levels in colon cancer patients.

METHODS: A total of 255 colon cancer patients treated at the Affiliated Tumor Hospital of Xinjiang Medical University from June 1st 2005 to June 1st 2008 were enrolled in the study. All patients received radical surgery as their primary treatment method. Preoperative fibrinogen was detected by the Clauss method, and all patients were followed up after surgery. Preoperative fibrinogen measurements were correlated with a number of clinicopathological parameters using the Student *t* test and analysis of variance. Survival analyses were performed by the Kaplan-Meier method and Cox regression modeling to measure 5-year disease-free survival (DFS) and overall survival (OS).

RESULTS: The mean preoperative fibrinogen concentration of all colon cancer patients was 3.17 ± 0.88 g/L. Statistically significant differences were found between preoperative fibrinogen levels and the clinicopathological parameters of age, smoking status, tumor size, tumor location, tumor-node-metastasis (TNM) stage, modified Glasgow prognostic scores (mGPS), white blood cell (WBC) count, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and carcinoembryonic antigen (CEA) levels. Univariate survival analysis showed that TNM stage, tumor cell differentiation grade, vascular invasion, mGPS score, preoperative fibrinogen, WBC, NLR, PLR and CEA all correlated with both OS and DFS. Alpha-fetoprotein (AFP) and body mass index correlated only with OS. Kaplan-Meier analysis revealed that both OS and DFS of the total cohort, as well as of the stage Ⅱ and Ⅲ patients, were higher in the hypofibrinogen group compared to the hyperfibrinogen group (all *P* < 0.05). In contrast, there was no significant difference between OS and DFS in stage Ⅰ patients with low or high fibrinogen levels. Cox regression analysis indicated preoperative fibrinogen levels, TNM stage, mGPS score, CEA, and AFP levels correlated with both OS and DFS.

CONCLUSION: Preoperative fibrinogen levels can serve as an independent prognostic marker to evaluate patient response to colon cancer treatment.

Core tip: Inflammatory cytokines have been implicated in the development of several malignancies, including colon cancer. Specifically, fibrinogen has been correlated with some clinicopathological factors of cancer. However, the prognostic value of fibrinogen measurements remains unclear, particularly in colon cancer patients. In this study, preoperative fibrinogen levels were correlated with a poor prognosis in a cohort of colon cancer patients. These data suggest that preoperative fibrinogen levels can serve as an independent prognostic factor for colon cancer patients following radical surgery.

INTRODUCTION

Recently, the incidence of gastrointestinal cancer has increased as standards of living have improved. Colon cancer is one of the most common malignancies of the digestive track in humans. Early detection is strongly correlated with an improved prognosis, thus it is important to develop simple, non-invasive methods to accurately detect colon cancer and assess patient prognosis. Recent evidence indicates that fibrinogen, a major protein in the blood clotting process, is linked to a number of malignancies[1-4]. Elevated fibrinogen levels have been correlated with tumor progression, invasiveness, and metastasis[5-7]. However, the role of fibrinogen in colon cancer remains unclear.

To assess the prognostic significance of fibrinogen for colon cancer patients, preoperative fibrinogen levels, clinicopathological parameters, and follow-up data were analyzed from a cohort of 255 colon cancer patients undergoing radical surgery. The results indicate that preoperative fibrinogen levels correlate with a number of cancer clinicopathological parameters, and are negatively correlated with 5-year survival rates. Therefore, fibrinogen measurements could provide a useful prognostic tool for colon cancer patients.

MATERIALS AND METHODS

Patients and clinicopathological parameters

Clinicopathological parameters and follow-up data were assessed from 255 colon cancer patients (135 male, 120 female) who received radical surgery in the Affiliated Tumor Hospital of Xinjiang Medical University between June 1st 2005 and June 1st 2008. Mean patient age was 59.47 ± 12.63 years. Prior to participation, a diagnosis of colon cancer was confirmed by histopathology for all patients. Tumor-node-metastasis (TNM) stage was determined according to the American Joint Committee on Cancer/International Union Against Cancer TNM staging system of colorectal cancer (2010, 7th edition). The American Society of Anesthesiologists score of the patients was 1 in 198 cases and 2 in 57 cases. No patient received preoperative chemotherapy or immunotherapy. The presence of complex metastases, such as uncertain lumps, micrometastases (particularly in the liver), and abdominal/pelvic lymph node metastases, were diagnosed using enhanced computed tomography, magnetic resonance imaging, positron emission tomography-computed tomography, and puncture biopsies.

The following criteria were used to exclude patients: confirmed metastasis (39 cases), use of procoagulant or anticoagulant drugs within 8 wk of the enrollment (11 cases), hepatitis infection (23 cases), kidney disease (9 cases), myocardial infarction (14 cases), hypertension (47 cases), or other infectious or hematologic diseases which could influence fibrinogen levels (22 cases). Postoperative adjuvant chemotherapy was administered to stage Ⅱ patients with high-risk factors (including poor differentiation, large lumps, T4 stage, less than 1 cm of tumor resection margin, fewer than 12 lymph nodes for postoperative biopsy) and stage Ⅲ patients.

Blood samples were obtained by phlebotomy; 5-7 d prior to surgery, 2 mL of blood was collected from each patient. Preoperative fibrinogen levels were measured by the Clauss standard method with bovine thrombin (100 NIH U/mL).

Follow-up assessments

After surgery, patients underwent follow-up assessments once every 3 mo for the first 2 years, and then once every 6 mo until 5 years after surgery. Follow-ups were either by outpatient or inpatient review, or by telephone. Thirty patients did not participate in follow-up analyses because they did not maintain any communication with physicians after surgery. In addition, 3 patients developed dysthymia and were unable to cooperate with the study procedures, one patient committed suicide due to the burden of the cancer, and 2 patients did non participate in follow-up assessments for unknown reasons. Therefore, the total follow-up rate in the study was 88.2%.

Ethics

The study design and procedures described below were approved by the Ethics Committee of the Affiliated Tumor Hospital of Xinjiang Medical University (No. W-201305). All patients provided informed written consent prior to their participation.

Statistical analysis

All data is presented as mean ± SD. Univariate analyses of preoperative fibrinogen and each clinicopathological parameter were performed using the Student *t*-test and

Table 1 Correlations between preoperative fibrinogen and clinicopathological parameters

Parameters	*n*	Fibrinogen (g/L, mean ± SD)	*P* value
Age (yr)			
< 60	119	3.29 ± 1.01	0.047
≥ 60	136	3.07 ± 0.73	
Nationality			
Han	216	3.16 ± 0.87	0.892
Uygur	30	3.24 ± 0.92	
Others	9	3.12 ± 0.94	
BMI (kg/m²)			
< 18.5	8	3.54 ± 0.82	0.638
18.5-23.99	115	3.15 ± 0.94	
24-27.99	102	3.14 ± 0.83	
≥ 28	30	3.23 ± 0.79	
Smoking			
Never	173	3.06 ± 0.82	0.018
Light	18	3.43 ± 0.74	
Heavy	64	3.39 ± 0.99	
Grade (tumor differentiation)			
Low	203	3.12 ± 0.86	0.080
High	52	3.36 ± 0.92	
TNM			
I	29	2.70 ± 0.58	0.002
II	139	3.24 ± 0.95	
III	87	3.21 ± 0.78	
Tumor size (cm)			
< 4	51	2.81 ± 0.72	0.000
4-6	114	3.01 ± 0.73	
≥ 6	90	3.57 ± 0.98	
Type			
Mess type	104	3.13 ± 0.87	0.390
Ulceration	148	3.21 ± 0.89	
Infiltrative	3	2.58 ± 0.13	
Tumor location			
Left	155	3.06 ± 0.82	0.020
Right	89	3.38 ± 0.97	
Transverse	11	2.99 ± 0.55	
Perineural invasion			
Yes	7	3.40 ± 0.59	0.488
No	248	3.16 ± 0.88	
Vascular invasion			
Yes	13	3.29 ± 0.94	0.619
No	242	3.16 ± 0.87	
CEA (ng/mL)			
< 5	161	3.08 ± 0.89	0.038
≥ 5	94	3.32 ± 0.84	
AFP (ng/mL)			
< 5	231	3.17 ± 0.88	0.747
≥ 5	24	3.11 ± 0.82	
mGPS			
0	163	3.00 ± 0.77	0.000
1	71	3.37 ± 0.94	
2	21	3.80 ± 1.00	
WBC count			
< 5 × 10⁹/L	61	2.68 ± 0.56	0.000
≥ 5 × 10⁹/L	194	3.32 ± 0.90	
NLR			
< 5	238	3.13 ± 0.86	0.013
≥ 5	17	3.69 ± 1.02	
PLR			
< 150	134	2.96 ± 0.75	0.000
150-300	105	3.41 ± 0.96	
> 300	15	3.40 ± 0.83	

AFP: Alpha-fetoprotein; BMI: Body mass index; CEA: Carcinoembryonic antigen; mGPS: Modified Glasgow prognostic score; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; TNM: Tumor-node-metastasis; WBC: White blood cell.

analysis of variance. Survival rates were determined using the Kaplan-Meier method and the log-rank test to perform comparisons between the hypofibrinogen (< 2.61 g/L) and hyperfibrinogen (≥ 2.61 g/L) groups. Multivariate survival analysis was performed using the Cox regression model to determine relative risk (RR) and 95% confidence interval (CI). All statistical analyses were carried out using SPSS for Windows, version 18 (SPSS Inc., Chicago, IL, United States). Statistical significance was defined by $P \leqslant 0.05$.

RESULTS

Correlations between preoperative fibrinogen levels and clinicopathological parameters of colon cancer patients

The mean level of preoperative fibrinogen levels of all 255 colon cancer patients was 3.17 ± 0.88 g/L. Statistical analyses were performed to assess any relationships between fibrinogen levels and clinicopathological factors (Table 1). Preoperative fibrinogen levels were associated with age, smoking status, tumor size, tumor location, TNM stage, modified Glasgow prognostic (mGPS) score, white blood cell (WBC) count, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and carcinoembryonic antigen (CEA) levels ($P < 0.05$ for all parameters). Meanwhile, preoperative fibrinogen was not related to the patient's nationality, body mass index (BMI), tumor grade, gross tumor type, tumor invasion into the nervous or lymphatic system, or serum alpha-fetoprotein (AFP) levels.

Prognostic analysis of clinicopathological parameters in colon cancer patients

To determine the prognostic significance, preoperative fibrinogen and other clinicopathological factors were correlated with the 5-year disease-free survival (DFS) and overall survival (OS) rates of the patient cohort (Table 2). Results show that TNM stage, tumor grade, vascular invasion status, mGPS score, preoperative fibrinogen, WBC count, NLR, PLR, and CEA levels were all significantly correlated with both OS and DFS rates (all $P < 0.05$). In addition, AFP and BMI were significantly correlated with OS ($P < 0.05$). In contrast, no significant relationship was observed between prognosis and age, nationality, smoking status, gross tumor type, tumor location, or perineural invasion status.

Survival analysis of patients with different preoperative fibrinogen levels

Given the correlation observed between preoperative fibrinogen and DFS and OS rates, the effect of fibrinogen levels on patient survival was examined. Patients were divided into hyperfibrinogen (> 2.61 g/L) or hypofibrinogen (< 2.61 g/L) groups. Kaplan-Meier survival analyses were performed to determine 5-year OS and DFS rates for each group. Among the entire cohort, both OS and DFS rates were higher in the hypofibrinogen group compared with the hyperfibrinogen group (Figure 1A; $P <$

Table 2 Univariate survival analyses of clinicopathological parameters

Parameters	*n*	5-yr DFS	χ^2	*P* value	5-yr OS	χ^2	*P* value
Age (yr)							
< 60	119	49.3%	0.301	0.583	64.90%	0.616	0.432
≥ 60	136	47.7%			61.80%		
Nationality							
Han	216	51.3%	3.185	0.203	64.60%	3.477	0.176
Uygur	30	34.4%			48.80%		
Others	9	33.3%			76.20%		
BMI (kg/m²)							
< 18.5	8	37.5%	3.905	0.272	50%	9.296	0.026
18.5-23.99	115	46.5%			55.60%		
24-27.99	102	54.4%			74.00%		
≥ 28	30	39.7%			59.30%		
Smoking							
Never	173	49.1%	0.079	0.961	65.00%	0.153	0.927
Light	18	50.0%			60.20%		
Heavy	64	47.7%			61.40%		
Grade							
Low	203	52.7%	5.948	0.015	67.10%	4.482	0.034
High	52	32.7%			49.30%		
TNM							
I	29	78.7%	38.724	0.000	86.20%	28.420	0.000
II	139	57.3%			70.60%		
III	87	25.2%			43.90%		
Type							
Mess type	104	54.3%	2.523	0.283	68%	3.088	0.213
Ulceration	148	44.1%			59.30%		
Infiltrative	3	27.2%			0		
Tumor location							
Left	155	51.8%	2.992	0.224	67.20%	5.563	0.062
Right	89	42.0%			54.30%		
Transverse	11	54.5%			81.80%		
Perineural invasion							
Yes	7	42.9%	0.551	0.458	42.90%	2.108	0.147
No	248	48.6%			63.90%		
Vascular invasion							
Yes	13	15.4%	8.432	0.004	30.80%	7.747	0.005
No	242	50.3%			65.10%		
CEA (ng/mL)							
< 5	161	56.6%	18.630	0.000	71.20%	15.269	0.000
≥ 5	94	33.6%			49.10%		
AFP (ng/mL)							
< 5	231	49.7%	3.568	0.059	65.20%	5.117	0.024
≥ 5	24	35.0%			43.20%		
mGPS							
0	163	58.9%	79.236	0.000	77.80%	90.552	0.000
1	71	60.2%			49.80%		
2	21	0.0%			4.80%		
WBC count							
< 5 × 10⁹/L	61	60.9%	4.032	0.045	76.70%	4.870	0.027
≥ 5 × 10⁹/L	194	44.8%			59.30%		
NLR							
< 5	238	50.1%	6.060	0.014	64.70%	4.754	0.029
≥ 5	17	25.0%			43.80%		
PLR							
< 150	134	55.6%	11.095	0.004	71.20%	11.772	0.003
150-300	105	43.0%			57.20%		
> 300	15	20.0%			33.30%		
Fibrinogen (g/L)							
< 2.61	74	77.0%	26.717	0.000	87.20%	20.255	0.000
≥ 2.61	181	36.9%			53.60%		

DFS: Disease-free survival; OS: Overall survival; BMI: Body mass index; TNM: Tumor-node-metastasis; CEA: Carcinoembryonic antigen; AFP: Alpha-fetoprotein; mGPS: Modified Glasgow prognostic scores; WBC: White blood cell; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

0.05). Furthermore, hyperfibrinogen was associated with significantly reduced OS and DFS rates in stage II and III colon cancer patients (Figure 1C, D; *P* < 0.05), but not in patients with stage I disease (Figure 1B). However,
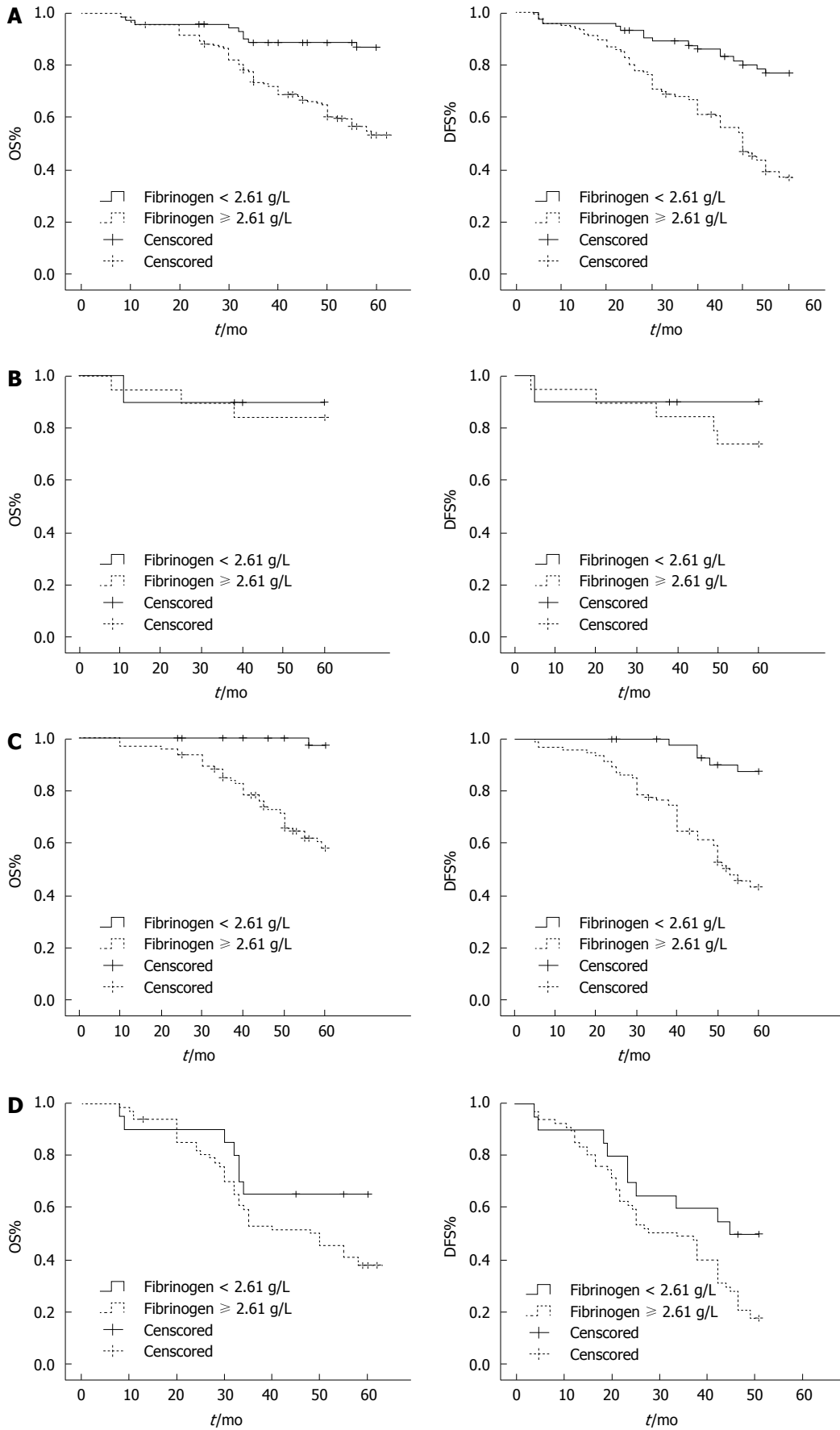
Figure 1 Kaplan-Meier curves of hyperfibrinogen and hypofibrinogen colon cancer groups. A: Entire patient cohort; B: Stage Ⅰ; C: Stage Ⅱ; D: Stage Ⅲ. 1 and 2 stand for the 5-yr overall survival (OS) and 5-yr disease-free survival (DFS), respectively. Both OS and DFS of the entire cohort, stage Ⅱ, and stage Ⅲ patients were significantly higher in the hypofibrinogen (< 2.61 g/L) group than in the hyperfibrinogen (≥ 2.61 g/L) group (*P* < 0.05).

Table 3 Cox proportional hazards model analyses for overall survival and disease-free survival

Parameters	5-yr OS			5-yr DFS		
	P value	RR	95%CI	*P* value	RR	95%CI
PLR	0.330	0.825	0.560-1.215	0.274	0.835	0.604-1.154
NLR	0.262	1.541	0.724-3.282	0.109	1.701	0.889-3.255
WBC count	0.384	1.318	0.708-2.452	0.547	1.161	0.715-1.886
AFP	0.002	2.583	1.406-4.744	0.008	2.111	1.218-3.656
CEA	0.010	1.779	1.146-2.762	0.002	1.762	1.223-2.539
Vascular invasion	0.456	1.359	0.606-3.047	0.528	1.260	0.614-2.585
Fibrinogen	0.001	3.324	1.620-6.821	0.000	2.940	1.707-5.064
BMI	0.401	0.888	0.674-1.171	-	-	-
TNM	0.000	2.583	1.704-3.916	0.000	2.405	1.722-3.360
Grade	0.538	0.851	0.511-1.420	0.892	0.970	0.629-1.497
mGPS	0.000	2.968	2.137-4.122	0.000	2.400	1.799-3.201

RR: Relative risk; CI: Confidence interval; PLR: Platelet-lymphocyte ratio; NLR: Neutrophil-lymphocyte ratio; WBC: White blood cell; AFP: Alpha-fetoprotein; CEA: Carcinoembryonic antigen; BMI: Body mass index; TNM: Tumor-node-metastasis; mGPS: Modified Glasgow prognostic scores.

Table 4 Studies on fibrinogen in different malignancies

Ref.	Country	*n*	Pre-therapeutic plasma fibrinogen (g/L)	Cancer type	Prognosis DFS/OS
Takeuchi *et al*[1] (2007)	Japan	105	3.86 ± 1.02	Esophageal cancer	No, neither
Polterauer *et al*[2] (2009)	Austria	313	4.17 ± 1.30	Cervical cancer	Yes, both
Polterauer *et al*[3] (2009)	Austria	422	4.50 ± 1.50	Ovarian cancer	Yes, both
Ghezzi *et al*[4] (2010)	Italy	336	hyper: 40.8%	Endometrial cancer	Yes, both
Zhao *et al*[5] (2012)	China	160	4.72 ± 1.46	Non-small cell lung cancer	DFS, no; OS, yes
Son *et al*[6] (2013)	South Korea	624	3.25 ± 0.88	Non-metastatic colon cancer	Yes, both
Zhu *et al*[7] (2013)	China	275	3.92 (0.68-9.80)	Non-small cell lung cancer	Yes, both

DFS: Disease-free survival; OS: Overall survival.

the lack of a significant association with stage I disease may be related to the relatively small sample size for this patient group.

Survival analysis of different clinicopathological parameters

Cox regression analyses showed that preoperative fibrinogen, TNM stage, mGPS score, CEA and AFP levels were significantly associated with both 5-year OS and 5-year DFS ($P < 0.05$). For DFS, the strongest predictive factor was preoperative fibrinogen levels (RR: 2.940; 95%CI: 1.707-5.064, $P < 0.05$), followed by TNM stage, mGPS, AFP and CEA levels. Similarly, fibrinogen was the strongest predictor for OS (RR: 3.324; 95%CI: 1.620-6.821, $P < 0.05$), followed by mGPS, TNM stage, AFP and CEA (Table 3). These data indicate that preoperative fibrinogen plays an important role in the prognosis of colon cancer patients who receive radical surgery.

DISCUSSION

Recent evidence has indicated that there are links between inflammation and cancer development[8]. In addition to the genetic basis of cancer, the host inflammatory response can play an important role in tumor progression[9,10]. In particular, inflammatory cytokines are associated with a number of cancer types and contribute to tumorigenesis by promoting tumor cell proliferation,

invasion, or metastasis, which can have dramatic effects on patient prognosis. Several inflammatory markers that are readily detectable in plasma are currently being investigated as prognostic factors for cancer patients, as well as for their role in tumor biology. These markers include monocyte chemo-attractant proteins[11,12], WBC count, NLR[13,14], PLR[11,15], and fibrinogen[16], among others. However, there is currently no consensus concerning their efficacy to assess patient prognosis[1-3].

Fibrinogen is synthesized in the liver as a 350 kDa glycoprotein. Fibrinogen plays an important role in blood coagulation, thrombosis, wound healing, and platelet aggregation. Moreover, recent studies suggest fibrinogen is associated with cancer development (Table 4). As a component of the extracellular matrix, fibrinogen can affect cell behavior through interactions with other matrix proteins, or the cell itself. Fibrinogen has been associated with increased tumor growth and metastatic potential, although the precise mechanism remains unclear. One potential mechanism involves fibrinogen's influence on tumor cell proliferation, migration, and signaling through interactions with multiple integrin and non-integrin receptors. Another possible mechanism is the promotion of tumor angiogenesis, as fibrinogen has been shown to cooperate with growth factors, including vascular endothelial and fibroblast growth factors, to stimulate angiogenesis[17-19]. Furthermore, the fibrinolytic system derived from fibrinogen also plays a facilitating role in both an-

giogenesis and the proliferation process of tumor cells[20].

Several lines of evidence indicate that fibrinogen can promote tumor cell metastasis. The fibrinolytic system stimulates adhesion between tumor cells and platelets or endothelial cells, thereby promoting the dissemination of tumor cells into the bloodstream[21]. Studies using fibrinogen-deficient mice have indicated that fibrinogen is an important factor in the metastasis of circulating tumor cells[22]. In addition, fibrinogen can suppress natural killer cell-mediated tumor cell clearance, leading to an increase in the number of metastatic cells[23]. Taken together, these data suggest that fibrinogen is involved in tumor cell invasion and metastasis, further supporting its potential as a prognostic factor for cancer patients.

In clinical studies, pre-treatment fibrinogen levels have been associated with clinicopathological factors in a number of cancers. Fibrinogen has been correlated with the depth of tumor invasion, tumor size, and WBC and platelet counts[1]. Elevated fibrinogen levels are associated with lymph node metastasis and distant metastasis. Fibrinogen has also been correlated with clinicopathological factors such as age and BMI[3]. In our study, we analyzed additional clinicopathological parameters in colon cancer patients, and found that preoperative fibrinogen levels correlated with several cancer-relevant factors, including age, smoking status, tumor size, tumor location, TNM stage, mGPS score, WBC count, NLR, and PLR. The results of this study also support previous reports demonstrating that smoking, which confers a high risk of tumor development, is correlated with serum fibrinogen levels[24]. However, the mechanisms linking smoking and fibrinogen in cancer patients remain unclear.

Tumor progression is the result of complex interactions between tumor cells and the host environment[25] and the host inflammatory response. Tumors can occur at sites of inflammation, such as during hepatitis virus or *H. pylori* infection, and can also trigger the release of pro-inflammatory cytokines to promote an inflammatory microenvironment that favors tumorigenesis[26,27]. The elevation of fibrinogen levels in colon cancer patients may be the result of tissue damage and subsequent inflammatory responses[28]. For example, tumors can induce a hypercoagulable and hypoxic state through a variety of mechanisms, including the stimulation of an inflammatory response[18,21,29]. Thus, it is likely that elevated fibrinogen reflects the host-tumor response[15]. However, tumor cells can produce endogenous fibrinogen, suggesting that other sources may also contribute[18]. Consistent with this evidence, results from this study indicate that serum fibrinogen is closely related with other inflammatory markers, such as the mGPS score, WBC count, NLR and PLR, suggesting that fibrinogen reflects the inflammatory status of colon cancer tumors.

A systemic inflammatory response prior to surgery may reflect the presence of an additional disease or a change in the patient's physiology[30]. Several studies have demonstrated that fibrinogen levels can serve as an independent prognostic factor for cancer patients. For example, fibrinogen levels were closely associated with both 5-year DFS and OS in a cohort of 313 cervical cancer patients[2]. A similar analysis of a cohort of 422 ovarian cancer patients led to the same conclusion[3]. In colon cancer patients, systemic inflammatory markers can predict patient survival following radical resection[15] and provide independent prognostic risk factors for tumor specificity and OS for these patients[31].

A Cox regression statistical analysis in the present study showed that preoperative fibrinogen level was closely associated with prognosis of patients with colon cancer, which is in contrast to the results of Takeuchi *et al*[1], who found that serum fibrinogen was not associated with prognosis in 105 esophageal cancer patients. Furthermore, survival analyses indicated that both the 5-year OS and DFS of the entire cohort, as well as of stage II and stage III patients, were significantly higher in the hypofibrinogen group compared to the hyperfibrinogen group. These results are consistent with previous studies investigating inflammation and colon cancer, and suggest that fibrinogen can serve as a useful prognostic marker for colon cancer patients.

In conclusion, this study demonstrates that fibrinogen is closely associated with several clinicopathological features and 5-year survival rates of colon cancer patients. Furthermore, elevated preoperative fibrinogen levels were found to predict poor survival in colon cancer patients. These data suggest that preoperative fibrinogen is a promising prognostic marker for colon cancer patients receiving radical surgery. Moreover, fibrinogen-based therapies may provide a novel therapeutic approach for treating colon cancer.

COMMENTS

Background
Inflammation, including inflammatory cytokines, plays an important role in the incidence, invasion, and metastasis of several tumors. However, as an inflammation precursor, the role of fibrinogen in tumors, particularly colon cancer, remains unclear.

Research frontiers
Increasing evidence indicates that the host inflammatory response plays an important role in tumor development and progression. Inflammatory mediators and cytokines secreted by inflammatory cells are elevated in tumors and promote proliferation, invasion or metastasis, which consequently have an impact on patient prognosis. These inflammatory markers, including monocyte chemoattractant proteins, white blood cell counts, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and fibrinogen, are easily detected in plasma and therefore could represent useful prognostic markers. However, the prognostic value of inflammatory markers, particularly fibrinogen, remains unclear.

Innovations and breakthroughs
While there have been a number of studies on the relationship of fibrinogen and cancer, few have analyzed this relationship in colon cancer patients. In this study, the prognostic significance of preoperative fibrinogen in colon cancer patients was investigated. The results illustrate that preoperative fibrinogen is negatively correlated with prognosis in colon cancer patients who received radical surgery, suggesting that preoperative fibrinogen is a promising prognostic marker for colon cancer patients.

Applications
The study indicates that preoperative fibrinogen is an independent prognostic factor for colon cancer patients that undergo radical surgery. Consequently, preoperative fibrinogen may serve as a potential prognostic marker for colon

cancer patients. Moreover, anti-fibrinogen therapies may provide a novel strategy for treating colon cancer.

Terminology
Fibrinogen is a plasma glycoprotein that is involved in blood clot formation. Levels of this protein have been associated with tumor progression and metastasis in many cancer types.

Peer review
This study comprehensively analyzes the prognostic significance of preoperative fibrinogen levels in patients with colon cancer. The results suggest that preoperative fibrinogen is a promising independent prognostic factor for patients with colon cancer, and may provide a new target for colon cancer therapy.

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