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Circulating C-reactive protein and colorectal cancer risk: a report from the Shanghai Men's Health Study

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Chronic inflammation has been implicated in the pathogenesis of colorectal cancer. The objective of this study was to evaluate the association of prediagnostic circulating levels of C-reactive protein (CRP), a biomarker of systemic inflammation, with subsequent development of colorectal cancer. Prediagnostic plasma CRP levels were examined among 288 colorectal cancer cases and 576 individually-matched controls nested within the Shanghai Men's Health Study (2002–06), a population-based cohort study of 61 482 Chinese men. The association between CRP levels and colorectal cancer risk was investigated. Baseline plasma CRP levels were 53% higher among men who subsequently developed colorectal cancer than among those who remained free of the disease (1.15 versus 0.75 μg/ml; $P < 0.001$). Multivariate analyses showed a dose-dependent relationship between CRP and colorectal cancer risk (P trend = 0.003); men in the highest tertile (CRP > 1.19 μg/ml) had 1.88-fold (95% confidence interval (CI): 1.24–2.86) increased odds of developing colorectal cancer compared with men in the lowest tertile (CRP < 0.45 μg/ml). The association was only significant for colon cancer, when cancer site was considered, and was predominantly seen for cases diagnosed within 4 years of blood collection; adjusted odds ratios for the highest versus the lowest tertiles were 3.28 (95% CI: 1.28–8.37), 3.68 (95% CI: 1.62–8.38) and 1.05 (95% CI: 0.56–1.97), respectively, for cases diagnosed <2, 2–4 and >4 years after blood collection. The findings from our study suggest that circulating CRP level is positively associated with colorectal cancer risk in Chinese men, and this association, at least in part, is explained by inflammation-related cancerous or precancerous processes.

Introduction

Colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death in the USA, with an estimated total of 143 460 new cases and 51 690 deaths in 2012 (1).The lifetime risk of being diagnosed with cancer of the colon or rectum is ~5% for both men and women in the USA. In the past decade, the incidence rate of colorectal cancer has rapidly increased in Asian countries where incidence has traditionally been low, particularly among men, a change probably due to the adoption of a Westernized lifestyle (2,3).

Increasing evidence suggests that inflammation plays a key role in the pathogenesis of colorectal cancer. Patients with a history of chronic inflammatory bowel diseases, such as Crohn's disease and ulcerative colitis, have an increased risk of developing colorectal cancer (4–8), whereas regular use of non-steroidal anti-inflammatory drugs, such as aspirin, confers not only a significant reduction in colorectal cancer risk and adenoma recurrence, but also a lower risk of dying from colorectal cancer (9–13). Several well-established risk factors for colorectal cancer, such as smoking, physical inactivity, overweight and obesity (14), are known to be related to chronic inflammation.

C-reactive protein (CRP) is a sensitive but non-specific marker of systemic inflammation produced primarily by hepatocytes under transcriptional control by interleukin-6 in response to infection, trauma, surgery, burns, tissue infarction, advanced cancer and chronic inflammatory conditions (15). The association between circulating CRP levels and colorectal cancer has been previously evaluated in various populations (16–25). Several case–control studies have reported that colorectal cancer patients had a significantly higher level of CRP in preoperative blood compared with healthy controls (26–28). It has been suggested that high levels of CRP may be a result of disease progression and an indicator of poor outcomes (29–32). However, data from prospective cohort studies, where blood is collected before cancer diagnosis, have been inconsistent (16–23,33). Of eight prospective studies published before 2008, four demonstrated positive associations between circulating CRP levels and colorectal cancer incidence (16–19), whereas the remainder reported generally null or even inverse relationships (20–23). A recent report from the European Prospective Investigation into Cancer and Nutrition indicated a significant non-linear association between circulating CRP concentrations and colon cancer risk but not rectal cancer risk among men (33).

We evaluated the association of prediagnostic circulating CRP levels with subsequent development of colorectal cancer among 864 men in a case–control study nested within the Shanghai Men's Health Study (SMHS), a large population-based prospective cohort study conducted among Chinese men.

Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; RR, relative risk; SMHS, Shanghai Men's Health Study; WHR, waist:hip ratio.

Materials and methods

Study population

Details of the study design and methods have been described elsewhere (34,35). Briefly, between 2002 and 2006, the SMHS recruited 61 482 men who were aged 40–74 years, were free of cancer, and lived in one of eight urban communities of Shanghai, China (participation rate: 74.0%). At baseline, an in-person interview was conducted to collect information on sociodemographic characteristics (education, occupation and income), personal habits (smoking, alcohol consumption), occupational history, disease history and medication use, dietary habits, physical activity and other characteristics using a structured questionnaire. Anthropometric measurements, including current weight, height and circumferences of the waist and hips, were taken. Participants were asked to donate biological samples, including a blood or cheek cell sample and a spot urine sample, at the end of the interview. For blood sample collection, a 10 ml blood sample was drawn into an ethylenediaminetetraacetic acid vacutainer tube. The samples were kept in a portable Styrofoam box with ice packs (0–4°C), processed within 6 h and stored at −80°C until assays were conducted. The study was approved by the Institutional Review Boards for human research at Vanderbilt University in the USA and Shanghai Cancer Institute in China, and written informed consent was obtained from all study participants.

Case identification and control selection

The cohort has been followed for occurrence of cancer through a combination of annual record linkages with the Shanghai Cancer Registry and the Shanghai Vital Statistics databases and through in-home interviews taking place every 2–3 years. The response rate for the first (2004–07) and second (2008–11) follow-up surveys were 97.6 and 93.2%, respectively. Each year, the roster of the SMHS is linked with the Shanghai Cancer Registry database to identify cancer cases that occurred between the in-person surveys and among individuals who did not participate in the follow-up survey. All possible matches are verified by home visits and review of medical charts from the diagnostic hospital. Of the 369 colorectal cancer cases identified between the baseline enrollment and December 2009, 289 cases who donated a blood sample at baseline were included in the present study (colon cancer, $n = 173$; rectal cancer, $n = 116$).

The incidence-density method was used to select controls. For each case, two controls were selected from among cohort members who donated a blood sample at baseline and were free of any cancer at the time of cancer diagnosis for the index case. Controls were individually matched to cases on age at baseline (± 2 years), date (≤30 days) and time (morning or afternoon) of blood collection, vitamin use during the past week and interval since last meal (≤2 h).

Measurement of plasma levels of CRP

Plasma CRP levels were measured by using a Millipore Human CRP enzyme-linked immunosorbent assay kit (cat. no. CYT298) following the manufacturer's protocol. Briefly, 100 µl of diluted plasma samples were incubated in microtitration wells coated with polyclonal anti-human CRP antibody at room temperature for 30 minutes. After a thorough wash, polyclonal anti-human CRP antibody labeled with horseradish peroxidase was added to the wells and incubated with the immobilized antibody–CRP complex. Following another washing step, the remaining horseradish peroxidase-conjugated antibody was allowed to react with the substrate of tetramethylbenzidine. The reaction was stopped by the addition of acidic solution, and absorbance of the resulting yellow color product was measured spectrophotometrically at 450 nm. A standard curve and two controls (high and low) were run in each plate. All samples were measured in duplicate and the values were averaged. Samples from the matched case–control sets were analyzed in the same plate. The lower limit of detection of the assay is 0.20 ng/ml. All plasma samples were diluted (≥1:225) for measurement, and no samples had measurements below the detection limit. The interplate coefficients of variation for the two controls were 4.7% (high) and 6.7% (low), and the coefficients of variation for duplicate samples were <8.1% for all samples.

Statistical analyses

Case–control differences for selected baseline characteristics were assessed by using the chi-square test. The analysis of variance test was applied to compare CRP levels between cases and controls. CRP level was categorized by the tertile distribution of controls. The association between CRP levels and risk of colon and rectal cancer was analyzed using conditional logistic regression, with and without adjustment for conditions related to chronic inflammation, and possible confounders. Covariates adjusted for included smoking status; regular exercise; body mass index (BMI); waist:hip ratio (WHR); family history of any cancer; prior history of selected chronic inflammation-related diseases diagnosed before the baseline survey, including cardiovascular disease, diabetes, hypertension, prostatic hypertrophy, gastritis, gastrointestinal ulcer, bronchitis and polyps; use of antibiotics, non-steroidal anti-inflammatory drugs or antihypertension medication. Analyses were also carried out separately by cancer site (colon or rectum) and by years of follow-up.

Two-sided P values <0.05 were considered to be statistically significant. All statistical analyses were carried out using SAS software, version 9.3 (SAS Institute, Cary, NC).

Results

A total of 288 colorectal cancer cases and 576 controls were included in the analysis after exclusion of one colorectal cancer case with a CRP level >100 µg/ml (who may have had a transient acute infection) and two matched controls. The selected baseline characteristics for colorectal cancer cases and matched controls, including demographic variables, lifestyle factors, anthropometric measurements and disease history, are shown in Table I. The mean age was 63.1 years for cases. The demographic characteristics, including age at sample collection, education, income, occupation and marital status, did not substantially differ between cases and controls. No significant differences were found between cases and controls for smoking, alcohol consumption or exercise participation. Compared with controls, more cases were in the higher BMI and WHR categories (P = 0.014 and 0.001, respectively). A family history of cancer was more common among cases than controls (P = 0.011). More cases reported having a prior history of diseases that may be related to chronic inflammation than controls (P < 0.001).

Table II presents the baseline mean levels of plasma CRP in colorectal cancer cases and matched controls. The geometric means of plasma CRP were 53% higher among men who subsequently developed colorectal cancer compared with men who remained free of disease (1.15 versus 0.75 µg/ml; P < 0.001). In analyses stratified by tumor site, higher levels of CRP were observed for both colon cancer (1.23 versus 0.72 µg/ml; P < 0.001) and rectal cancer (1.03 versus 0.80 µg/ml; P = 0.033) compared with controls. The geometric means for the CRP levels of colon and rectal cancer cases were 71 and 29% higher, respectively, than the geometric means of controls.

Table I. Selected baseline characteristics of colorectal cancer cases and matched controls: SMHS (2002–06)[a]

Baseline characteristics	Cases (n = 288)	Controls (n = 576)	P
Age at sample collection (%)			
<60 years	34.0	33.7	
60–69 years	39.6	38.0	
≥70 years	26.4	28.3	0.826
Education (%)			
Primary school or below	12.5	14.1	
Middle school	34.3	30.6	
High school	23.7	29.6	
College or above	29.5	25.7	0.209
Income (%)			
<1000 yuan/month	52.3	55.6	
1000–1999	38.4	37.2	
≥2000	9.3	7.2	0.448
Occupation (%)			
Professional	35.5	37.7	
Clerical	20.1	17.0	
Manual laborer	44.4	45.3	0.494
Currently married (%)	86.1	86.7	0.815
Smoking			
Non-smoker	36.4	39.4	
Former smoker or light smoker	33.5	36.3	
Heavy smoker (≥10 cigarettes/day)	30.1	24.3	0.178
Regular alcohol consumption (%)	32.0	31.8	0.965
Regular exercise			
No	51.2	46.2	
METs <2.69	24.2	26.8	
METs ≥2.69	24.6	27.0	0.352
BMI			
<25	58.4	65.5	
25–29.9	36.4	32.4	
≥30	5.2	2.1	0.014
WHR			
<0.88	26.5	33.2	
≥0.88	24.3	30.6	
≥0.92	49.3	36.2	0.001
Family history of cancer (%)	38.0	29.4	0.011
Number of selected diseases[b]			
0–1	50.8	63.4	
2	26.0	22.9	
≥3	23.2	13.7	<0.001

MET, metabolic equivalent.
[a]Adjusted for age at sample collection.
[b]Includes diabetes, hypertension, cardiovascular diseases, prostatic hypertrophy, gastritis, gastrointestinal ulcer, bronchitis and polyps.

Associations between plasma CRP levels and risk of colon and rectal cancer are presented in Table III. Plasma CRP was positively associated with colorectal cancer risk in a dose-dependent manner. The relative risks (RRs) of developing colorectal cancer increased from 1.0 to 1.63 (95% confidence interval (CI): 1.11–2.40) and 2.32 (95% CI: 1.59–3.38) with increasing tertiles of plasma CRP (P trend <0.001). Positive associations were observed for both colon cancer (RR = 2.45, 95% CI: 1.53–3.91 for the upper versus lower tertiles; P trend <0.001) and rectal cancer risk (RR = 2.08, 95% CI: 1.11–3.91 for the upper versus lower tertiles; P trend = 0.031). After further adjustment for potential confounders and conditions that may be related to chronic inflammation, the association remained significant for colorectal cancer and colon cancer but lost significance for rectal cancer (for the upper versus lower tertiles, RR = 1.88, 95% CI: 1.24–2.86, P trend = 0.003 for colorectal cancer; RR = 2.05, 95% CI: 1.20–3.50, P trend = 0.008 for colon cancer and RR = 1.61, 95% CI: 0.81–3.21, P trend = 0.213 for rectal cancer). The association became stronger after excluding men who used antibiotics during the

Table II. Baseline plasma CRP levels of colorectal cancer cases and matched controls: SMHS (2002–06)[a]

	CRP levels (μg/ml)		Difference (%)	*P*
	Cases	Controls		
All colorectal cancers (288 sets)				
Geometric mean (95% CI)	1.15 (1.01–1.30)	0.75 (0.69–0.82)	53.3	<0.001**
Median (25th–75th percentile)	1.07 (0.54–2.42)	0.75 (0.36–1.68)	42.7	<0.001***
Colon cancer (172 sets)				
Geometric mean (95% CI)	1.23 (1.04–1.46)	0.72 (0.64–0.81)	70.8	<0.001**
Median (25th–75th percentile)	1.32 (0.53–2.71)	0.74 (0.34–1.56)	78.4	<0.001***
Rectal cancer (116 sets)				
Geometric mean (95% CI)	1.03 (0.85–1.25)	0.80 (0.70–0.91)	28.8	0.033**
Median (25th–75th percentile)	1.01 (0.58–2.06)	0.76 (0.37–1.78)	32.9	0.045***

[a]Adjusted for matched set and age at sample collection.
***P* values were derived from two-way analysis of variance for the case–control difference using log-transformed CRP data,
****P* values were derived from Wilcoxon signed rank sum test for case–control difference.

Table III. Association of baseline plasma CRP levels and subsequent risk of colorectal cancer: SMHS (2002–06)

CRP (μg/ml)	Cases	Controls	RR (95% CI)[a]	RR (95% CI)[b]	RR (95% CI)[c]
Colorectal cancer					
<0.45	60	192	1.0	1.0	1.0
0.45–1.19	94	191	1.63 (1.11–2.40)	1.51 (1.00–2.28)	1.61 (1.04–2.49)
>1.19	134	193	2.32 (1.59–3.38)	1.88 (1.24–2.86)	1.97 (1.26–3.08)
P for trend			<0.001	0.003	0.004
Colon cancer					
<0.45	36	117	1.0	1.0	1.0
0.45–1.19	48	110	1.43 (0.86–2.36)	1.44 (0.83–2.49)	1.62 (0.90–2.93)
>1.19	88	117	2.45 (1.53–3.91)	2.05 (1.20–3.50)	2.23 (1.25–3.99)
P for trend			<0.001	0.008	0.007
Rectal cancer					
<0.45	24	75	1.0	1.0	1.0
0.45–1.19	46	81	1.91 (1.04–3.50)	1.57 (0.82–3.01)	1.57 (0.80–3.08)
>1.19	46	76	2.08 (1.11–3.91)	1.61 (0.81–3.21)	1.58 (0.76–3.30)
P for trend			0.031	0.213	0.256

[a]Conditional logistic regression.
[b]Stratified by matched sets and adjusted for smoking status, regular exercise, BMI, WHR, family history of cancer, number of selected diseases reported at baseline, use of antibiotics in the 7 days before blood collection, use of antihypertension medication and ever use of non-steroidal anti-inflammatory drugs.
[c]Excluding men who had used antibiotics in the 7 days before blood collection.

7 days before blood collection (RR = 1.97, 95% CI: 1.26–3.08 for the upper versus lower tertiles; *P* trend = 0.004 for colorectal cancer). Additional analyses stratified by BMI and WHR found no evidence of interaction between these variables and plasma CRP levels (*P* interaction = 0.583 for BMI and 0.738 for WHR, data not shown).

The median time between blood sample collection and cancer diagnosis was 3.45 years. Additional analyses were carried out based on the time interval between blood sample collection and cancer diagnosis (<2, 2–4 and >4 years). A positive association was found for cases diagnosed <2 years after blood collection and for those diagnosed 2–4 years after blood collection (Table IV). The RRs increased as CRP increased from 1.0 for the lowest tertile (reference) to 1.77 for the middle tertile and 3.28 for the highest tertile for cases diagnosed <2 years after blood collection (*P* trend = 0.012) and from 1.0 for the lowest tertile (reference) to 2.40 for the middle tertile and 3.68 for the highest tertile for cases diagnosed between 2 and 4 years after blood collection (*P* trend = 0.002). No association was observed between CRP levels and colorectal cancer risk when diagnosis occurred >4 years after blood collection (RR = 1.05, 95% CI: 0.56–1.97 for the highest tertile compared with the lowest tertile; *P* trend = 0.942). Direct comparison of mean plasma CRP levels also showed significant or marginally significant case–control differences when cases were diagnosed <2 years or between 2 and 4 years after blood collection (*P* = 0.020 and 0.068, respectively), whereas no difference was seen for cases diagnosed >4 years after blood collection (*P* = 0.236). Sensitivity analyses, in which men who had used antibiotics in the 7 days before blood collection were excluded, showed similar association patterns.

Discussion

In this nested case–control study conducted among Chinese men, we found a positive association between prediagnostic circulating CRP levels, a sensitive biomarker of systemic inflammation, and colorectal cancer risk. The positive association was predominantly seen for colorectal cancer cases diagnosed within 4 years of blood collection.

Our findings are in line with the results of several previous prospective cohort studies. Erlinger *et al.* (16) found a significant association between baseline CRP levels and the subsequent risk of colon cancer in a case–control study nested in the Campaign Against Cancer and Heart Disease/CLUE II cohort. Similar positive associations between CRP and colorectal cancer risk were observed among male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study cohort (17) and in the Japan Public Health Center-Based Study cohort (18). These three studies reported a persistent association between plasma CRP and colorectal cancer risk after excluding colorectal cancer cases that occurred during the first 2 and 5 years (16), 5 and 10 years (17) and 2 years (18) of follow-up, respectively. The largest study to date, a case–control study nested within the European Prospective Investigation into Cancer and Nutrition study (1992–2003), which included 1096 incident colorectal cancer cases and 1096 controls, reported a significant,

Table IV. Association of baseline plasma CRP levels and subsequent risk of colorectal cancer by time interval between blood collection and cancer diagnosis: SMHS (2002–06)[a]

Interval (years)	CRP (μg/ml), geometric mean (95% CI)	*P*	CRP (μg/ml)			*P* trend
			<0.45	0.45–1.19	>1.19	
All participants						
<2 years						
Colorectal cancer cases	1.28 (0.98–1.66)		13	24	40	
Controls	0.86 (0.72–1.03)	0.020	48	53	53	
RR (95% CI)			1.0	1.77 (0.74–4.24)	3.28 (1.28–8.37)	0.012
2–4 years						
Colorectal cancer cases	0.86 (0.69–1.09)		20	27	39	
Controls	0.66 (0.56–0.78)	0.068	74	52	46	
RR (95% CI)			1.0	2.40 (1.06–5.39)	3.68 (1.62–8.38)	0.002
>4 years						
Colorectal cancer cases	0.99 (0.83–1.18)		27	43	55	
Controls	0.87 (0.77–0.98)	0.236	70	86	94	
RR (95% CI)			1.0	1.16 (0.62–2.18)	1.05 (0.56–1.97)	0.942
Excluding participants who had used antibiotics in the 7 days before blood collection						
<2 years						
Colorectal cancer cases	1.21 (0.93–1.58)		12	23	35	
Controls	0.88 (0.73–1.06)	0.061	45	51	48	
RR (95% CI)			1.0	2.14 (0.82–5.57)	3.43 (1.17–10.0)	0.025
2–4 years						
Colorectal cancer cases	0.87 (0.70–1.10)		18	26	35	
Controls	0.64 (0.55–0.75)	0.032	70	49	42	
RR (95% CI)			1.0	2.65 (1.08–6.50)	4.73 (1.90–11.8)	0.001
>4 years						
Colorectal cancer cases	0.93 (0.78–1.12)		26	40	47	
Controls	0.87 (0.76–0.98)	0.524	63	80	88	
RR (95% CI)			1.0	1.07 (0.55–2.07)	0.95 (0.48–1.87)	0.833

[a]RRs and geometric means were stratified by matched sets and adjusted for smoking status, regular exercise, BMI, WHR, family history of cancer, number of selected diseases reported at baseline, use of antibiotics in the 7 days before blood collection, use of antihypertension medication, and ever use of non-steroidal anti-inflammatory drugs.

non-linear association between circulating CRP levels and colon cancer risk but not rectal cancer risk with a median follow-up time of 3.7 years. Colon cancer risk was significantly increased among men (RR = 1.74, 95% CI: 1.11–2.73 for the upper versus lower tertiles; *P* trend = 0.01), but not among women (RR = 1.06, 95% CI: 0.67–1.68 for the upper versus lower tertiles; *P* trend = 0.13). In that study, the results also did not change appreciably after excluding subjects with a follow-up time of <3 years (33). In contrast, we found that CRP levels were not significantly associated with the risk of colorectal cancer for cases diagnosed >4 years after blood collection. It should be noted that the SMHS has a relatively short follow-up and the number of colorectal cancer cases diagnosed >4 years after blood collection was small. Our study, thus, may not have had adequate power to assess weak to moderate associations for cases diagnosed >4 years after blood collection. On the other hand, Ito *et al.* (21) reported no association between CRP levels and colorectal cancer risk among subjects enrolled in the Japan Collaborative Cohort Study with a 10 year follow-up, and Zhang *et al.* (20) observed an inverse relationship between plasma CRP levels and colorectal cancer risk among US women enrolled in the Women's Health Study with a maximum length of follow-up of 10.8 years (21). Both of these studies included only a small number of cases (169 and 141, respectively) and most participants were female (169 and 78, respectively) (20,21). A recent meta-analysis of eight prospective studies published before 2008 revealed a weak, positive association between circulating CRP levels and colorectal cancer risk (RR = 1.12, 95% CI: 1.01–1.25) and found that the association was stronger among men compared with women and stronger in nested case–control studies compared with case–cohort studies (36). No data on the association between CRP levels and colorectal cancer risk by length of follow-up were provided in this meta-analysis. Taken together, current epidemiological evidence, in general, supports the notion that low-grade systemic inflammation is associated with an increased risk of colorectal cancer in men.

Despite the well-recognized link between inflammation and cancer (4), the molecular and cellular mechanisms mediating the association are not entirely clear. In general, it is believed that inflammatory responses play a pivotal role in tumor development, including initiation, promotion, malignant conversion, invasion and metastasis. The inflammatory environment, which consists of an increase in cytokines, chemokines and reactive oxygen and nitrogen species, results in DNA mutations, epigenetic changes and genomic instability that can contribute to tumor initiation (37,38). Sustained or chronic inflammation may promote tumor progression by inhibiting the apoptosis of genetically altered cells and accelerating proliferation and angiogenesis (37–40). Finally, the close interaction of cancer cells, immune cells, stromal elements and the factors produced by each can act to promote both inflammatory status and cancer progression and metastasis (38,41,42).

Increased CRP levels may reflect inflammatory status before the clinical onset of cancer and/or host inflammatory response to existing advanced cancer. Despite the prospective nature of this study and the exclusion of participants with cancer at baseline, we cannot completely exclude clinically undetected cancer at baseline. Our finding that the positive association was predominantly seen in cases diagnosed within 4 years of baseline suggests that increased CRP level may be more of a marker of disease occurrence and progression. On the other hand, we found that a history of chronic inflammatory diseases was associated with colorectal cancer in our study, suggesting an involvement of inflammation in colorectal carcinogenesis.

Among the strengths of our study are its population-based, prospective cohort design and high follow-up rates, which minimized the potential for selection bias. The high assay sensitivity is critical for measuring CRP in a population with relatively low inflammation status, such as Chinese men. The mean level of plasma CRP among controls in this study was 0.76 μg/ml, which is 60–70% lower than levels found in US and European populations (1.9–2.6 μg/ml) (16,17,33) and close to levels reported in the Japanese population

(0.45 μg/ml) (18,21). Our study is limited by the relatively modest follow-up time, which limited our ability to evaluate the time sequence of the CRP–colorectal cancer association in more depth. In addition, the lack of data on other inflammation biomarkers, such as interleukin-6 and other proinflammatory cytokines, also hampered a more complete understanding of the role of inflammation in colorectal carcinogenesis.

In conclusion, we found that elevated circulating CRP levels were associated with higher risk for colorectal cancer in Chinese men, and this positive association was predominantly seen among colorectal cancer cases diagnosed within 4 years of blood collection. Our study results suggest that increased CRP level is a marker of colorectal occurrence and progression. Future studies are needed to evaluate the value of using CRP to guide the surveillance of high-risk populations for colorectal cancer.

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