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Original Research Article

Baseline C - Reactive Protein is Associated with Incident Cancer and Survival in Patients with Cancer

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Abstract

Aim: We hypothesized that baseline plasma C-reactive protein (CRP) levels are linked with incidence cancer in the general population and early death in cancer patients.

Methods: 500 baseline CRP-measured participants were followed for 1 year. The follow-up was 100% complete. We excluded individuals with a cancer diagnosis at baseline.

Results: CRP greater than 3 mg/L and the highest quartile had multifactorial adjusted hazard ratios for early cancer death. Localized cancer patients with elevated CRP died earlier than those with metastases.

Conclusion: Cancer-free people with elevated CRP risk cancer of any kind, lung cancer, and possibly colorectal cancer. Elevated baseline CRP also predicts early cancer death, especially in individuals without metastases.

Keywords: Baseline C - reactive protein, Cancer, Survival.

Introduction

A person may be predisposed to cancer by having an inflammatory milieu because of continuous low-grade inflammation, according to one theory [1]. Although C-reactive protein (CRP) is a member of the pentraxin family of conventional acute phase reactant proteins, a mild increase in CRP level has been seen in chronic inflammatory conditions [2]. Prior research has found links between blood CRP levels and lung, breast, and colorectal cancers [3], but there is conflicting or no evidence for links with other cancers. The first hypothesis contends that elevated CRP levels are a sign of cancer or a precancerous condition, whereas the second contends that elevated CRP and chronic inflammation may play a causal role in the development of cancer. As a result, it is still unknown if and to what extent CRP levels are related to cancer incidence as well as early death in cancer patients [4]. We investigated the relationship between baseline plasma levels of CRP and incident cancer risk in the overall population, taking into account the three most prevalent malignancies (breast, colorectal, and lung cancer), and we adjusted

for regression dilution bias. Also, we looked at the claim that individuals with cancer of any kind are more likely to die young if their baseline plasma levels of CRP are high.

Methods

The Rama Medical College in Hapur, Uttar Pradesh, was the site of the prospective cohort study. 500 people who had their plasma CRP evaluated between 2021 and 2022 were included in the investigation of plasma CRP levels with incident cancer. Due to the presumption that their ability to produce CRP would be compromised, we did not include participants who had liver cirrhosis that had been diagnosed before or during the study period. Also, we did not include participants in the analysis of the corresponding cancer subtypes who had received a cancer diagnosis of any kind or of another malignancy prior to study admission. We had 100% follow-up throughout the trial period. Cancer patients were tracked from the time of their diagnosis until either death or emigration, whichever happened first, during the follow-up period.

STATA version 10.0, a statistical analysis program, was used to examine the data (StataCorp, College Station, TX). P values were determined using Kruskal-Wallis one-way analysis of variance tests for continuous variables and two tests for categorical variables.

Results

Table 1: Baseline Characteristics of subjects

Characteristic	N	%	N	%	N	%	p- value
Sex, women	80	50.5	300	55.1	120	52.0	0.06
Ageatentry, years							<0.001
Median	40		56		60		
Interquartile range	30-55		44-70		52-71		
No. of cigarettes smoked per day							<0.001
Median	0		0		1		
Interquartile range	0-9		0-15		0-18		
Smoking							<0.001
Never	20	31.4	50	25.1	20	22.5	
Former	10	33.0	100	27.0	30	25.0	
Current	50	35.1	150	45.4	70	51.5	
Body mass index, kg/m^2							<0.001
<18.5	8	3.5	20	2.0	12	1.0	
18.5-24.9	40	65.1	130	51.0	38	35.0	
25-29.9	20	20.0	80	35.1	50	37.6	
≥30.0	12	4.2	70	11.0	20	24.0	
Current oral contraceptive Therapy among pre-menopausal women	60	15.0	120	27.2	100	45.5	<0.001
Postmenopausal status among women	200	66.0	350	68.6	220	68.0	0.35
Current hormone replacement Therapy among postmenopausal women	55	15.3	320	20.0	150	24.5	0.01

Table 2: Cancer incidence by plasma levels of C-reactive protein (P-CRP) stratified for cancer stage.

P-CRP (mg/L)	Participants	Localized	Metastases
Any cancer <1	18	P = 0.40	P = 0.001
1 to 3	60		
>3	30		
Lung cancer <1	10	P =0 .61	P =0 .03
1 to 3	100		
>3	28		
Colorectal cancer <1	22	P = 0.80	P = 0.02
1 to 3	70		
>3	30		
Breast cancer <1	10	P = 0.71	P = 0.95
1 to 3	32		
>3	12		
Other <1	20	P = 0.50	P = 0.10
1 to 3	38		
>3	20		

When we stratified for cancer type, stage, and histology, and for time from blood sampling to diagnosis, elevated levels of CRP were associated with early death separately in patients with other cancer, localized cancer. However, tests of interaction were all non-significant, suggesting that elevated CRP levels are associated with early death irrespective of cancer type and histology and time from blood sampling to diagnosis, but that elevated CRP levels are associated with early death in patients with cancer having localized disease, but not in those with metastases.

Discussion

In this prospective cohort trial, which included about 500 people followed for up to a year, we discovered that rising levels of CRP were linked to a higher risk of incident cancer of any kind, lung cancer, and perhaps colorectal cancer, but not breast cancer. Furthermore, we discovered that increased CRP levels were linked to early demise following a cancer diagnosis. What biological process underlies the link between CRP levels and the risk of developing cancer? The idea that increased CRP levels are a sign of latent cancer is supported by a number of findings. First, as a tumour grows, the tissues around it may become inflamed, which raises CRP levels in the blood [3].

Second, it has been demonstrated that some malignant cells express CRP and emit interleukin-6 and interleukin-8, which encourage the formation of CRP in the liver. Tumor cells are known to produce a variety of cytokines and chemokines that attract leukocytes [5,6]. Finally, CRP may be a component of the body's immune system's response to the tumour [3]. Yet, there is mounting proof that a number of cancers are caused by chronic inflammation, for which CRP serves as a marker [6,7].

It is obvious that inflammatory cells operate as tumour promoters, creating an environment that is conducive to tumour growth, causing DNA damage, encouraging angiogenesis, and favouring the spread and metastasis of neoplasms [6]. We are unable to discriminate between high CRP being a sign of occult cancer or inflammation and

raised CRP being a cause of carcinogenesis in the current association research.

The average interval from blood sampling to cancer diagnosis in the CRP category, however, was greater than 3 mg/L, indicating that elevated CRP levels may be more than merely a sign of occult cancer. The link between CRP levels and incident any cancer, on the other hand, was diminished when we eliminated incident cancer cases detected within a year of blood sample.

We discovered that elevated CRP levels were linked with any, lung, and colorectal cancer with metastases at diagnosis but not with localised cancer exclusively, providing additional evidence that CRP is a marker of occult cancer. CRP has been utilised as a predictive marker in a number of investigations, but only two studies with a small sample size have quantified CRP using a high-sensitivity assay [8,9]. According to Il'yasova *et al*. [8] and Heikkila *et al*. [9], a log unit increase in CRP level was associated with a hazard ratio of 1.4 (95% CI, 1.1 to 1.8) for the early mortality of cancer patients. Our study's findings, which involved a lot more individuals, confirm these conclusions and, as a result, the usefulness of CRP as a predictive marker in cancer patients.

Confounding and bias in the selection of participants are potential drawbacks of our study.

Conclusion

our research has shown that elevated CRP levels in people who appear to be cancer-free are linked to a higher risk of developing incident cancer of any kind, lung cancer, and probably colorectal cancer. Moreover, we have shown that elevated CRP levels at baseline are linked to early death following a cancer diagnosis, particularly in patients without metastases.

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