RESEARCH ARTICLE

Risk Factors for Colorectal Cancer in Thailand

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Abstract

Background: Colorectal cancer (CRC) is one of the most common cancers worldwide. This study aimed to investigate the risk factors for colorectal cancer in the Thai population. Materials and Methods: A cohort study was carried out in Khon Kaen, Thailand, including 71 cases of histologically confirmed CRC patients among 19,861 participants, aged 30-69 years, who were recruited for a cohort study during the period 1990-2001. Participants were followed-up until 31 December, 2013. To identify factors associated with the incidence of colorectal cancer, hazard ratios were evaluated using Cox proportional hazard regression. Results: No environmental variables could be shown to be significantly related to the risk of CRC. Although in our sample, CRC was more prevalent among males, ex-smokers, and those who drank alcohol beverages ≥ 50 gram/day, but we could not demonstrate significantly associations (HRmale= 1.67, 95% CI, 0.80-3.49, HR ex-smokers = 1.34, 95% CI, 0.52-3.46, and HRalc≥ 50 = 1.08, 95% CI, 0.43-2.71). Individuals within the sample with a family history of cancer, working hour >8 hours per day, and current-smokers appeared to have decrease risk of CRC, but again these relationship could not be shown to be significantly associated (HRfam cancer= 0.96, 95% CI, 0.85-1.09, HRwork>8= 0.84, 95% CI, 0.36-1.93, and HRcurrent-smoker = 0.51, 95% CI, 0.18-1.38). Conclusions: We found no evidence of environmental factors effecting the risk of CRC. There is a need for further research to determine why factors identified risk in other populations appear to not be associated with CRC risk in Thais.

Keywords: Colorectal cancer - risk factors - Thailand

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Introduction

Globally, colorectal cancer (CRC) is the third most common form of cancer in males and the second most common cancer in females (Ferlay et al., 2013). Although CRC is stabilizing or decreasing in the most western developed countries, the incidence of CRC is rapidly increasing in Asia, in general, and in Thailand, in particular (Sung et al., 2005; Yee et al., 2009; Cho and Kim, 2011; Ferlay et al., 2013). The incidence of CRC in Thailand now ranks as the third most common cancer in males and fifth in females (Ferlay et al., 2013).

It is established that CRC is a complex disease, and its incidence is related to both genetic, and environmental factors, especially those associated with a Western lifestyle. Several studies have indicated dietary habit and alcohol intake, inactive lifestyle, smoking, obesity, family history of colorectal cancer, and especially diet with high fat, as possible risk factors for developing CRC (Wang et al., 2010; Durko and Malecka-Panas, 2014; De Stefani et al., 2012; Ganesh et al., 2009). However, the degree and significance of the various environmental risk factors varies widely across studies, and populations, this needs future investigate.

Previous colorectal cancer studies in Thailand reported that red meat (beef and/or pork), and alcohol consumption associated with colorectal cancer in the Thai population (Promthet et al., 2010; Promthet et al., 2012). Although several cohort studies of CRC have been conducted in other countries (Hsing et al., 1998), no CRC cohort study has ever been conducted in Thailand. The present prospective study aims to identify which environmental factors associated with CRC in the Thai population.

Materials and Methods

This was a prospective cohort study, in which data were obtained from the Khon Kaen Cohort Study (KKCS), Faculty of Medicine, Khon Kaen University, in Northeast Thailand. The KKCS was conducted from 1991 to 2001, and recruited participant aged 30 to 69 years, and living in the Khon Kaen Province. The cohort included 19,861 participants with data obtained by structured questionnaire. Based on the Khon Kaen provincial cancer registry, 71 cases were histologically confirmed CRC among the 13,489 female, and 6,372 male cohort members. Follow-up was completed for all participants.

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Table 1. Baseline Characteristics of Subjects

Baseline charateristics	Subjects (n =19,861)	percent
Sex		
Male	6,372	32.1
Female	13,489	67.9
Age at recruitment (Years)		
<40	2,776	14.0
41-50	7,190	36.2
51-60	6,947	35.0
>60	2,948	14.8
Mean (S.D.)	51 (8.65)	
Marital status		
Single	456	2.4
Married	16,228	84.6
Separate, widow	2,501	13.0
Education		
Illiteracy	515	2.7
Primary school	17,958	92.8
Secondary or above	876	4.5
Occupation		
Agriculture	14,324	84.3
Others	1,484	8.7
Unemployed	1,182	7.0
Working hours/day (hours)		
Unemployed	1,182	7.3
<8	4,163	25.6
8	8,382	51.6
>8	2,513	15.5
BMI history (kg/m2)		
< 18.5	6,169	39.4
18.5 - 22.9	1,051	6.7
23 - 24.9	2,982	19.1
25 – 29.9	4,418	28.2
30 +	1,023	6.6

Data collection

All participants of the KKCS were followed up until December 31, 2013, and all data of the KKCS participants were linked to the Khon Kaen Population-based Cancer Registry by the RECLINK program to identify patients with a diagnosis of CRC. All CRC diagnoses were histologically confirmed, and the date of diagnosis was obtained from medical records.

Data for analyses were extracted from the KKCS database which, collected at baseline, included the demographic and environmental variables, sex, age at recruitment, marital status, education level, occupation, working hour per day, history of body mass index (BMI), family history of cancer, history of smoking, duration of smoking, number of cigarette per year, history of alcohol drinking, duration of alcohol drinking, frequency of drinking, and units of alcohol (grams/day). Person-times were computed from date of recruitment to KKCS, date of diagnosis, date of loss to follow-up or withdrawal, and date at the end of study.

Statistical analysis

Crude and adjusted estimates of associations between potential environmental risk factors and CRC were estimated using hazard ratios (HRs) with 95% confidence interval derived from Cox proportional hazard regression analysis. All analyses were conducted using STATA Version 10.0 (StataCorp., 2007), and a significance level of 0.05 was used throughout.

Ethical approval

The present study was approved by the Khon Kaen University Ethics Committee for Human Research (reference no. HE561328), and was adhered to the Declaration of Helsinki and the Good Clinical Practice Guidelines of the International Conference on Harmonisation.

Table 2. Univariate Analysis of Environmental and Demographic Factors

Factors	Numbers	Number of CRC	Person-time (person-yesrs)	IR/ 100,000	HR (95% CI)	p-value
Sex						0.241
Female	13,489	44	212,837	21	1	
Male	6,372	27	97,774	27	1.34 (0.83-2.16)	
Age at recruitment (years)						0.0002
< 40	2,776	6	51,624	11	1	
41-50	7,190	16	116,710	13	1.27 (0.50-3.26)	
51-60	6,947	32	102,554	31	3.03 (1.26-7.29)	
> 60	2,948	17	39,722	42	4.29 (1.68-10.98)	
Marital status						0.148
Single	456	1	7,378	13	1	
Married	16,228	56	256,054	21	1.63 (0.23-11.81)	
Separate, widow	2,501	14	36,612	38	2.94 (0.39-22.37)	
Education						0.530
Illiteracy/primary school	18,473	65	289,961	22	1	
Secondary school/above	876	2	13,659	14	0.66 (0.16-2.68)	
Occupation						0.394
Agriculture	14,324	46	215,467	21	1	
Others	1,484	6	23,122	25	1.20 (0.51-2.81)	
Unemployed	1,182	8	20,213	39	1.74 (0.81-3.70)	
Working hours/day (hours)						0.438
8	8,382	27	125,549	21	1	
< 8	4,163	17	61,342	27	1.31 (0.71-2.40)	
>8	2,513	7	39,099	17	0.82 (0.36-1.88)	
Unemployed	1,182	8	20,214	39	1.70 (0.77-3.77)	

Table 2 (continued). Univariate Analysis of Environmental and Demographic Factors

BMI history (kg/m2)						0.544
18.5 - 22.9	1,051	4	15,568	25	1	
< 18.5	6,169	20	96,092	20	0.80 (0.27-2.35)	
23 - 24.9	2,982	8	45,895	17	0.67 (0.20-2.24)	
25 - 29.9	4,418	17	66,762	25	0.98 (0.33-2.93)	
30 +	1,023	1	15,165	6	0.26 (0.03-2.29)	
History of family cancer						0.412
No	13,503	44	201,454	21	1	
Yes	4,781	22	79,603	27	1.24 (0.74-2.08)	
Smoking						0.132
Non-smoker	14,146	48	224,014	21	1	
Ex-smoker	1,520	9	22,605	39	1.89 (0.93-3.86)	
Current-Smoker	2,931	7	47,050	14	0.69 (0.31-1.53)	
Duration of smoking (years)						0.553
Non-smoker	14,140	48	223,943	21	1	
1-10	370	2	5,502	36	1.74 (0.42-7.16)	
11-20	714	1	12,066	8	0.38 (0.05-2.78)	
> 20	3,362	13	52,018	24	1.17 (0.63-2.16)	
No. of cigarette / year						
Non-smoker	13,467	47	209,620	22	1	0.119
Low (1-5,776)	1,857	5	34,063	14	0.59 (0.23-1.53)	
High (5,776-62,051)	1,508	9	22,203	40	1.83 (0.9-3.74)	
Alcohol drinking						0.772
Non-drinker	4,988	15	70,460	21	1	
Ex-drinker	1,163	5	17,816	28	1.27 (0.46-3.54)	
Current-drinker	2,817	10	49,738	20	0.85 (0.37-1.95)	
Duration of drinking (years)						0.992
Non-drinker	4,971	15	70,199	21	1	
1-10	967	4	16,886	23	1.02 (0.33-3.12)	
11-20	1,146	5	20,171	24	1.06 (0.38-2.97)	
>20	1,819	6	29,590	20	0.89 (0.34-2.33)	
Frequency of drinking						0.972
Non-drinker	4,971	15	70,199	21	1	
Daily	540	2	7,805	25	1.15 (0.26-5.05)	
Weekly	1,209	5	18,143	27	1.24 (0.45-3.45)	
Monthly	3,689	11	56,843	19	0.86 (0.39-1.89)	
< 1/ month	2,587	8	38,118	20	0.96 (0.40-2.29)	
Unit of alcohol (grams/day)						0.453
Non-drinker	4,971	15	70,199	21	1	
< 50	6,180	18	95,012	18	0.84 (0.42-1.69)	
≥50	1,837	8	25,796	31	1.46 (0.62-3.47)	

Table 3. Multivariate Analysis of Potential Risk Factors

Factors	Numbers	Number of CRC	Person-time (person-yesr)	Crude HR (95% CI)	Adjusted HR (95% CI)	p-value
Sex						0.187
Female	13,489	13,489	13,489	1	1	
Male	6,372	6,372	6,372	1.34 (0.83-2.16)	1.67 (0.80-3.49)	
History of family cancer						0.525
No	13,503	44	201,454	1	1	
Yes	4,781	22	79,603	1.24 (0.74-2.08)	0.96 (0.85-1.09)	
Working hours/day (hours)						0.490
8	8,382	27	125,549	1	1	
< 8	4,163	17	61,342	1.31 (0.71-2.40)	1.32 (0.72-2.42)	
>8	2,513	7	39,099	0.82 (0.36-1.88)	0.84 (0.36-1.93)	
Unemployed	1,182	8	20,214	1.70 (0.77-3.77)	1.83 (0.40-2.02)	
Smoking						0.104
Non-smoker	14,146	48	224,014	1	1	
Ex-smoker	1,520	9	22,605	1.89 (0.93-3.86)	1.34 (0.52-3.46)	
Current-Smoker	2,931	7	47,050	0.69 (0.31-1.53)	0.51 (0.18-1.38)	
Unit of alcohol (grams/day)						0.569
Non-drinker	4,971	15	70,199	1	1	
< 50	6,180	18	95,012	0.84 (0.42-1.69)	0.68 (0.32-1.44)	
≥50	1,837	8	25,796	1.46 (0.62-3.47)	1.08 (0.43-2.71)	

Results

In total, a sample of 19,861 subjects with a total observation time of 310,611 person-years were observed which included 71 cases of histologically confirmed CRC. The general demographic characteristics of all cohort members are summarized in Table 1. Most participants were female, aged at least 41 years old at recruitment, never attended school or had only primary school level education, and were employed as farmers. The result of the univariate analysis are given in Table 2. The univariate analysis identified only age at recruitment as significantly associated with the risk of CRC, especially age more than 50 year old (HRage 51-60= 3.03, 95% CI, 1.26-7.29, and HRage >60= 4.29, 95% CI, 1.68-10.98).

The results from the multivariable cox regression are shown in Table 3. None of the potential risk factors were significantly related to the risk of CRC. In our sample, we note that the survival experience was poorer among males, although sex could not be shown to be associated with CRC (HRsex= 1.67, 95% CI, 0.80-3.49). In our sample those who were ex-smoker, and those who drink alcohol beverage more than 50 gram per day were more at risk, but again, this is cannot be inferred to the populations (HRex-smoker= 1.34, 95% CI, 0.52-3.46, and HRalc >50=1.08, 95% CI, 0.43-2.71). Whereas, those who had a family history of cancer, those who working hour >8 hours per day, and those who were current-smoker, the survival experience appeared better, and these factors appeared to decrease risk of CRC. However, these could not be show to be significantly protective of CRC (HRfam-cancer=0.96, 95% CI, 0.85-1.09, HRworking hour=0.84, 95% CI, 0.36-1.93, and HRcurrent-smoker= 0.51, 95% CI, 0.18-1.38).

Discussion

The objective of this cohort study was to determine the environmental risk factors for CRC in the Thai population. To the best of our knowledge, this is the first prospective cohort study of the association between environmental factors and CRC risk in the Thai population. Surprising our study did not find significant associations between any of the factors and the subsequent development of colorectal cancer.

In the present study, family history of cancer could not be shown to be increase CRC risk, and indeed our result indicate that it may be protective. This is consistent with a case-control study of the The CpG island methylator phenotype (CIMP) status of 3,119 primary population-based colorectal cancer tumors from the multinational Colon Cancer Family Registry, reported that family history of CRC had decreased risk for CIMP, that represents a subset of colorectal cancer (Weisenberger et al., 2015). However, our result are in contrast with most previous studies which report family history of CRC to increase the risk for CRC (Johns and Houlston, 2001; Zhivotovskiy et al., 2012; Castiglione et al., 2012; Turati et al., 2013; Askling et al., 2001; Stegeman et al., 2013). Indeed, family history of any cancer has been shown to be associated with CRC in the Thai population (Sriamporn et al., 2007; Promthet et al., 2010; Poomphakwaen et al., 2014). Our inability to identify family history as a risk factor may stem from limited information from the case report form. Our study employed a question regarding family history of any type of cancer, not specifically CRC.

We found that alcohol consumption was not associated with CRC. Studies on the effect of alcohol on CRC are mixed. Some previous studies have shown that alcohol consumption is associated with CRC (Cho and Kim, 2011; Zhivotovskiy et al., 2012). A study of patients who underwent colonoscopic polypectomy of colorectal adenoma in Korea reported alcohol drinking was related to the development of advanced colorectal adenoma, especially in the patients with alcoholic liver diseases (Song et al., 2015). However, a meta-analysis investigating the association between alcohol intake and colorectal serrated polyp with the dose-response of alcohol intake indicates the light alcohol intake does not increase risk of colorectal serrated polyp (Wang et al., 2015). Also a case-control study in India (Ganesh et al., 2009), and a previous study in the Thai population found no association between alcohol consumption and CRC (Sriamporn et al., 2007; Poomphakwaen et al., 2014).

The present study did not show smoking to be associated with CRC. This is consistent with some other studies. For instance , no relationship between smoking and CRC was found in a US Prospective cohort study of white males (Hsing et al., 1998), Nor did previous studies in Japan (Nisa et al., 2010) or Holland (Tiemersma et al., 2002), or indeed, earlier colorectal case-control studies in Thailand (Promthet et al., 2010; Poomphakwaen et al., 2014). However, several colorectal cancer studies have shown a relationship between smoking and CRC development (Botteri et al., 2008; Phipps et al., 2011; Leufkens, et al., 2011; Gong et al., 2012; Zhivotovskiy et al., 2012; Peng et al., 2013; Stegeman et al., 2013).

Our study did have some limitations. First we had a small number of cases which may have impacted the power of our analysis. However, there was little indication that any of the effects were clinically risky, and failed to be identified only because of low power. On the contrary, we found most risk factors identified in other studies to have negligible risk and even to be marginally protective. Second, all environmental variables in our study came from a single interview of participants on entry into the KKCS. It is quite possible that many subject may have changed their habit after recruitment.

The present study is the first cohort study of CRC in Thailand and our study involved a large cohort. We found no association between life style, environmental factors and the risk of CRC development. We found little evidence to suggest smoking, and alcohol were risk factors for CRC. Further study is needed to investigate why environmental risk factors of CRC identified as important in other populations appear to have little impact on risk of CRC in Thais. The impact of dietary habit and gene polymorphism on CRC risk need further investigate in this population.

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