

RESEARCH COMMUNICATION

Risk Factors for Colorectal Cancer in Northeast Thailand: Lifestyle Related

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Abstract

Background: The incidence of colorectal cancer is variable around the world. Hiroshima, Japan had the highest incidence in men in 1997 with an age-standardized rate of 86.7 per 100,000 and New Zealand had the highest, at 40.6 per 100,000, in women. The incidence of colorectal cancer in Thailand is rather low and the latest figures for Northeast of Thailand are 7.1 per 100,000 for men and 4.7 for women. The reasons for these differences between countries are possibly due to variation in dietary habits, alcohol drinking or other cofactors. **Methods:** A case-control study was conducted in Khon Kaen, Northeast Thailand during 2002-2006 to study risk factors for colorectal cancer in a low risk area. Totals of 253 colorectal cancer cases (males 135, females 118) and 253 age- and sex-matched controls were recruited. Information on dietary habits, alcohol drinking, smoking and other information were collected by a structured questionnaire. Blood samples were collected for further study. Both univariate and multivariate analyses were carried out. **Results:** In the final model of multivariate analysis, the significant risk factors for colorectal cancer were a family history of cancer (OR=1.9 95%CI=1.2-2.9) and meat consumption (OR=1.0 95%CI=1.0007-1.0026). For BMI, subjects with higher BMI unexpectedly had a lower risk of colorectal cancer (OR=0.5 95%CI=0.3-0.8). **Conclusion:** Our study confirmed risk factors for colorectal cancer i.e. meat consumption and cancer in the family (genetic problem). However, the results for BMI are the reverse of expected, underlining one limitation of hospital-based case-control studies, in which cases are ill and admitted to the hospital at late stage.

Key Words: Colorectal cancer - case-control study - risk factors - Thailand

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Introduction

The incidence of colorectal cancer is variable around the world. Hiroshima, Japan has the highest incidence in men with the age-standardized rates of 86.7 per 100,000 and New Zealand has a highest incidence in women 40.6 per 100,000 (Parkin et al., 2002). The incidence of colorectal cancer in Thailand is rather low. From population-based cancer registration data in Thailand during 1988-2000 (Vatanasapt et al., 1993; Deerasamee et al., 1999; Sriplung et al., 2003), colorectal cancer has shown an increasing trend in both males and females in all centers. In 1990, an estimated total of 1,910 new colon cancers occurred in Thailand with a male/female ratio of 1.25 : 1. The annual age-standardized incidence rates were low (5.5 and 3.7 per 100,000 for men and women respectively). For rectal cancer the annual age-standardized incidence rates were also quite low (3.4 and 2.2 per 100,000 for men and women respectively) (Vatanasapt et al., 1993).

In 1999, the estimated annual age-standardized incidence rates of colorectal cancer were 11.8 and 7.8 per 100,000 in males and females respectively (Sriplung et al., 2003). The highest incidence rate of colorectal cancer for both sexes is in Bangkok (age-standardized incidence rate 16.6 for males and 11.0 for females followed by Lampang, Chiang Mai, Songkhla and Khon Kaen which has incidence rates of 7.1 and 4.7 per 100,000 in males and females, respectively. On a world basis, the estimated age-standardised incidence rates by world region in 2002 for South East Asia, with an average incidence similar to that of Thailand, is among the low-risk regions of the world (Ferlay et al., 2004).

The risk of developing colorectal cancer appears to be associated with a diet that is low in fiber and high in calories, protein and fat, especially in red meat. In addition, obesity, sedentary life styles and alcohol consumption have been implicated as potential risk factors (Kinsella, 1993; Potter et al., 1986; Giovannucci et al., 1995). In a study in Bangkok, nitrite-treated meat increased colorectal

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cancer risk; while dietary fibre decreased risk; there was an elevated risk of colorectal cancer in those with a history of bowel polyps (Lohsoonthorn and Danvivat, 1995).

A reduced risk of colorectal cancer has been linked to the use of NSAIDs such as aspirin. (Giovannucci et al., 1995). In Thailand, especially in the Bangkok area, there has been striking change in life style, especially with respect to eating and smoking habits, which may explain the higher incidence rate.

As part of a multi-centre study of 'The epidemiological study of host and environmental factors for stomach and colorectal cancers in Southeast Asian Countries', in this investigation we focused on possible determinants of colorectal cancer in the population of northeast Thailand who came to get treatment at Srinagarind and Khon Kaen Regional Hospital in Khon Kaen Thailand.

Materials and Methods

Subjects

A total of 253 new colorectal cases were recruited from Srinagarind Hospital and Khon Kaen Regional Hospital, Khon Kaen Province, between October 2002 and October 2006. All were from Khon Kaen or neighbouring provinces, histologically confirmed to be colorectal cancers and were interviewed within 3 months of first diagnosis. In the same period, a control was recruited for each case matched by sex, age (± 3 years) and province of residence. Subjects with gastrointestinal disease or other cancers were excluded. All subjects gave informed consent to their participation in the study; subjects who refused, were too old or unable to do the interview were excluded from the study. A 5 ml blood sample was obtained from cases and controls for further study which is not reported in this study. The controls had a variety of diseases, the main ones being diseases of the eye, genito-urinary system and inflammation.

Interview

Subjects were interviewed by two trained interviewers, using a structured questionnaire. The questionnaire comprised two sections. The first section included demographic and socio-economic status, smoking history allowing for various periods of different consumption, physical activity, family history. The second section was a food frequency questionnaire structured by meals. The interview referred to habits before the subjects became sick with their present illness (one year earlier). All subjects were reminded of this condition throughout the interview.

Statistical analysis

The association between individual variables and colorectal cancer was assessed using conditional logistic regression to account for the matching of cases and controls. A multiple variable model analysis used a backward elimination approach to identify a final set of variables independently associated with colorectal cancer, age, sex and place of resident were included in these analyses, a cut-off level of 0.1 was used to retain variables in the backward elimination approach.

All results are presented as odds ratios (OR) with the associated 95% confidence intervals (95% CI). Those confidence intervals not containing unity were considered statistically significant.

Occupation activity was categorized into 3 levels as heavy labour work, moderate work and light work based on working types. Example, heavy labour workers are persons who are work in farms, gardens, building construction industry etc, moderate workers are persons who mostly work by standing or sitting but move around such as salesmen, hair stylists, servants and policeman, and, light workers are persons who mostly sit such as managers and clerks.

For the analysis of cigarette smoking, there were categorized as smokers and nonsmokers. Smokers included those who smoked filtered, unfiltered cigarettes and yamuan (a home-made cheroot). Duration of smoking, and average number of cigarettes per year were computed based on all smoking periods reported and dichotomized on the median of the controls. Average number of cigarette was calculated as annual cigarettes consumption (filtered and unfiltered) plus 1.5 times annual yamuan consumption. The 1.5 correction factor was used to allow for the longer size of yamuan compared with the regular cigarettes. The amount of cigarettes was categorized based on the 50th percentile of the controls and dichotomized into low and high levels.

For the analysis of alcohol drinking, there were two categories for alcohol drinking: drinkers and nondrinkers. Ever drinkers, was defined as who have consumed at least one type of all alcoholic beverages (beer, sato, white alcohol, maekong and other whiskies) and consumed within range of ever day to once a month. Those who did not drink or have consumed all alcoholic beverages with frequently less than one time a month were categorized as nondrinkers.

For the analyses of types of dietary intake within a previous year (vegetable, fruits fish/shellfish: fresh/sea water, meat and fried meat), there were categorized two levels as low and high. Frequencies of each dietary intake, and an amount of intake per year were computed based on each type of dietary intakes reported and dichotomized on the median of the controls.

Body mass index (BMI) was computed as weight (kg) divided by the square of height (m²) which are categorized into two levels (< 25, normal weight and ≥ 25 ; non-normal; 25 to 29, overweight plus ≥ 30 , obese). Exercise was categorized into two levels (exercise and non-exercise) Exercisers were defined as those who played sports at least 3 times a week. Others were considered non-exercisers.

Results

Table 1 shows the distribution of general characteristics by case and control status. Since this is a matched case-control study, the distributions of age, sex and province of residence were the same in cases and controls. There were 135 males and 118 females, median age is 54. The majority were educated lower than high school. Most of subjects were hard labour workers. The median income per month for both cases and controls are similar (3000

Table 1. Characteristics of Cases (Colorectal Cancer) and Controls (Patients with Other Diseases)

Characteristic	Cases (n = 253)	Controls (n = 253)	OR _c (95 % CI)	OR _{adj} (95 % CI)
Male sex, n (%)	135 (53.4)	135 (53.4)		
Age group, n (%)				
≤39	33 (13.0)	36 (14.2)		
40-49	60 (23.7)	51 (20.2)		
50-59	73 (28.9)	85 (33.6)		
60-69	74 (29.3)	63 (24.9)		
≥ 70	13 (5.14)	18 (7.11)		
Median age yr (range)	54 (4-79)	55 (6-76)		
Education level, n (%)				
≤ High school	190 (75.1)	205 (81.03)	1.0	1.0
> High school	63 (24.9)	48 (18.97)	1.4 (0.9-2.2)	1.4 (0.9-2.2)
Occupation activity, n (%)				
Heavy labour work	176 (70.1)	177 (70.80)	1.0	1.0
Moderate work (standing)	43 (17.1)	43 (17.20)	1.0 (0.6-1.6)	1.1 (0.7-1.8)
Light work (sitting)	32 (12.8)	30 (12.00)	1.1 (0.6-1.8)	0.9 (0.5-1.5)
Income(Baht)				
Median (range)	3000 (250-80,000)	3000 (416-45,000)		

OR_c, Crude Odd Ratio; OR_{adj}, Adjusted Odd Ratio; 95% CI, 95% confidence interval; n, number

Baht per month).

Table 2 shows potential risk factors for colorectal cancer from the univariate analysis. Subjects who have relative with cancer have higher risk than those who never have. However, those who have higher BMI have lower risk. Those who have regularly exercise have lower risk for colorectal cancer.

There is a slightly higher risk (non-significant) of colorectal cancer in smokers relative to non-smokers and in smokers of unfiltered cigarettes compared to filtered cigarettes smokers (non significant). There was no evidence of a dose-response effect with respect to duration of smoking or amount smoked.

Most cases (146/253; male, 40 and female, 106) and controls (169/253; male, 57 and female, 112) were non-drinkers. The risk associated with alcohol consumption did not achieve statistical significance.

Table 3 shows univariate analyses of types of dietary

intake based on the food frequency questionnaire. Using the low level as referent group, there was association between meat and colorectal cancer. There is no association with other dietary consumption.

Table 4 shows the association between risk factors which found from the multivariate analysis with colorectal cancer. The significant risk factors for colorectal cancer are the history of family with cancer (OR=1.9, 95%CI=1.2-2.9) and meat consumption (OR=1.0, 95%CI=1.0007-1.0026). For BMI, subjects with higher BMI have lower risk for colorectal cancer (OR=0.5, 95%CI=0.3-0.8).

Discussion

The North East region has been, for many decades, the most impoverished part of Thailand. Until the introduction of various industries in the last 20 years, the

Table 2. Univariate Analysis of Potential Characteristics Associated with Colorectal Cancer

Characteristics	Cases (n = 253)	Controls (n = 253)	OR _c (95% CI)	OR _{adj} (95% CI)
Family history of cancer, n (%)				
No	158 (62.7)	191 (75.8)	1	1
Yes	94 (37.3)	61 (24.2)	1.9* (1.3-2.8)	1.9* (1.3-2.8)
BMI, n (%)				
< 25 k/m ²	215 (86.3)	188 (75.2)	1	1
≥ 25 k/m ²	34 (13.7)	62 (24.8)	0.5* (0.3-0.8)	0.5* (0.3-0.8)
Regularly exercise, n (%)				
No	191 (75.5)	207 (81.8)	1	1
Yes	62 (24.5)	46 (18.2)	0.7 (0.4-1.1)	0.7 (0.4-1.1)
Ever drink Alcohol, n (%)				
No	146 (57.7)	169 (66.8)	1	1
Yes	107 (42.3)	84 (33.2)	1.5* (1.02-2.1)	1.7* (1.1-2.7)
Amount of cigarettes per yr, n (%)				
None	133 (54.1)	140 (56.4)	1.0	1.0
Low (50-4563)	60 (24.4)	55 (22.2)	1.1 (0.7-1.8)	1.5 (0.5-4.2)
High (4,564-25,550)	53 (21.5)	53 (21.4)	1.1 (0.7-1.6)	1.2 (0.5-2.8)

OR_c, Crude Odd Ratio; OR_{adj}, Adjusted Odd Ratio; 95% CI, 95% confidence interval; *P < .05; n, number

Table 3. Univariate Analysis of Amount of Dietary Intakes Associated with Colorectal Cancer

Types (frequency per year)	Cases (n = 253)	Controls (n = 253)	OR _c (95% CI)	OR _{adj} (95% CI)
Vegetable/Fruits, n (%)				
Low (198-528)	132 (52.2)	132 (52.4)	1.0	1.0
High (529-1110)	121 (47.8)	120 (47.6)	1.0 (0.7–1.4)	1.0 (0.7–1.4)
Vegetable Only, n (%)				
Low (84-291)	122 (48.2)	126 (50.0)	1.0	1.0
High (292-666)	131 (51.8)	126 (50.0)	1.1 (0.8–1.5)	1.1 (0.7–1.5)
Fruit Only, n (%)				
Low (42-228)	137 (54.2)	136 (53.7)	1.0	1.0
High (229-588)	116 (45.8)	117 (46.3)	1.0 (0.7–1.4)	1.0 (0.7–1.4)
Fish/Shellfish:Fresh/Sea water, n (%)				
Low (0-395)	118 (46.6)	124 (49.2)	1.0	1.0
High (396-1472)	135 (53.4)	128 (50.8)	1.2 (0.8–1.7)	1.2 (0.8–1.7)
Meat, n (%)				
Low (0-238)	106 (42.0)	129 (51.0)	1.0	1.0
High (239-2398)	146 (58.0)	124 (49.0)	1.4* (1.0-2.0)	1.4* (1.0-2.0)
Fried Meat, n (%)				
Low (0-157)	119 (48.4)	128 (51.0)	1.0	1.0
High (158-782)	127 (51.6)	123 (49.0)	1.1 (0.8–1.6)	1.1 (0.8–1.6)

OR, odds ratio; OR_{adj}, Adjusted Odd Ratio; 95% CI, 95% confidence interval; *P < .05; n, number

population was very largely rural, relying on cultivation of rice, as the staple crop.

Five decades of research into the role of different dietary factors in promoting or preventing cancer have resulted in a broad consensus that fresh fruit and vegetables are protective factors (WCRF, 1997). On this basis, there is little reason to conclude that the low risk of colorectal cancer in North East Thailand is a consequence of a “healthy” diet. Typically, the local diet is based on consumption of sticky rice, which is flavoured with various sauces, often with fermented ingredients and typically rather salty and spiced with liberal use of chilli. Some proteins may be added in the form of meat, fish (generally small fish caught in rivers and ponds). Vegetable consumption is commonly in the form of salads, again flavoured with salty, fermented, spicy sauces. Fruit consumption has not been common, except as incidental snacks (especially banana).

We found slight negative association of vegetable and fruit intake on colorectal cancer which is similar to many studies (Potter et al., 1993; Steinmetz et al., 1996; WCRF 1997).

Table 4. Final Multivariate Model of Significant Factors Independently Associated with Colorectal Cancer

Variables	OR ^a	95% CI
Family history of cancer		
No	1	
Yes	1.9*	1.2–2.9
Meat consumption		
Low	1	
High	1.0*	1.0007–1.0026
BMI		
< 25 k/m ²	1	
≥ 25 k/m ²	0.5*	0.3–0.8

^aOdds ratio based on a backward elimination conditional logistic regression model. *P < .01

There is an association of meat consumption and colorectal cancer in our study which similar to the study in Europe found that those who eat red meat more than 160 g/day has higher risk for colorectal cancer compare to those who consume less than 20 g/day (Norat et al., 2005). Similar finding were found in other studies (Oba et al., 2006; Robertson et al., 2005; Correa et al., 2005; Larsson et al., 2005; Lin et al., 2004).

However these associations were not precise due to the fact that most of our subjects had similar eating habits, thus limiting the ability to assess even the slightest effects of these variables.

An increased risk of colorectal cancer among smokers has been observed in our study but not significant. There are similar finding in numerous studies, both case-control and cohort (Slattery et al., 1990; Tavani et al., 1998; Giovannucci et al., 1994; Akhter et al., 2007). However, the lack of association which is often observed in a hospital-based case-control studies may be due to the high prevalence of smoking related diseases in the control series.

We observed that alcohol drinking was positively associated with colorectal cancer in a univariate analysis but not in multivariate analysis. In a population base prospective cohort study in Singapore (Tsong et al., 2007) found that alcohol consumption is risk for colorectal cancer (hazard ratio = 1.72, 95 % confidence interval = 1.33-2.22). The similar finding also found in other studies (Akhter et al., 2007; Moskal et al., 2007).

We found that people who had relative with cancer have higher risk with colorectal cancer. Similar finding found in many studies (Burt et al., 1985; Slattery et al., 2003; Shah et al., 2007).

BMI, subjects with higher BMI have lower risk for colorectal cancer (OR=0.5, 95%CI=0.3-0.8). This finding seems to be opposite of the finding in a cohort study (Adams et al., 2007) which found that BMI, body mass index (BMI) has been associated with increased risk of

colorectal or colon cancer in men, but the relation is weaker and less consistent for women. However that may be due to one of the limitations of hospital-based case-control study that the cases have been ill and admitted to the hospital at late stage, means that cases already weight loss for a long period. Exercise (physical activity) found to be protective for colorectal cancer in univariate analysis but not significant similar to the study of Friedenreich et al.(2006).

In conclusion, our study confirmed the risk factors for colorectal cancer i.e. meat consumption, cancer in the family (genetic problem). But the BMI seems to be reverse finding that might be due to one of the limitations of hospital-based case-control study that the cases have been ill and admitted to the hospital at late stage. We do not find the association with vegetable/fruit intake on colorectal cancer risk. We do not find the association with food preparations on colorectal cancer risk. We observed a slightly higher risk for smokers and alcohol drinkers compared to the nonsmokers and nondrinkers. These associations were not precise due to the fact that most of our subjects had similar eating habits, thus limiting the ability to assess even the slightest effects of these variables.

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References

Adams KF, Leitzmann MF, Albanes D, et al (2007). Body mass and colorectal cancer risk in the NIH-AARP cohort. *Am J Epidemiol*, **21**.

Akhter M, Kuriyama S, Nakaya N, et al (2007). Alcohol consumption is associated with an increased risk of distal colon and rectal cancer in Japanese men: The Miyagi Cohort Study. *Eur J Cancer*, **43**, 383-90.

Akhter M, Nishino Y, Nakaya N, et al (2007). Cigarette smoking and the risk of colorectal cancer among men: a prospective study in Japan. *Eur J Cancer Prev*, **16**, 102-7.

Burt RW, Bishop T, Cannon LA, et al (1985). Dominant inheritance in adenomatous polyp and colorectal cancer. *N Engl J Med*, **312**, 1540-44.

Correa Lima MP, Gomes-da-Silva MH (2005). Colorectal cancer: lifestyle and dietary factors. *Nutr Hosp*, **20**, 235-41.

DeerasameeS, Martin N, Sontipong S, et al (1999). Cancer in Thailand Vol.II , 1992-1994. IARC Technical Report No. 34, Lyon.

Ferlay J, Bray F, Pisani P, et al (2004). GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide. IARC Cancer Base No.5, version 2.0. IARC Press, Lyon,

Friedenreich C, Norat T, Steindorf K, et al (2006). Physical activity and risk of colon and rectal cancers: the European prospective investigation into cancer and nutrition. *Cancer Epidemiol Biomarkers Prev*, **15**, 2398-407.

Giovannucci E, Egan KM, Hunter DJ, et al (1995). Aspirin and the risk of colorectal cancer in women. *N Engl J Med*, **333**, 609-14.

Giovannucci E, Rimm EB, Stampher MJ, et al (1994). A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. men. *J Natl Cancer Inst*, **86**, 183-91.

Kinsella AR (1993). Colorectal cancer: a scientific perspective, Cambridge University press.

Larsson SC, Bergkvist L, Wolk A (2005). High-fat dairy food and conjugated linoleic acid intakes in relation to colorectal cancer incidence in the Swedish Mammography Cohort. *Am J Clin Nutr*, **82**, 894-900.

Lin J, Zhang SM, Cook NR, et al (2004). Dietary fat and fatty acids and risk of colorectal cancer in women. *Am J Epidemiol*, **160**, 1011-22.

Lohsoonthorn P, Danvivat D (1995). Colorectal cancer risk factors: a case-control study in Bangkok. *Asia Pac J Public Health*, **8**, 118-22.

Moskal A, Norat T, Ferrari P, et al (2007). Alcohol intake and colorectal cancer risk: a dose-response meta-analysis of published cohort studies. *Int J Cancer*, **120**, 664-71.

Norat T, Bingham S, Ferrari P, et al (2005). Meat, fish, and colorectal cancer risk: the European Prospective Investigation into cancer and nutrition. *J Natl Cancer Inst*, **97**, 906-16.

Oba S, Shimizu N, Nagata C, et al (2006). The relationship between the consumption of meat, fat, and coffee and the risk of colon cancer: a prospective study in Japan. *Cancer Lett*, **244**, 260-7.

Parkin DM, Whelan SL, Ferlay J, et al (2002). Cancer Incidence in Five Continents, Vol. VIII. IARC Scientific Publications No. 155. Lyon: International Agency for Research on Cancer

Parkin DM, Whelan SL, Ferlay J, et al (1997). Cancer Incidence in Five Continents, Vol.VII. IARC Scientific Publications No.143, IARC, Lyon, France.

Parkin DM, Bray F, Ferlay J, et al (2001). Estimating the world cancer burden: Globocan 2000. *Int J Cancer*, **94**, 153-6.

Potter JD, McMichael AJ (1986). Diet and cancer of the colon and rectum: a case-control study. *J Natl Cancer Inst*, **75**, 557-69.

Potter JD, Slattery ML, Bostick RM, et al (1993). Colon cancer: review of the epidemiology. *Epidemiol Rev*, **15**, 499-545.

Robertson DJ, Sandler RS, Haile R, et al (2005). Fat, fiber, meat and the risk of colorectal adenomas. *Am J Gastroenterol*, **100**, 2789-95.

Slattery ML, Levin TR, Ma K, et al (2003). Family history and colorectal cancer: predictors of risk. *Cancer Causes Control*, **14**, 879-87.

Slattery ML, West DW, Robinson LM, et al (1990). Tobacco, alcohol, coffee, and caffeine as risk factors for colon cancer in a low-risk population. *Epidemiology*, **1**, 144-5.

Sriplung H, Sontipong S, Martin N, et al (2003). Cancer in Thailand Vol.III, 1995-1997. Bangkok : Bangkok Medical Publisher.

Steinmetz KA, Potter JD (1996). Vegetables, fruit and cancer prevention: a review. *J Am Diet Assn*, **96**, 1027-39.

Tavani A, Gallus S, Negri E, et al (1998). Cigarette smoking and risk of cancer of colon and rectum: a case-control study from Italy. *Eur J Epidemiol*, **14**, 675-81.

Tsong WH, Koh WP, Yuan JM, et al (2007). Cigarettes and alcohol in relation to colorectal cancer: The Singapore Chinese Health Study. *Br J Nutr*, **97**, 430-4.