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A case-control study on environmental and familial risk factors for colorectal cancer in Hong Kong: chronic illnesses, medication and family history

Key Messages

1. Individuals with a family history of colorectal cancer as well as individuals with medical illnesses including diabetes, stroke, haemorrhoids, chronic constipation, and colorectal polyp should be informed of their increased risk of colorectal cancer due to a combination of genetic and lifestyle factors.
2. To maximise cost-effectiveness in cancer prevention, the individuals stated above should be targeted for preventive health measures that include lifestyle modifications and regular screening programmes.
3. Further study into the possible protective effect of aspirin and non-steroidal anti-inflammatory drugs in the local population should be undertaken.

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Introduction

Of all colorectal cancers, 80% to 90% are sporadic and 10% to 20% are familial. The cause of sporadic colorectal cancer is multifactorial with environmental factors playing a major role. First-degree relatives of patients with colorectal cancer have an increased risk for colorectal cancer. The risk is greater if diagnosis is made at a young age and if other first-degree relatives are affected. Case-control studies on familial risk have not been performed in Asian countries except Japan.[1]

Certain medical and colorectal diseases have been associated with colorectal cancer due to shared lifestyle factors or genetic predisposition. Identification of these high-risk individuals in the local population is important so that targeted preventive measures can be devised.

Risk modification involving lifestyle changes can be difficult to implement. Therefore, modifiers of colorectal cancer risk, which can be introduced, may be of major public health importance. Two possible prescribable modifiers are aspirin and non-steroidal anti-inflammatory drugs (NSAIDs). Two case-control studies in the United States confirmed their protective effect.[2,3] The role of these modifiers in the Asian population is unknown.

This report describes the result of a hospital-based case-control study conducted in three Hospital Authority hospitals from April 1998 to March 2000.

Methods

Among the 1120 and 970 subjects identified for the case and control groups, 822 cases and 926 controls, respectively, were successfully recruited and interviewed. Using a validated questionnaire, subjects provided the following information: (1) past medical history including the nature of the disease and age at diagnosis; (2) a detailed family history of colorectal neoplasia and other malignancy in first- and second-degree relatives including the nature of neoplasia and age at diagnosis; (3) analgesia intake in the past 10 years including the type, frequency and the amount used. Multivariate analysis was performed for significant factors identified on univariate analysis with adjustment for possible confounders including demographic features (sex, age, marital status, education level), family history if appropriate and environmental risk factors (smoking habit, drinking habit, physical activity level, and nutrient intake).

Results

Familial predisposition

Using clinical criteria alone, eight (0.9%) cases were confirmed to be suffering from hereditary colorectal cancer syndrome. This rate was much lower than the previously reported rate of 5% to 10%, probably due to a difference in diagnostic criteria used (clinical vs genetic) and the method of case ascertainment (case series vs registry data).

Table 1. Family history and colorectal cancer risk*

	All cases, n=822	Colon cancer, n=452	Rectal cancer, n=357	Controls, n=926
Family history of CRC	60	30	28	24
Adjusted OR	3.14	2.83	3.49	
95% CI	(1.89-5.22)	(1.56-5.14)	(1.91-6.37)	
History of CRC in FDR	46	24	20	20
Adjusted OR	2.81	2.74	2.97	
95% CI	(1.60-4.93)	(1.41-5.31)	(1.50-5.88)	
History of CRC in parent	24	12	11	8
Adjusted OR	3.73	3.91	3.84	
95% CI	(1.62-8.61)	(1.50-10.19)	(1.45-10.15)	
Family history of polyp	6	2	4	1
Adjusted OR	7.33	4.46	14.32	
95% CI	(0.87-61.52)	(0.39-50.91)	(1.53-133.70)	
Family history of other cancer	14	5	9	6
Adjusted OR	3.17	1.99	4.95	
95% CI	(1.18-8.52)	(0.57-6.98)	(1.65-4.87)	

* CRC denotes colorectal cancer, and FDR first-degree relative

Table 2. Family history according to age at cancer diagnosis for cases*

	Age (<50 yrs)	Age (≥50 yrs)	P value	OR (95% CI)
Total No.	93	729		
Family history of CRC	18	42	0.000	3.93 (2.15-7.19)
FDR with CRC	12	34	0.003	3.03 (1.51-6.08)
Parents with CRC	11	13	0.000	7.39 (3.21-17.03)
Family history of colorectal polyp	3	3	0.022	8.07 (1.60-40.57)
CRC syndrome	3	2	0.000	25.07 (4.98-126.13)
Mean No. of family members with CRC	1.88 ± 2.34	1.07 ± 0.34	0.034	

* CRC denotes colorectal cancer, and FDR first-degree relative

A family history of colorectal cancer (in either first- or second-degree relatives) was reported by 60 (7.3%) cases and 24 (2.6%) controls. Forty-six (5.6%) cases and 20 (2.2%) controls had at least one first-degree relative suffering from colorectal cancer (Table 1). A family history of colorectal cancer was significantly associated with increased colon and rectal cancer risk. The same findings were obtained for a history of colorectal cancer in a first-degree relative, particularly if the first-degree relative was a parent. Since many known personal and environmental confounders were adjusted for in our analysis, the results indicated that genetic predisposition is a likely cause for the increased risk observed.

A family history of colorectal polyp in a first-degree relative was associated with rectal cancer risk ($OR_{adjusted}$= 14.32; 95% CI, 1.53-133.70) [Table 1].

A history of other cancers in their family members was also associated with colorectal cancer risk ($OR_{adjusted}$= 3.17; 95% CI, 1.18-8.52). In subsite analysis, the association remained the same for rectal cancer ($OR_{adjusted}$=4.95; 95% CI, 1.65-4.87) [Table 1].

Comparing cases diagnosed before and after 50 years of age, we found that family history of colorectal neoplasia was stronger for those suffering from colorectal cancer before 50 years of age. These younger cases had a higher number of family members suffering from colorectal cancer and they themselves were more likely to be suffering from hereditary colorectal cancer syndrome (Table 2).

Underlying medical diseases

Diabetes mellitus and stroke were associated with a significant increase in colorectal cancer risk and subsite analysis for colon cancer. Hypertension was associated with increased colon cancer risk before and after adjustment for potential confounders ($OR_{adjusted}$=1.33; 95% CI, 1.03-1.72).

Colorectal diseases including colorectal polyp, haemorrhoids and chronic constipation were associated with increased colorectal cancer risk. For colorectal polyp and haemorrhoids, the association remained significant for the subsites of colon and rectal cancer. As the mean age at haemorrhoid diagnosis was much younger than the mean age at colorectal cancer diagnosis (44.3±16.8 years vs 66.8±12.0 years), it is unlikely that the high prevalence of haemorrhoids was due to misinterpreting symptoms of colorectal cancer as a diagnosis of haemorrhoids. The observed association for chronic constipation became insignificant in subsite analysis.

Analgesia intake

Controls had a significantly higher analgesia usage rate than cases (73.5% vs 65.7%, P=0.001) [Table 3]. Ever exposure to analgesia in the past 10 years was associated with significantly reduced colorectal cancer risk

Table 3. Analgesia intake in the past 10 years and colorectal cancer risk

	All cases n=822	Colon n=452	Rectum n=357	Controls n=926
Ever use analgesia	534	298	227	
Adjusted OR	0.75	0.8	0.67	
(95% CI)	(0.60-0.94)	(0.61-1.05)	(0.50-0.90)	
Regular use of aspirin or NSAID*	27	15	10	51
Adjusted OR	0.53	0.5	0.5	
(95% CI)	(0.32-0.89)	(0.26-0.95)	(0.24-1.03)	

* NSAID denotes non-steroidal anti-inflammatory drugs

($OR_{adjusted}$=0.75; 95% CI, 0.60-0.94) and rectal cancer ($OR_{adjusted}$=0.67; 95% CI, 0.50-0.90). Only 64 (7.9%) cases and 98 (10.7%) controls used analgesia on a regular basis, that is, more than 1 month in the past 10 years.

Regular use of either aspirin or NSAIDs was associated with significantly reduced risk of colorectal cancer ($OR_{adjusted}$=0.53; 95% CI, 0.32-0.89).

Because of this relatively low regular usage rate, we could not demonstrate any significant association between the extent of aspirin or NSAIDs exposure with colorectal cancer risk.

Conclusions

Family history of colorectal cancer was an important risk factor for colon and rectal cancer in our population. Such a family history was stronger for cases diagnosed before 50 years old. These findings suggest genetic predisposition to be the most likely cause for the increased risk. Medical illnesses including diabetes mellitus and stroke, colorectal diseases such as haemorrhoids, chronic constipation and colorectal polyp were associated with an increased risk of colorectal cancer. Regular intake of aspirin or NSAIDs was associated with reduced colorectal cancer risk.

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