RESEARCH ARTICLE

Dietary Fibre and the Risk of Colorectal Cancer: a Case-Control Study

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Abstract

Background: Colorectal cancer is one of the most commonly occurring cancers in China. Dietary fibre has been thought to decrease the risk of colorectal cancer in Western countries. However, studies investigating the association between dietary fibre (particularly soluble and insoluble fibres) and colorectal cancer have hitherto been lacking in China. Objective: This case-control study examined the effect of dietary fibre intake on the risk of colorectal cancer, stratified by tumour site. Materials and Methods: The study included 265 cases (colon cancer, 105; rectal cancer, 144; colon and rectal cancer, 16) and 252 controls residing in Qingdao. A food frequency questionnaire that included 121 food items was used to collect dietary information. Odds ratio (OR) and 95% confidence intervals (CI) were calculated using unconditional logistic regression analysis. Results: For food groups, controls in the study consumed more vegetables, soy food and total fibre than did colorectal cancer patients ($p<0.05$). The intakes of fruit, meat and sea-food did not differ significantly between cases and controls. However, we did not find any association between soy food intake and colon cancer. We observed inverse associations between total fibre intake and colorectal, colon and rectal cancer (Q4 *vs* Q1: OR=0.44, 95%CI, 0.27-0.73; OR=0.40, 95%CI, 0.21-0.76; OR=0.52, 95%CI, 0.29-0.91). Vegetable fibre intake showed similar inverse associations (Q4 *vs* Q1: OR=0.51, 95%CI, 0.31-0.85; OR=0.48, 95%CI, 0.25-0.91; OR=0.53, 95%CI, 0.29-0.97). In addition, inverse associations were observed between soluble fibre and insoluble fibre and both colorectal cancer and colon cancer. No relationship was found between colorectal cancer and fruit, soy or grain fibre intakewhen the results were stratified by tumour site. Conclusions: The present study suggests that vegetable fibre and total fibre play very important roles in protecting against colorectal cancer. Soluble and insoluble fibres were inversely associated with only colorectal cancer and colon cancer.

Keywords: Dietary fibre - fibre sources - colorectal cancer - case-control study

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Introduction

Colorectal cancer is one of the most commonly occurring cancers in the world. The incidence rate has been on the rise; from 2003 to 2007, it was 28.08 per 100,000 males and ranked third among all cancer cases in China (Chen et al., 2012). Etiological studies have shown that diet is a very important factor in colorectal carcinogenesis (Armstrong et al., 1975). Although some studies have been conducted on dietary fibre and the risk of colorectal cancer in western countries, the evidence has been inconsistent (Burkitt, 1971; Negri et al., 1998; Jansen et al., 1999; Slattery et al., 2004; Lin et al., 2005; Michels et al., 2005). Burkitt hypothesised that dietary fibre might be a protective factor for colorectal cancer (Burkitt, 1971). Some studies also reported an inverse association about fibre and colorectal cancer (Negri et al., 1998; Slattery et al., 2004). However, some recent studies have not shown a protective effect of dietary fibre on colorectal cancer (Lin et al., 2005; Michels et al., 2005).

Fibre can be classified into soluble fibre and insoluble fibre, according to differences in water solubility. According to food sources, fibre can be further classified into grain, soy, vegetable, and fruit fibre and so on. One study showed that vegetable fibre can reduce the risk of colorectal cancer (Nomura et al., 2007), whereas other studies reported that vegetable fibre was not associated with a decreased risk of colorectal cancer (Terry et al., 2001; Lin et al., 2005). Some animal studies also have shown that various types of fibre have different effects on colon cancer (Bingham, 1990; Slavin et al., 1990; Schatzkin, 2000). Therefore, the relationship between dietary fibre and colorectal cancer is a conflicting subject. Moreover, few studies have been conducted on the associations between soluble and insoluble fibre and

To further understand the association among food groups, fibre and colorectal cancer, we conducted a case-control study in Qingdao. We also analysed the relationships between fibre from different foods and colorectal cancer.

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Materials and Methods

Study population

Cases were admitted to Affiliated Hospital of Qingdao University Medical College, Qingdao Municipal Hospital, Qingdao Central Hospital from October 2013 to June 2014. Controls were individuals who had medical examinations in Qingdao Huici Heath Examination Centre within the same time frame. Ethical approval was obtained from Registered Ethic Committee of the Affiliated Hospital of Qingdao University Medical College.

The inclusion criteria for selecting cases were as follows: newly diagnosed with electronic colonoscopy and pathology report, aged 30-70 years, living in Qingdao, and able to complete the interview independently. Ineligible cases were excluded for the following reasons: *(i)* suffered from cancer previously (n=12); *(ii)* in-complete or inconsistent dietary data (n=20); or *(iii)* familial adenomatous or hereditary non-polyposis colon cancer (n=15). Overall, 265 (colon cancer: 105; rectal cancer: 144; colon and rectal cancer: 16) eligible cases were included in the study.

The inclusion criteria for selecting controls were as follows: *(i)* matched for age (≤3 years) and sex with cases; *(ii)* no disease of intestine after medical check-up and no history of intestinal disease; and *(iii)* no family history of colorectal cancer in a first-degree relative. We selected 271 controls; of these, 19 were ineligible because of incorrect information. In total, 252 controls were included for the analysis.

Data collection

Data were collected through face-to-face interviews conducted by trained investigators. All participants completed a questionnaire that included two sections: a health-related factors questionnaire and a semi-quantitative food frequency questionnaire. Cases were asked to recall their consumption frequency and the typical amount consumed of various foods one year before diagnosis, and controls were asked to report the same information about the one year before the interview date. The health-related factors questionnaire included sociodemographic characteristics and lifestyle habits. The semi-quantitative food frequency questionnaire included 121 food items, which were categorised into 9 groups: cereal and cereal products; soy and soy products; vegetables; fruit; nut; fish; meat (pork, beef, lamb, poultry); eggs; and milk and dairy products. We provided colour photos of food to aid recall. The interview took approximately half an hour. The energy and fibre intakes were estimated using the 2004 China Food Composition Table (Yang et al., 2004). Soluble and insoluble fibre intakes were calculated according to a Chinese study (Yin et al., 2004).

Statistical analysis

Data were analysed with SPSS version 17.0. Differences between continuous variables were examined using t-tests. Chi-square tests were used to examine differences among categorical variables. T-tests were also used to assess the differences in mean intakes of some food groups between cases and controls. To estimate the risk of colorectal cancer from dietary fibre, we used unconditional logistic regression models. Fibre intake was grouped into four categories using quartiles as cut-off points based on the distribution of controls. The odds ratios (ORs) and 95% confidence intervals (CI) for each category used the lowest categories as the reference. Age, sex, smoking habits, drinking habits, physical activity, body mass index (BMI), and total energy were selected as potential confounding factors. Tests for trends were conducted using chi-square tests. $p<0.05$ was considered statistically significant.

Results

The characteristics of the study population are described in Table 1. There were no meaningful differences in age and gender because controls were matched with

Table 1. The Characteristics of the Study Population

Variables		Controls (n=252)	Colorectal cancer (n=265)	Colon cancer (n=121)	Rectal cancer (n=160)
Age (mean±SD)		57.87±9.75	59.16±9.86	59.29±10.53	59.24±9.25
Gender (n,%)	Male	148 (58.7)	150 (56.6)	68 (56.2)	94 (58.8)
	Female	104 (41.3)	115 (43.4)	53 (43.8)	66 (41.2)
Physical activity (n,%)	Less	77 (30.6)	98 (37.0)	45 (37.2)	59 (14.3)
	Moderate	85 (33.7)	92 (34.7)	43 (35.5)	52 (12.6)
	More	90 (35.7)	75 (28.3)	33 (27.3)	49 (11.9)
BMI(kg.m-2)	<18	4 (1.6)	4 (1.5)	1 (0.8)	3 (1.9)
	18-24.9	135 (53.6)	130 (49.9)	65 (53.7)	71 (44.4)
	25-29.9	102 (40.5)	119 (44.9)	51 (42.1)	78 (48.8)
	>30	11 (4.4)	12 (4.5)	4 (3.3)	8 (5)
Smoking (n,%)	Yes	77 (30.6)	92 (34.7)	42 (34.7)	59 (36.9)
	No	175 (69.4)	173 (65.3)	79 (65.3)	10 (63.1)
Drinking (n,%)	Yes	86 (34.1)	104 (39.2)	39 (32.2)	72 (45.0)*
	No	166 (65.9)	161 (60.8)	82 (67.8)	88 (55.0)
Total energy	<1654.45	63 (25)	56 (21.1)	26 (21.5)	31 (19.4)
	1654.45-1932.75	63 (25)	61 (23.0)	28 (23.1)	37 (23.1)
	1932.76-2285.43	63 (25)	72 (27.2)	32 (26.4)	45 (28.1)
	>2285.43	63 (25)	76 (28.7)	35 (28.9)	47 (29.4)

* significantly different compared with controls; $p<0.05$

cases. No significant differences were observed in BMI, physical activity, total energy, smoking habits or drinking habits between controls and cases with colorectal cancer or colon cancer. A significant difference was observed in drinking habits between controls and cases with rectal cancer ($p<0.05$).

Table 2 shows the mean intake of various food groups in cases and controls. For grains, fruit, meat, and sea-food, we did not find significant differences among colorectal, colon, rectal cancer and controls ($p>0.05$). For vegetables and total fibre, controls reported higher intakes than did cases with colorectal, colon and rectal cancer ($p<0.05$). For soy food intake, significant differences were observed between controls and cases with colorectal and rectal cancer, but not colon cancer.

Associations between various types of fibre and colorectal cancer are shown in Table 3. Similar inverse associations were also found between the highest intakes of vegetable fibre, soluble dietary fibre, insoluble dietary fibre, total fibre and the risk of colorectal cancer (Q4 *vs* Q1: OR=0.51, 95%CI: 0.31-0.85; OR=0.53, 95%CI: 0.33-0.88; OR=0.50, 95%CI: 0.30-0.82; OR=0.44, 95%CI: 0.27-0.73). The risk of colorectal cancer was not correlated with grain, fruit or soy fibre (Q4 *vs* Q1: OR=0.85, 95%CI: 0.53-1.38; OR=0.70, 95%CI: 0.43-1.15; OR=0.71, 95%CI: 0.43-1.15). With increasing intakes of total fibre, vegetable, insoluble and soluble dietary fibres, the risk of colorectal cancer showed a decreasing trend ($p<0.05$).

Associations between the intake of various types of fibre and colon cancer are shown in Table 4. High intakes of vegetable, soluble, insoluble and total fibre were associated with a reduced risk of colon cancer (Q4 *vs* Q1: OR=0.48, 95%CI: 0.25-0.91; OR=0.51, 95%CI: 0.27-0.96; OR=0.46, 95%CI: 0.24-0.88; OR=0.40, 95%CI:

Table 2. The Consumption of Food Groups among Cases and Controls

Food groups	Controls	Colorectal cancer		Colon cancer		Rectal cancer	
(g/d)	(mean±SD)	(mean±SD)	*P*-value	(mean±SD)	*P*-value	(mean±SD)	*P*-value
Grain	351.47±142.72	348.16±146.87	0.795	346.36±143.24	0.747	355.37±154.13	0.794
Vegetable	311.60±127.79	241.48±112.02	<0.001*	244.81±126.16	<0.001*	244.49±106.73	<0.001*
Fruit	164.92±62.80	156.04±58.87	0.098	153.87±44.20	0.051	156.48±66.85	0.196
Soy food	21.91±12.10	19.49±11.77	0.021*	20.06±12.75	0.176	19.40±11.26	0.036*
Meat	65.17±36.63	70.73±42.23	0.110	69.05±45.73	0.416	72.21±39.15	0.069
Sea food	60.60±40.80	60.35±46.75	0.949	60.36±48.05	0.963	63.61±51.53	0.532
Total fiber	22.98±8.40	20.52±8.50	0.001*	20.49±9.30	0.010*	20.83±8.21	0.011*

1. The intake of soy was assessed by dry weight; 2. Meat contains pig, pork, mutton and poultry; 3. P-value for difference between cases and controls; 4.*significantly different compared with controls. $p<0.05$

Table 3. Odds Ratios (ORs) and 95% Confidence Intervals (CI) of Colorectal Cancer according to Intake Quartiles of Food and Fiber

Variables	Q1 (low)	Q2	Q3	Q4 (high)	P_{Trend}
Total fiber					
Intake(g/d)	<17.36	17.36-22.31	22.31-27.60	>27.60	0.001*
controls/cases	63/ 99	63/66	63/56	63/44	
OR(95%CI)	1	0.67(0.42-1.06)	0.57(0.35-0.91)	0.44(0.27-0.73)	
Grain fiber					
Intake(g/d)	<4.17	4.17-7.78	7.78-10.11	>10.11	0.582
controls/cases	63/75	63/61	63/65	63/64	
OR(95%CI)	1	0.81(0.50-1.32)	0.87(0.54-1.40)	0.85(0.53-1.38)	
Vegetable fiber					
Intake(g/d)	<6.74	6.74-9.43	9.43-11.06	>11.06	0.018*
controls/cases	63/82	63/71	63/70	63/42	
OR(95%CI)	1	0.87(0.54-1.39)	0.85(0.53-1.37)	0.51(0.31-0.85)	
Fruit fiber					
Intake(g/d)	<2.08	2.08-3.18	3.18-5.05	>5.05	0.123
controls/cases	63/81	63/68	63/59	63/57	
OR(95%CI)	1	0.84(0.52-1.35)	0.73(0.45-1.18)	0.70(0.43-1.15)	
Soy fiber					
Intake(g/d)	<0.64	0.64-1.33	1.33-2.40	>2.40	0.186
controls/cases	63/78	63/66	63/66	63/55	
OR(95%CI)	1	0.85(0.52-1.37)	0.85(0.32-1.37)	0.71(0.43-1.15)	
Soluble fiber					
Intake(g/d)	<2.22	2.22-3.58	3.58-5.09	>5.09	0.013*
controls/cases	63/81	63/64	63/64	63/56	
OR(95%CI)	1	0.77(0.48-1.24)	0.71(0.44-1.14)	0.53(0.33-0.88)	
Insoluble fiber					
Intake(g/d)	<9.03	9.03-12.57	12.57-14.97	>14.97	0.004*
controls/cases	63/92	63/70	63/57	63/46	
OR(95%CI)	1	0.76(0.48-1.21)	0.62(0.38-1.00)	0.50(0.30-0.82)	

Adjusted for age, gender, BMI, physical activity, energy intake, smoking, drinking; *significantly different compared with controls. $p<0.05$

Table 4. Odds Ratios (ORs) and 95% Confidence Intervals (CI) of Colon Cancer according to Intake Quartiles of Food and Fiber

Variables	Q1 (low)	Q2	Q3	Q4 (high)	P_{Trend}
Total fiber					
controls/cases	63/47	63/27	63/28	63/19	0.006*
OR(95%CI)	1	0.57 (0.32-1.03)	0.60 (0.33-1.07)	0.40 (0.21-0.76)	
Grain fiber					
controls/cases	63/37	63/25	63/32	63/27	0.446
OR(95%CI)	1	0.68 (0.37-1.25)	0.87 (0.48-1.56)	0.73 (0.40-1.34)	
Vegetable fiber					
controls/cases	63/40	63/30	63/32	63/19	0.041*
OR(95%CI)	1	0.75 (0.42-1.35)	0.80 (0.45-1.43)	0.48 (0.25-0.91)	
Fruit fiber					
controls/cases	63/35	63/30	63/29	63/27	0.405
OR(95%CI)	1	0.86 (0.47-1.56)	0.83 (0.45-1.52)	0.77 (0.42-1.42)	
Soy fiber					
controls/cases	63/38	63/28	63/31	63/24	0.194
OR(95%CI)	1	0.74 (0.40-1.34)	0.82 (0.45-1.47)	0.63 (0.34-1.17)	
Soluble fiber					
controls/cases	63/41	63/30	63/29	63/21	0.042*
OR(95%CI)	1	0.73 (0.41-1.32)	0.71 (0.39-1.28)	0.51 (0.27-0.96)	
Insoluble fiber					
controls/cases	63/41	63/35	63/26	63/19	0.012*
OR(95%CI)	1	0.85 (0.48-1.51)	0.63 (0.35-1.16)	0.46 (0.24-0.88)	

Adjusted for age, gender, BMI, physical activity, energy intake, smoking, drinking; *significantly different compared with controls. $p<0.05$

Table 5. Odds Ratios (ORs) and 95% Confidence Intervals (CI) of Rectal Cancer according to Intake Quartiles of Food and Fiber

Variables	Q1 (low)	Q2	Q3	Q4 (high)	P_{Trend}
Total fiber					
controls/cases	63/54	63/41	63/34	63/31	0.011*
OR(95%CI)	1	0.77(0.45-1.30)	0.57(0.33-1.00)	0.52(0.29-0.91)	
Grain fiber					
controls/cases	63/42	63/37	63/40	63/41	0.621
OR(95%CI)	1	0.91(0.52-1.58)	0.84(0.48-1.47)	0.89(0.51-1.54)	
Vegetable fiber					
controls/cases	63/46	63/45	63/42	63/27	0.056
OR(95%CI)	1	0.96(0.56-1.64)	0.92(0.53-1.57)	0.53(0.29-0.97)	
Fruit fiber					
controls/cases	63/52	63/40	63/32	63/36	0.063
OR(95%CI)	1	0.77(0.45-1.32)	0.62(0.36-1.09)	0.62(0.36-1.09)	
Soy fiber					
controls/cases	63/43	63/38	63/39	63/40	0.544
OR(95%CI)	1	0.91(0.52-1.58)	0.89(0.51-1.54)	0.84(0.48-1.47)	
Soluble fiber					
controls/cases	63/47	63/43	63/36	63/34	0.037*
OR(95%CI)	1	0.76(0.44-1.30)	0.63(0.36-1.10)	0.57(0.33-1.01)	
Insoluble fiber					
controls/cases	63/40	63/40	63/46	63/34	0.055
OR(95%CI)	1	0.70(0.41-1.21)	0.69(0.40-1.18)	0.57(0.33-1.01)	

Adjusted for age, gender, BMI, physical activity, energy intake, smoking, drinking; *significantly different compared with controls. $p<0.05$

0.21-0.76). These inverse associations were not found between grain fibre, fruit fibre, or soy fibre and colon cancer. Intakes of vegetable fibre, insoluble fibre, soluble fibre and total fibre showed a trend to reduce the risk of colon cancer ($p<0.05$).

Associations between various types of fibre and rectal cancer are shown in Table 5. For rectal cancer, the risk decreased with increasing intakes of vegetable fibre and total fibre (Q4 *vs* Q1: OR=0.53, 95%CI: 0.29-0.97; OR=0.52, 95%CI: 0.29-0.91). Rectal cancer was not associated with grain fibre, soy fibre, fruit fibre, soluble fibre, fibre, soluble fibre or insoluble fibre. Though no significant relationship was observed between soluble fibre and rectal cancer, the risk of rectal cancer displayed a decreasing trend with increased soluble fibre intake ($p<0.05$).

Discussion

Previous studies on intake of food groups and the risk of colorectal cancer have had inconsistent findings (Pietinen et al., 1999; Michels et al., 2000; Sandhu et al., 2001; Tabatabaei et al., 2011). In our study, the intakes of grain products, meat, sea-food and fruit did not differ

significantly between cases and controls. We also did not find differences when the results were stratified by tumour site. The findings of our study suggest that intake of vegetables reduced the risk of colorectal cancer. Similar results were found in colon and rectal cancer. We observed that soy food could decrease the risk of colorectal cancer and rectal cancer.

The protective effect of vegetables observed in our study was consistent with some previous findings. A study conducted by Marta Banque et al. (2012) showed an inverse association between intake of vegetables and colorectal cancer. However, intake of fruit was not related to the risk of colorectal, colon and rectal cancer. A study in Japan also did not support the inverse association between fruit and colorectal cancer (Sato et al., 2005). Fruit may lack some beneficial factors, such as low energy and low sugar content (Franceschi et al., 1997). A study carried out in Shanghai showed that soy food reduced the risk of colorectal cancer in women (Yang et al., 2009), similar to our findings. It may be that soy foods are rich in folic acid, calcium, isoflavones and so on. These nutrients have protective effects against colorectal cancer. Previous studies have shown that these nutrients can maintain DNA synthesis and methylation (Mason et al., 1996), modulate signal pathways in malignant transformation (Li et al., 2005), inhibit cell growth and induce apoptosis (Bennink, 2001). Foods that lack these nutrients are related to an increased risk of colorectal cancer (Potter, 1999). Although some studies have shown that sea-food intake may protect against colon cancer (Franceschi et al., 1997; Kato et al., 1997), our study did not find an effect on colon or rectal cancer. However, we cannot rule out all confounding factors, including recall bias. In western countries, some studies have shown that high intake of meat may increase the risk of colorectal cancer (Larsson et al., 2005; Norat et al., 2005). However, some studies in Japan did not show clear associations between colorectal cancer, colon cancer and rectal cancer (Kojima et al., 2004; Sato et al., 2006). Similar to studies in Japan, the mean intake of meat did not differ between cases and controls.

In our study, we observed inverse associations between total fibre and vegetable fibre intake and the risk of colorectal cancer. The protective effect of fibre could be due to various mechanisms. *(i)* In the large bowel, fibre can increase stool bulk, dilute faecal carcinogens, shorten faecal transit time and reduce the contact of carcinogens with the colon epithelium (Bingham, 1990; Schatzkin, 2000). *(ii)* Fibre can bind to the bile acid, which can produce carcinogens (Wakai et al., 2007). *(iii)* Fibre can be fermented by gut flora to short-chain fatty acids. Butyrate is a one of the main short-chain fatty acids in the human colon, which has the ability to inhibit carcinogenesis (Goncalves et al., 2013). *(iv)* Fibre can reduce hyperinsulinemia by delaying the starch absorption (Hawk et al., 2002). Moreover, one study has shown that hyperinsulinemia is related to colorectal cancer (Ma et al., 2004). Inverse associations were observed between soluble fibre and insoluble fibre and colon cancer but not rectal cancer. The results of a Japanese collaborative study are consistent with our findings (Wakai et al., 2007). The reasons may be that rectum is empty in most of the time, thus reducing the effect of fibre (McNeil et al., 1981) or because the fermentable rates of fibre and bacterial growth are highest in the colon (Mai et al., 2003). However, one study showed that insoluble fibre had a strong inverse relationship with rectal cancer (Slattery et al., 2004). The reason may be that it is not possible to absolutely separate the effect of the two fibres in an observational study.

In terms of fibre from different food sources, we find an inverse association between vegetable fibre and the risk of colon or rectal cancer, similar to the result of a study conducted in Hawaii and Los Angeles (Nomura et al., 2007). However, this study (Nomura et al., 2007) reported an inverse association between fruit fibre and colorectal cancer risk (Q5VSQ1: OR=0.59, 95%CI: 0.40-0.71). This discrepancy in findings may be due to the different types of fruits people eat in Qingdao, as different fruit fibres may have different effects on colorectal cancer. Therefore, the different proportion of fruit fibre may lead to these observed differences. Soy food intake was inversely related to colorectal cancer and rectal cancer, but we did not find inverse associations between soy fibre intake and the risk of colorectal cancer. Another Chinese study (Zhong et al., 2014) reported that soy fibre did not reduce the risk of colorectal cancer and suggested that some nutrients contained in soy food have protective effects against colorectal cancer. However, another study found that blue lupin kernel fibre could improve colonic function and had beneficial effects on decreasing the risk of colorectal cancer (Fechner et al., 2013). Grain fibre did not show an inverse association with colorectal cancer in our study, and a prospective study of 88757 women also did not report a significant relationship between grain fibre and the risk of colorectal cancer (Fuchs et al., 1999). However, another cohort study reported a decrease in the risk of colorectal cancer associated with the intake of grain fibre (Schatzkin et al., 2007).

In conclusion, the present case-control study suggests that vegetables and fibre (including vegetable fibre, soluble fibre, and insoluble fibre) are associated with a decreased risk of colorectal cancer and colon cancer. Intake of vegetables and soy foods was inversely related to rectal cancer risk. More in-depth studies are needed to confirm the relationship between fruit and colorectal cancer stratified by gender.

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