BASIC RESEARCH

Peanut consumption and reduced risk of colorectal cancer in women: A prospective study in Taiwan

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Abstract

AIM: To examine whether peanut consumption is associated with a reduced risk of colorectal cancer in a prospective cohort with a 10-year follow-up.

METHODS: In 1990-1992, residents (12 026 men and 11 917 women aged 30 to 65 years) in 7 townships, Taiwan, were interviewed and recruited into a cancer-screening cohort and annually followed up. Colorectal cancer cases in this cohort were identified from cancer registry and death certificates. Incidence rates of this disease by the end of 2001 were calculated by gender for the primary study variable and covariates. The dietary intake was assessed by means of weekly food frequency measures, including frequently consumed food groups and folk dishes including sweet potato, bean products, peanut products, pickled foodstuffs, nitrated or smoked foodstuffs.

RESULTS: During the study period, 107 new colorectal cancer cases (68 men and 39 women) were confirmed. The multivariate Cox's proportional hazard model showed that the relative risk (RR) of peanut consumption was 0.73 [95% confidence interval (CI) = 0.44-1.21] for men and 0.42 (95% CI = 0.21-0.84) for women. However, frequent intake of pickled foodstuffs was harmful for women (RR = 2.15, 95% CI = 0.99-4.65). The risk of colorectal cancer was also elevated among cigarette smokers but not significant ($P < 0.05$).

CONCLUSION: This study suggests that frequent intake of peanut and its products may reduce colorectal cancer risk in women, demonstrating the anti-proliferating effect of peanut intake.

INTRODUCTION

Etiological studies showed that more than 85% colorectal cancer cases are associated with environmental factors[1,2], particularly the dietary factor[3]. Among dietary constituents implicating in colorectal carcinogenesis, consumption of vegetables and fruits has a beneficial effect[4]. But the effect of pulse (legume) consumption is conflicting[5]. An ecological study reported consumption of pulses is inversely related with colon cancer mortality of males in 38 countries (correlation coefficient = -0.7)[6]. Previous studies showed that components, such as folic acid, protease inhibitors, phytosterols (PS), saponins, inositol hexaphosphate (phytic acid, PA), isoflavones and resveratrol in grains, nuts and seeds may have anti-carcinogenic effects[7,8]. Several studies reported consumption of pulses is inversely related with colorectal cancer[9-12], but other studies have failed to show this protective effect[13-16]. As a good source of PS, PA and resveratrol, peanut has been thought to have an effect against carcinogenesis[17]. The suppression effect of PS, PA and resveratrol on colon cancer has been supported *in vitro* and *in vivo* as well[18-20]. Whether the laboratory findings are relevant to the hypothetically protective effect of peanut on cancers remains unexplored.

Colorectal cancer has become the second most fatal malignancy in developed countries and the third most frequent cancer worldwide[21,22]. While the incidence rate of colorectal cancer also increases in Taiwan, the mortality rate of the disease has a 74% rise from 1993 to 2002.

Table 1 Incidence and relative risk of colorectal cancer by social demographic characteristics in a Taiwan community-based cancer screening cohort (1991-2001)

Characteristic	Subject number	Person-yr	Colorectal cancer			
			Case number	Rate[1]	RR[2] (95% CI[3])	*P*
Age (yr)						
<50	12 902	129 055	18	13.9	1.00	
50-59	6 679	66 812	51	76.3	5.47 (3.20-9.36)	<0.01
+60	2 534	24 944	38	152.0	11.0 (6.30-19.4)	<0.01
Gender						
Women	11 192	112 007	39	34.8	1.00	
Men	10 923	108 805	68	62.5	1.81 (1.22-2.68)	<0.01
Education (yr)						
None	4 576	45 806	30	65.5	1.00	
≤6	9 126	91 009	56	61.5	0.94 (0.61-1.47)	0.79
>6	8 383	83 698	21	25.1	0.39 (0.22-0.67)	<0.01
Unknown	30	300	0	—	—	
Ethnic group						
Fukien	14 938	149 709	73	48.8	1.01 (0.67-1.52)	0.96
Others[4]	7 128	70 612	34	48.2	1.00	
Unknown	49	491	0	—	—	
Residential area						
Potzu	3 362	33 680	23	68.3	1.51 (0.95-2.39)	0.08
Other[5]	18 753	187 132	84	44.9	1.00	
Married						
Yes	20 354	203 204	99	48.7	1.00	
No	1 671	16 699	8	47.9	0.98 (0.48-2.02)	0.97
Unknown	90	909	0	—	—	
All	22 115	220 812	107	48.5		

[1]Rate in 10^5 persons/year; [2]Relative risk; [3]95% Confidence interval; [4]Including mainland Chinese, Hskka and aborigines; [5]Including Sanchi, Chutung, Kaoshu, Makung, Hushi and Paihsa.

Peanut is a common food in the world and in Taiwan as well. The association between peanut consumption and colorectal cancer has not been well studied. The purpose of this study was to determine the association between peanut consumption and colorectal cancer risk in a community-based cancer-screening cohort with a 10-year follow-up.

MATERIALS AND METHODS

Cohort recruitment and inclusion criteria
The details of this prospective cohort study conducted in 7 townships (Sanchi, Chutung, Potzu, Kaoshu, Makung, Huhsi and Paihsa) and their precincts, Taiwan, have been described elsewhere[23]. A total of 23 943 persons (12 026 men and 11 917 women) who were at least 30 years old and gave their consent to a baseline interview in person, physical examinations and annual follow-up activities, were recruited between July 1990 and June 1992 in this cohort study. At the same time, we conducted the laboratory tests of serum cholesterol and triglyceride for all participants.

Questionnaire interviews
Well-trained public health nurses employed at local health stations in the study townships assisted to conduct home visits to all participants. With consent, structured questionnaire interviews were conducted for information regarding socio-demographic characteristics (age, gender, education level, ethnicity group, residential area, and marital status), anthropometric measures (height and weight), cigarette and alcohol use, dietary consumption, personal and family history of cancers. Dietary intake was assessed by means of weekly food frequency measures (0-1, 2-3, and >3 meals/week), including frequently consumed food groups and folk dishes including sweet potato, bean products, peanut products, pickled foodstuffs, nitrated or smoked foodstuffs.

Cigarette smoking and alcohol drinking were evaluated by their amount and duration. Total cigarette smoking was estimated in terms of packs/year (packs per day multiplying the years of cigarette smoking in the follow-up). Alcohol drinking in data analyses used a dichotomous classification: yes versus no. Height and weight were measured once at the baseline. This study also collected information on reproductive health, including the use of oral contraceptives or intrauterine devices (never or ever use) and menopausal status (yes or no) for females.

Follow-up and data linkage
All participants were annually followed up for their health status. In addition to the active follow-up by home visit or telephone interviews, data from the National Cancer Registry and death certificates were also used to identify and verify newly developed colorectal cancer and other types of cancer. Diagnoses of colorectal cancer were confirmed by reviewing the medical records and death certificates. Colon and rectal cancer cases were combined in this study because of the small sample size and potential for their mutual misclassification in some death certificates[24].

Statistical analysis
After exclusion of the participants with cancer occurred prior to the recruitment (*n*=1336) or cancer cases (*n*=492) other than colorectal cancer, a cohort of 22 115 (92%) persons remained for the present study analysis. In addition to calculation of the incidence of the disease, the Cox's proportional hazard model was used to estimate the relative risk (RR) and 95% confidence interval (CI) associated with socio-demographic factors, cigarette and alcohol use, body mass index (BMI), cholesterol, triglyceride and diet. The association with menopause was also considered for women. None of the female cases was a smoker or a alcohol user, the RR due to these two factors was calculated only for men. Because of the limited sample size, diet consumptions and other covariates were mostly categorized into two or three strata in the data analysis. BMI was categorized into four strata (<24.2, 24.2-26.4, 26.4-28.2, >28.2 kg/m^2). For incidence and RR calculation, the number of persons/year under observation was computed for each stratum of categorized risk factors. The dose-response relationship across the level of life style variables was observed by treating each ordinal-score variable as a continuous variable in proportional hazard regression. A score selection procedure (the highest likelihood score statistic) was used to determine the covariates included in the final multivariate Cox's proportional hazard model beginning with all lifestyle and dietary variables. All analyses were performed using the SAS version 8.2 software (SAS Institute, Inc., Cary, North Carolina). All statistical tests were two-sided.

Table 2 Incidence of colorectal cancer and relative risk by lifestyle factor in a Taiwan community-based cancer screening cohort among men (1991-2001)

Characteristic	Cases number	Rate[1]	RR[2]	95% CI[3]	P
BMI (kg/m^2)					
<24.2	33	54.7	1.00		
24.2-26.4	16	62.5	1.15	0.63-2.08	0.65
26.4-28.6	11	73.5	1.35	0.68-2.67	0.39
28.6 +	8	101.4	1.87	0.86-4.04	0.11
P for trend			0.11		
Cholesterol (tertile[4])					
1	15	41.5	1.00		
2	18	49.5	1.19	0.60-2.36	0.62
3	35	96.5	2.32	1.27-4.25	<0.01
P for trend			0.004		
Triglyceride (tertile[5])					
1	20	54.2	1.00		
2	21	58.4	1.07	0.58-1.98	0.83
3	27	75.1	1.38	0.78-2.46	0.27
P for trend			0.26		
Cigarette smoking (pack-yr)					
0	22	45.2	1.00		
1-25	21	56.7	1.26	0.69-2.28	0.46
26 +	24	105.0	2.32	1.30-4.13	<0.01
Unknown	1	896.0	—		
P for trend			0.006		
Alcohol drinking					
No	52	59.9	1.00		
Yes	16	73.8	1.23	0.71-2.16	0.46

[1]Incidence rate per 10^5 persons/year; [2]Relative risk; [3]95% Confidence interval; [4]The tertile of cholesterol level (mg/dL) was <163, 163-197, 197+; [5]The tertile of triglyceride level (mg/dL) was <87, 87-145, 145+.

Table 3 Incidence of colorectal cancer and relative risk by lifestyle factor in a Taiwan community-based cancer screening cohort among women (1991-2001)

Characteristic	Cases number	Rate[1]	RR[2]	95% CI[3]	P
BMI (kg/m^2)					
<24.2	12	19.3	1.00		
24.2-26.4	12	50.3	2.61	1.17-5.80	0.02
26.4-28.6	10	70.2	3.64	1.57-8.43	<0.01
28.6 +	5	42.4	2.19	0.77-6.23	0.14
P for trend			0.012		
Cholesterol (tertile[4])					
1	8	21.6	1.00		
2	10	26.4	1.22	0.48-3.10	0.67
3	21	56.8	2.64	1.17-5.95	0.02
P for trend			0.012		
Triglyceride (tertile[5])					
1	8	21.4	1.00		
2	13	34.2	1.60	0.66-3.86	0.30
3	18	49.2	2.30	1.00-5.28	0.05
P for trend			0.046		
Oral contraceptives					
Never use	27	38.2	1.00		
Ever use	7	21.7	0.57	0.25-1.31	0.19
Unknown	5	54.9			
Intrauterine devices					
Never use	15	35.8	1.00		
Ever use	19	31.2	0.87	0.44-1.72	0.69
Unknown	5	54.5			
Menopause					
No	10	14.9	1.00		
Yes	24	67.6	4.53	2.17-9.47	<0.01
Unknown	5	53.5			

[1]Incidence rate per 10^5 persons/year; [2]Relative risk; [3]95% Confidence interval; [4]The tertile of cholesterol level (mg/dL) was <165, 165-199, 199+; [5]The tertile of triglyceride level (mg/dL) was <75, 75-126, 126+.

RESULTS

A total of 107 new cases of colorectal cancer (56 in the colon, 51 in the rectum) were found during the 10-year follow-up period until December 31, 2001. Table 1 shows the incidence rate of 34.8 per 10^5 persons/year for women and 62.5 per 10^5 persons/year for men. Most participants who received only elementary education or no school education had a greater incidence than persons who received 6 or more years of education. There were no significant relationships between colorectal cancer and ethnicity and marital status. Residents living in Potzu had a higher risk for the disease than those living in other areas but not significant ($P = 0.08$).

The incidence of the disease was positively associated with BMI, serum cholesterol and cigarette smoking in men ($P < 0.01$, Table 2). The incidence increased from 54.7 per 10^5 persons/year in men with the BMI less than 24.2 kg/m^2 to 101.4 per 10^5 persons/year for those with the BMI greater than 28.6 kg/m^2. In women, the incidence rate of colorectal cancer was related with their BMI, cholesterol and triglyceride level ($P < 0.05$, Table 3). The highest incidence rate in women was 70.2 per 10^5 persons/year for those with their BMI being 26.4-28.6 kg/m^2. The results also showed that menopausal women had an increased risk for the disease with an incidence rate of 67.6 per 10^5 persons/year.

The analysis of food intake showed that the incidence rate of colorectal cancer was significantly increased in men who had more sweet potatoes and in women who had more pickled foodstuffs (Table 4). Beneficial effects were of the consumption of peanut products observed in both sexes but not significant. There were no significant associations between the colorectal cancer risk and the consumption of bean products, nitrate and smoked foodstuffs in both sexes.

The score selection in the final multivariate Cox's proportional hazard analysis was completed with 5 final covariates including age, resident area, cigarette smoking, consumption of peanut products and BMI, which were potentially associated with the risk of the disease in men. For women, three potential covariates including age, consumption of peanut products and pickled foodstuffs were selected. Among these covariates, age was a significant factor for colorectal cancer in both sexes. Obese men living in Potzu had an increased risk for colorectal cancer. The RR was 1.98 (95% CI = 0.91-4.30) for the highest level of BMI (>28.6 kg/m^2 vs <24.2 kg/m^2). Men who smoked cigarettes had an excess risk of 77% over non-smokers (RR = 1.77, 95% CI = 0.97-3.26). Women who had peanut products demonstrated a significant beneficial effect. The RR was 0.42 (95% CI = 0.21-0.84) for consuming 2 + meals/week compared with 0-1 meals/week. On the other hand, consumption of pickled foodstuffs also had a harmful effect on female colorectal cancer patients with a boarder line significance level (RR for +2 meals/week

Table 4 Incidence of colorectal cancer and relative risk associated with dietary factors in a Taiwan community-based cancer screening cohort (1991-2001)

Food variable (meals/wk)	Men			Women		
	Cases (Rate[1])	RR2 (95%CI[3])	P	Cases (Rate[1])	RR2 (95%CI[3])	P
Folk Vegetarian						
No	68 (63.9)	1.00		37 (34.1)	1.00	
Yes	0			2 (67.4)	1.98 (0.48-8.22)	0.35
Unknown	0	—		0	—	
Sweet potato						
0-1	8 (31.7)	1.00		8 (26.0)	1.00	
2+	60 (72.3)	2.26 (1.08-4.73)	0.03	31 (38.4)	1.48 (0.68-3.22)	0.32
Unknown	0	—		0	—	
Bean products						
0-1	24 (60.0)	1.00		13 (27.1)	1.00	
2+	43 (63.0)	1.04 (0.63-1.71)	0.88	26 (41.0)	1.51 (0.78-2.94)	0.23
Unknown	1	—		0	—	
Peanut products						
0-1	23 (70.8)	1.00		17 (40.4)	1.00	
2+	44 (58.1)	0.83 (0.50-1.37)	0.45	21 (30.4)	0.75 (0.40-1.43)	0.38
Unknown	1	—		1	—	
Pickled foodstuffs						
0-1	26 (68.9)	1.00		10 (21.2)	1.00	
2+	41 (58.2)	0.84 (0.51-1.37)	0.48	29 (45.2)	2.13 (1.04-4.37)	0.04
Unknown	1	—		0	—	
Nitrated foodstuffs						
0-1	59 (61.5)	1.00		34 (33.4)	1.00	
2+	6 (53.5)	0.87 (0.38-2.01)	0.74	4 (44.1)	1.32 (0.47-3.71)	0.60
Unknown	3	—		1	—	
Smoked foodstuffs						
0-1	60 (60.5)	1.00		36 (34.1)	1.00	
2+	5 (65.1)	1.08 (0.43-2.69)	0.87	2 (38.2)	1.12 (0.27-4.64)	0.88
Unknown	3	—		1	—	

[1]Incidence rate per 10^5 persons/year; [2]Relative risk; [3]95% Confidence interval.

Table 5 Relative risk from multivariate analysis by Cox's proportional hazard model of the community-based cancer screening cohort (1991-2001)

Variables	Men			Women		
	RR[1]	95% CI[2]	P	RR[1]	95% CI[2]	P
Age (yr)	1.13	1.09-1.17	<0.01	1.1[2]	1.08-1.17	<0.01
Residential area						
Potzu	2.13	1.24-3.68	<0.01	NI[4]		
Other[3]	1.00					
Cigarette smoking (pack-yr)						
0	1.00			NI[4]		
1-25	1.77	0.97-3.26	0.06			
26+	1.51	0.83-2.74	0.18			
Peanut products						
0-1	1.00			1.00		
2+	0.73	0.44-1.21	0.22	0.42	0.21-0.84	0.01
Picked foodstuffs						
0-1	NI 4			1.00		
2+				2.15	0.99-4.65	0.05
BMI (kg/m²)						
<24.2	1.00			NI[4]		
24.2-26.4	1.19	0.65-2.17	0.58			
26.4-28.6	1.26	0.62-2.57	0.53			
28.6+	1.98	0.91-4.30	0.09			

[1]Relative risk; [2]95% Confidence interval; [3]Including Sanchi, Chutung, Kaoshu, Makung, Hushi and Paihsa; [4]Not included in the model.

versus 0-1 meals/week was 2.15, 95% CI = 0.99-4.65).

DISCUSSION

The present study had several weaknesses due the relatively short follow-up time (10 years), the lack of detailed information on meat, vegetables and fruits consumption, physical activity, family history of colorectal neoplasm, aspirin and other non-steroidal anti-inflammatory drug use, colon-cancer screening practices and the relatively small number of cases for a cohort study. However, this well-defined population-based prospective approach reduced the selection bias and strengthened the complete ascertainment of cancer cases in the study.

It was reported that colorectal cancer is related with the consumption of vegetables and fruits and that the intake of vegetables and fruits can moderately lower the risk for colorectal cancer[5,25,26]. This 10-year follow-up study was not able to examine the effect of the consumption of vegetables and fruits. However, our results support the hypothesis that the consumption of peanut protects those who consume peanut products against colorectal cancer. This finding indicates that some specific components in peanut inhibit the carcinogenic mechanisms of colorectal cancer. Peanut is a good source of phytosterols (PS)[17], phytic acid (PA)[17,19,27] and resveratrol[28], which is con-

sumed more in Asians (particularly in vegetarians) than in Westerns[7]. PS consists of approximately 80% β-sitosterol and 20% campesterol and stigmasterol[17]. β-sitosterol is the main component offering the protective effect against colon cancer by inhibiting HT-29 colon cancer cells[29]. The consumption of PS inhibits the development of chemically-induced colon tumors in rats[18]. In addition, PS consumption normalizes the hyper-proliferating state in rat and mouse colon cells[30].

PA consisting of a myo-inositol ring and six symmetrically distributed phosphate moieties[19], is a natural antioxidant in the form of metal chelate that decreases the catalytic reactivity of polyvalent transition metals[27] and has the anti-carcinogenic effect on colon cancer risk[19,31]. In addition, resveratrol is a natural phytoalexin in grapes, red wines and other grape products[32], peanut and its products[28]. With a resorcin-type structure, resveratrol can inhibit cyclooxygease-2 (COX-2) activities in colon cancer cells[33,34] and depress the growth of colorectal aberrant crypt foci[20], suggesting a protective role in the carcinogenesis of colon cancer.

The association between peanut consumption and human colorectal cancer risk has not been well established. The present study provided cohort data suggesting a significant beneficial effect of peanuts in women. Though legume consumption offers protection against colon cancer[12], PA and resveratrol are also candidate components in legumes offering this protection. This does not rule out the role of other components such as folic acid, calcium, dietary fiber, protease inhibitors, oligosaccharides, saponins and isoflavones in peanuts and legumes in protecting against colorectal cancer[35].

Studies on cigarette smoking and colon adenoma rather than colorectal cancer have consistently reported an ele-

vated risk in the earlier twentieth century. However, recent prospective studies showed that smoking is positively related with colorectal cancer, especially in long-term heavy smokers[36,37]. Giovannuci et al [36] proposed that carcinogens in cigarette smoke might initiate colorectal tumors with an induction period of three to four decades. In our follow-up study, a moderately elevated risk was observed in male smokers with colorectal cancer cases. There is no authentic evidence that can explain why moderate smokers are at the highest risk for colorectal cancer.

We also found that the harmful effect of pickled foodstuff consumption was significantly associated with colorectal cancer in women. Pickled food intake has been considered as a probable risk factor for gastric cancer[38]. Our finding is in agreement with the result of a case-control study in Japan[39]. Pickled foodstuff rich in sodium is the main dish for folk vegetarians in Taiwan. However, its association with colorectal cancer has not been found in men, indicating a gender discrepancy.

Increased body mass has been associated with excess colorectal cancer mortality, especially in men[40]. A previous cases-control study conducted in Taiwan, has also reported a significant gender discrepancy in the risk associated with colorectal cancer[41]. These findings suggest that the mechanism underlying colorectal carcinogenesis is different between men and women. Gender difference should be considered in studies on the etiology of colorectal cancer.

In conclusion, high bean intake has a number of beneficial effects and high pickled foodstuff consumption may have a number of potentially adverse effects, but the evidence is yet insufficient. Frequent peanut intake can lower the risk for colorectal cancer in women. Intake of peanuts may have beneficial effect on other types of cancer and deserves further study.

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