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Foods and Food Groups Associated With the Incidence of Colorectal Polyps: The Adventist Health Study

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Abstract

Colorectal cancer (CRC) is a leading cause of cancer death in the United States. The majority of CRC arise in adenomatous polyps and 25–35% of colon adenoma risk could be avoidable by modifying diet and lifestyle habits. We assessed the association between diet and the risk of self-reported physician-diagnosed colorectal polyps among 2,818 subjects who had undergone colonoscopy. Subjects participated in 2 cohort studies: the AHS-1 in 1976 and the AHS-2 from 2002–2005. Multivariate logistic regression analysis was used to estimate the period risk of incident cases of polyps; 441 cases of colorectal polyps were identified. Multivariate analysis adjusted by age, sex, body mass index, and education showed a protective association with higher frequency of consumption of cooked green vegetables (OR 1 time/d vs. <5/wk = 0.76, 95% CI = 0.59–0.97) and dried fruit (OR 3+ times/wk vs. <1 time/wk = 0.76, 95%CI = 0.58–0.99). Consumption of legumes at least 3 times/wk reduced the risk by 33% after adjusting for meat intake. Consumption of brown rice at least 1 time/wk reduced the risk by 40%. These associations showed a dose-response effect. High frequency of consumption of cooked green vegetables, dried fruit, legumes, and brown rice was associated with a decreased risk of colorectal polyps.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer mortality in the United States and the third most common cancer in both men and women; number 3 after prostate cancer among males and number 3 after breast cancer among females (1). CRC incidence and mortality has decreased over the past 2 decades. This decrease reflects an increase in

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screening that allows the detection and removal of colorectal polyps before they progress to cancer (2). Since colon polyps are found in populations with high incidence of CRC, it is believed they share a common etiopathogenesis (3). Therefore, it is important to focus our attention on the prevention of colon adenomas.

Results from international and correlational studies suggest that environmental factors, especially dietary factors, play a vital role in the risk of CRC (4–7). To what degree diet affects the risk of colon polyps and CRC remains unclear. Many case-control (8–12) and prospective studies (13–19) have found a significant protective association with intake of fruits, vegetables, and grains. Other studies (20), including intervention studies (21,22), on the other hand, have yielded nonsignificant associations, although most have showed a marginally significant protective effect.

The mechanism for how certain foods may reduce the risk of CRC or colon polyps is still unclear. Bioactive components in plant foods may induce antioxidative properties, thereby reducing DNA damage, and may activate genes that detoxify carcinogenes (23), thereby inhibiting carcinogenesis (24). Some studies have concluded that plant foods provide the best polypharmacy against the development of malignancy in tissues (25,26). However, it seems that there is not a single nutrient that would be responsible for this protection but rather a combination of nutrients. It is also possible that the biological activity of one may depend on the presence or absence of other substances.

In this study, we prospectively examined the effect of a number of different foods and food groups, measured by frequency of consumption, on risk of self-reported colon polyps among subjects of the Adventist Health Study-1 cohort (27).

MATERIAL AND METHODS

Study Population

The study population was composed of the survivor cohort that responded to 2 lifestyle questionnaires, the Adventist Health Study-1 (AHS-1) administered from 1976–1977, and the Adventist Health Study-2 (AHS-2) from 2002–2004. The AHS-1 was designed to examine the risk of cancer, coronary heart disease, and all-cause mortality among non-Hispanic California Seventh-Day Adventists (27). The purpose of the AHS-2 was to provide more precise and comprehensive results investigating the relationship between selected foods and the risk of cancer (28). Details of how respondents to these 2 cohort studies were identified and their information linked have been described elsewhere (29). Information obtained from these studies (AHS-1 and AHS-2) was considered protected health information and authorized by the Loma Linda University Institutional Review Board (IRB).

Briefly, 5,095 subjects participated in these 2 cohort studies. For the purpose of this study, we excluded (1) prevalent cases of colorectal polyps (82 cases), (2) history of CRC prior to the diagnosis of colon polyps (7 cases), and (3) history of inflammatory intestinal conditions such as ulcerative colitis or Crohn’s disease (9 cases) and diverticulitis (104 cases). To try to minimize detection and selection bias, we excluded subjects who reported never having had a colonoscopy as well as those who reported having a colonoscopy later than the time of diagnosis of polyps (n = 2,075). The total number of subjects excluded was 2,277. Hence, the analytic population consists of 2,818 subjects.

Dietary Assessment

Dietary and lifestyle information was assessed with the use of a self-administered food-frequency questionnaire (FFQ) from the AHS-1 in 1976. This questionnaire included questions on demographics, past medical history, and psychosocial factors. The dietary

section consisted of 55 nonquantitative food-frequency questions in which participants were asked how often, on average, each food or beverage was consumed when following the usual routine. Most dietary questions had 8 frequency categories that ranged from “never or almost never” to “more than once per day.” Variables such as dairy products (whole milk, lowfat milk, nonfat milk, buttermilk, and cheese), and sweets/desserts had 7 frequency categories that ranged from “never” to “over 5 times per day.” There were questions about the type of bread consumed, with options being “white only,” “100% whole wheat only,” “sprouted only,” “other only,” “combination of white and whole wheat or sprouted wheat bread,” “combination of white plus other only,” “combination of whole wheat plus sprouted wheat only,” “combination of whole wheat or sprouted wheat plus other,” and “combination of white plus whole wheat or sprouted wheat plus other type of bread.” These bread categories were then collapsed into 3: “white,” “whole wheat,” and “other.”

Each of the food items were assessed individually. However, responses for the various dairy products and meat questions were also summed to form a dairy and meat index. The meat index was determined from responses to 6 questions on the current frequency of consumption of specific meat (beef–steak, beef–hamburger, other–beef or veal, fish, poultry, and pork), and one question on the current frequency of consumption of any meat. This index has been used previously in this population for assessment of associated colon cancer risk (18).

Case Ascertainment

Assessment of colorectal polyps was performed using the baseline AHS-2 lifestyle questionnaire. This included questions on whether they had ever had a colonoscopy. They were also asked about whether they had been told by a physician that they had any of a number of specific conditions including “rectal/colon polyps.” For each condition, they were also asked to specify the approximate time frame since first diagnosed with the condition. The 5 time periods since first diagnosis were “less than 5 years ago,” “5 to 9 years ago,” “10 to 14 years ago,” “15 to 19 years ago,” and “20+ years ago.” Those who had been diagnosed more than 20 yr ago were considered prevalent cases in 1976 and were, therefore, excluded from our study population. To ensure higher validity of the self-reported outcome, only cases diagnosed after a colonoscopy were used in this study. A total of 590 new cases of rectal/colon polyps were thus identified during the 26-yr follow-up since enrollment into the AHS-1. After exclusion criteria were applied to the cohort, 441 incident cases of rectal/colon polyps were included in the analytic population of 2,818 subjects.

Statistical Methods

The statistical package SAS version 9.1 was used in all analyses. The characteristics of participants with and without incident rectal/colon polyps were compared by independent *t* test for continuous variables and chi-square test for categorical variables. Frequency of intake of various foods was categorized into 3 or more meaningful categories for this population and to assure adequate number of cases in each exposure category as well as be able to assess trends.

Multivariable logistic regression analysis was used to assess the risk of rectal/colon polyps associated with the frequency of consumption of the different food variables. A basic model was initially created for each of the candidate food variables [total meat, total white meat (poultry + fish), total red meat (beef + pork), poultry, fish, pork, beef, salad, cooked green vegetables, tomatoes, legumes, nuts, dried fruit, citrus fruit, winter fruit, other seasonal fruit, brown rice, white rice, bread, total dairy products, cheese, whole milk, lowfat milk, nonfat milk, eggs, and sweets intake] controlling for age, gender, and body mass index (BMI). Only the food variables that showed a statistically significant association with rectal/colon polyps

were kept to be assessed, individually, in a multivariate model that adjusted for possible confounders, which included family history of CRC (birth mother or birth father with CRC), education, physical activity level, alcohol, smoking, constipation, intake of sweets, pain medication, multivitamins, and the different food variables. All possible confounders, which also included food variables, were introduced into these new models one at the time. Only those variables that changed the main effect of the exposure of interest 10% or more were included in the final model (30). None of the nonfood variables changed the main effect of the exposure of interest, but among the food variables, only meat intake met this criterion when assessing the effect of legume consumption. Likewise, salad intake changed the main effect of brown rice. Therefore, these variables were included in the final model. Education did not change the main effect of the food variables assessed, but it was included in the final model to adjust for socioeconomic status.

To investigate a possible relationship between the different food variables and age, gender, or BMI, we also tested for a multiplicative interaction using in the model the product term "food" × age, "food" × gender, and "food" × BMI.

RESULTS

During an average of 26 yr of follow-up, a total of 441 cases of rectal/colon polyps were identified in the analytic population of 2,818 subjects.

Nondietary characteristics of the study population are presented in Table 1. Rectal/colon polyp cases were older, had higher BMI, and tended to be more educated (college graduates or more) than noncases. A higher proportion of cases reported positive family history of CRC among first-degree relatives, and more men reported incident rectal/colon polyps than women. No significant difference was found between cases and noncases for physical activity, constipation, use of pain medication, or use of multivitamins.

Table 2 shows the association between food variables and rectal/colon polyps risk assessed in the basic model with adjustment for age, gender, and BMI. In this population, where more than 60% of the cases were vegetarians or nearly so (eat meat <1/wk) (Table 2), inverse associations were found for the frequency of consumption of cooked green vegetables, legumes, dried fruit, and brown rice. These associations were statistically significant when comparing the highest vs. the lowest category of intake. A dose-response effect (P trend < 0.05) was also evident for these exposure factors.

After controlling for the selected confounding factors and education (Table 3), cooked green vegetables were associated with a 24% reduction in the risk of rectal/colon polyps when comparing intakes of 1 time/day or more with <5 times/wk (P trend = .03). A dose-response effect (P trend = .02) was also evident for legume intake with a clear protective association. When comparing dried fruit intake of 3 times/wk or more vs. <1 time/wk, a 26% reduced risk of rectal/colon polyps was observed (P trend = .03). Finally, consumption of brown rice at least once a wk reduced the risk of rectal/colon polyps by about 40%. A dose-response effect was also evident.

When tested for a multiplicative interaction term between the different food variables and age, gender, and BMI, no statistical significance was attained.

DISCUSSION

In this 26-yr follow-up study, a higher frequency of consumption of cooked green vegetables, legumes, dried fruit, and brown rice was associated with a decreased risk of rectal/colon polyps.

Although many epidemiological studies (9,12,25,31–35) have shown the protective effect of fruits, vegetables, and grains on rectal/colon adenoma risk, others have not (20,35,36), or were limited to specific circumstances. In some studies, the protective association was limited only to vegetables (11,37,38), fruits (33,39), or grains (40). Finally, others have demonstrated an inverse relationship limited to size (40), number of adenoma (37), colon but not rectum (41) or specific colon subsites (37). Randomized clinical trials assessing colon polyp recurrence have not detected an association with these food sources (35,42,43). The differences in findings may be due to specific limitations of these studies, such as, in the case of experimental studies, the intervention period having been too short to have an effect on tumor development.

Similar to our findings, a study conducted by Millen et al. (41) as part of the Prostate, Lung, Colorectal, Ovarian (PLCO) Cancer Screening Program observed a decreased risk of adenoma with high vs. low intake of green vegetables. A case-control study performed on southern Californians also found that frequent consumption of green vegetables, fruits (including raisins and prunes), and grains (including brown rice) was associated with a decrease in polyp prevalence (9).

Many hypotheses have been developed to explain the relationship between diet and the risk of CRC (44–46). For the most part, dietary factors that correlate with a predisposition to colon cancer are also associated with a risk of colon adenoma (47). Thus, it is possible that the same hypotheses that relate diet to CRC may also explain its relationship with colon adenomas. These hypotheses tend to be based on the concept of high-risk diets, which may either contain high levels of carcinogens or lack one or more anticarcinogenic protective factors. It is also well known that diets with a high intake of fruits and vegetables contain dietary fiber and phytochemicals that may inhibit colon carcinogenesis (48,49).

Diets high in meat intake have been shown in different studies to increase the risk of CRC (18,50–54) and incident (12,55–58) and recurrent colon polyps (59). In fact, AHS-1 found that meat consumption predicted risk of CRC (18). Several mechanisms have been postulated to explain this (45,48,57–60). However, in our study we did not find associations between meat intake and incident polyps, although the confidence intervals still admit the possibility of modest effects that we did not detect. It is also possible that meat intake has more of an effect on the progression from polyps to carcinoma, instead of the transition from normal to neoplastic mucosa.

Cruciferous vegetables such as broccoli contain sulforaphane, which detoxifies carcinogenic compounds. Also, all green plant parts contain chlorophyll, which modifies genotoxic effects of known toxins (61). Among the most studied bioactive compounds of these vegetables associated with cancer protection are glucosinolates and isothiocyanates, which induce phase 2 detoxication enzymes and boost antioxidant status (23,62). Finally, it has also been reported that some nutrients found in these food variables are highly bioavailable after being cooked, which would improve their protective function (48).

Legumes are a source of fermentable dietary fiber, which is a precursor of luminal butyrate, a compound with antiinflammatory and antineoplastic properties (63,64). The high fiber content would also dilute potential carcinogens by decreasing the overall transit time of the fecal bulk, by binding bile acids (65) or by a volatile fatty-acid-mediated lowering of the colonic pH that could slow conversion of primary to secondary bile acids (66). Other bioactive constituents of legumes that have anticarcinogenic properties and could potentially account for a protective effect include saponins, protease inhibitors, inositol hexaphosphate, gamma-tocopherol, and phytosterols (67). In addition, legumes have a low glycemic index (GI), which is associated with a reduced risk of CRC (48). It is also possible that there is a

specific factor in legumes that modifies one or more of the hypothesized carcinogenic mechanisms that occur in the colon because of a higher red meat intake, as suggested by the study of Singh and Fraser (18). Other studies support our findings of legumes as a protective factor against incidence (14,37) and recurrence (21) of colon polyps.

Dried fruits may be protective mostly due to their high fiber content, which slows glucose absorption and thus promotes better glucose control. The fiber also reduces hyperinsulinemia and produces short-chain fatty acids that have been shown to reduce cancer cell growth in vitro (68).

The protective effect of brown rice may also be explained due to its high content of fiber. Additionally, its content of phytates and protease inhibitors may play an important role in its protection (48).

The major strength of our study is its prospective design with 26 yr of follow-up. This eliminates the possibility of recall bias when assessing food intake. About 80% of this population (unpublished information) did not make major changes in their dietary habits during these years of followup, which also reduces the risk of measurement error in the exposure status. The unique lifestyle of the Adventist population, with a very low percentage of alcohol or smoking habits, reduces the possibility of confounding by these nondietary factors.

Limitations of this study include the possibility that participants may have overestimated some of their food consumption as a result of increased awareness of the potentially beneficial effects on cancer, or due to social desirability. However, this type of misclassification should be nondifferential, biasing the results toward the null. Due to the lack of hospital records of colonoscopy, there is also the possibility of measurement error in the outcome assessment. But again, this misclassification is most likely to be nondifferential, biasing the result toward the null. Survivors from the baseline AHS-1 study who also enrolled in the AHS-2 may have been healthier than the original cohort, which could bias the estimates of colon polyps risk in the target population. The AHS-1 FFQ was limited in the total number of foods. Moreover, we could not adequately adjust for energy intake, an important known risk factor for colon polyps, although we did adjust for BMI. Thus, in order to reach a better understanding of the roles of individual food groups and nutrients, the use of an improved dietary instrument is required. Finally, different physiological mechanisms occur during food transit through the large intestine that may increase exposure to carcinogens that contribute to cancer risk. We only asked about rectal/colon polyps without asking about the specific site. Thus, this lack of information on the specific site of the polyps, as well as the lack of histological classification, constitutes another limitation of our study.

In conclusion, our findings identify some foods—cooked green vegetables, legumes, dried fruit, and brown rice—as significantly inversely associated with the risk of rectal/colon polyps. However, we are aware of the difficulty assessing nutritional factors and the need for additional and better-designed studies. The anticarcinogenic properties of foods are still being explored, and it is possible that interactions between various nutrients with anticarcinogenic properties will be able to better explain the observed findings.

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TABLE 1

Baseline subject characteristics among subjects with (cases) and without (noncases) rectal/colon polyps (The Adventist Health Study, California, 1976–2002)

Characteristic	Cases (*n* = 441)	Noncases (*n* = 2,377)	*P* Value
Age (mean ± SD)	73.4 ± 9.2	71.2 ± 9.7	<.01
Body mass index (kg/m^2)			
≤23.2	39.8%	50.1%	<.01
23.3–≤ 25.8	31.8%	26.3%	
25.9 +	28.4%	23.6%	
Gender			
Female	52.2%	61.2%	<.01
Male	47.8%	38.8%	
Family history (1st degree) of CRC			
Yes	9.7%	5.0%	<.01
No	90.3%	95.0%	
Education			
≤High school	14.8%	15.8%	.73
Some college	39.6%	40.6%	
College graduate +	45.6%	43.6%	
Physical activity			
None	32.4%	26.9%	.07
Low	12.7%	15.9%	
Moderate	18.1%	20.0%	
Vigorous	36.8%	37.2%	
Alcohol			
Never	90.8%	93.5%	.04
Ever	9.2%	6.5%	
Smoking			
Never	83.3%	85.5%	.22
Ever	16.7%	14.5%	
Constipation			
Never	8.8%	8.5%	.79
Ever	91.2%	91.5%	
Pain medication			
Never	96.3%	97.1%	.38
Ever	3.7%	2.9%	
Aspirin use			
Noncurrent	84.1%	82.1%	.34
1+/wk	15.9%	17.9%	
Multivitamin			
Never	58.3%	59.7%	.59
Ever	41.7%	40.3%	

TABLE 2

Adjusted* odds ratio (OR) of rectal/colon polyps according to specific foods (The Adventist Health Study, California, 1976–2002)

Variable	Cases	OR	95% CI	*P* Trend
Total meat intake				
Never	168	1.00		.76
>0–<1/wk	111	1.06	0.80–1.41	
1+/wk	162	1.04	0.80–1.35	
Poultry				
Never	214	1.00		.56
>0–<1/wk	187	1.03	0.82–1.30	
1+/wk	40	1.13	0.77–1.68	
Beef				
Never	202	1.00		.62
>0–<1/wk	112	0.89	0.68–1.16	
1+/wk	127	1.09	0.84–1.41	
Fish				
Never	215	1.00		.64
>0–<1/wk	187	0.94	0.75–1.18	
1+/wk	39	1.25	0.85–1.85	
White meat				
Never	191	1.00		.40
>0–<1/wk	187	0.92	0.73–1.16	
1+/wk	63	1.27	0.92–1.77	
Red meat				
Never	202	1.00		.64
>0–<1/wk	112	0.89	0.68–1.16	
1+/wk	127	1.08	0.84–1.41	
Salad				
<5/wk	168	1.00		.94
5–6/wk	108	0.95	0.72–1.26	
1+/day	165	1.01	0.79–1.30	
Cooked green vegetables				
<5/wk	193	1.00		.03†
5–6/wk	102	0.78	0.59–1.04	
1+/day	146	0.76	0.60–0.98	
Tomatoes				
<3/wk	144	1.00		.93
3–4/wk	147	0.89	0.68–1.16	
5+/wk	150	1.01	0.78–1.32	
Legumes				
<1/month	48	1.00		

Variable	Cases	OR	95% CI	*P* Trend
1/mo–3/wk	294	0.96	0.68–1.35	.05
3+/wk	99	0.73	0.49–1.08	
Nuts				
<1/wk	147	1.00		
1–4/wk	195	0.78	0.62–1.02	.19
5+/wk	99	0.84	0.62–1.13	
Dried fruit				
<1/wk	189	1.00		.03†
1–2/wk	119	0.77	0.59–1.006	
3+/wk	133	0.76	0.58–0.98	
Citrus fruit				
<1/wk	156	1.00		.58
1–2/wk	137	1.001	0.77–1.31	
3+/wk	148	0.93	0.71–1.21	
Winter fruit				
<3/wk	105	1.00		.92
3–6/wk	198	0.87	0.66–1.06	
1+/day	138	0.99	0.74–1.35	
Other fruit				
<1/wk	100	1.00		.18
1–2/wk	118	0.85	0.63–1.17	
3+/wk	223	0.82	0.62–1.08	
Brown rice				
Never	102	1.00		.02†
<1/month	121	0.94	0.69–1.28	
1–2/month	152	0.84	0.62–1.13	
1+/wk	66	0.67	0.47–0.95*	
White rice				
Never	128	1.00		.67
<1/month	113	1.14	0.85–1.53	
1–2/m	154	1.22	0.93–1.61	
1+/wk	46	0.93	0.63–1.36	
Bread				
White	28	1.00		.69
Wheat	269	0.88	0.56–1.39	
Other	141	0.97	0.60–1.56	
Cheese				
<1/wk	118	1.00		.74
1–2/wk	163	0.85	0.65–1.12	
>2/wk	160	0.94	0.71–1.24	
Whole milk				

Variable	Cases	OR	95% CI	*P* Trend
Never	169	1.00		.26
<1/wk–<1/day	162	0.97	0.76–1.24	
1+/day	110	1.20	0.91–1.58	
Lowfat milk				
Never	187	1.00		.23
<1/wk–<1/day	114	0.95	0.72–1.24	
1+/day	140	0.86	0.67–1.10	
Nonfat milk				
Never	270	1.00		.26
<1/wk–<1/day	86	0.87	0.66–1.16	
1+/day	85	0.87	0.67–1.15	
Eggs				
<1/wk	174	1.00		.32
1–2/wk	185	0.88	0.69–1.11	
2+/wk	82	0.88	0.65–1.19	
Dairy				
<1/day	57	1.00		.55
1/day–<2/day	152	1.04	0.73–1.48	
2+/day	232	0.95	0.68–1.32	
Sweets				
<1/wk	66	1.00		.10
1–2/wk	141	1.08	0.77–1.51	
3–6/wk	148	1.18	0.84–1.66	
1+/day	86	1.32	0.91–1.92	

*Adjusted by age, gender, and body mass index.

†*P* value < 0.05.

TABLE 3

Final multivariate adjusted model with odds ratio for rectal/colon polyps according to selected dietary factors (The Adventist Health Study, California, 1976–2002)

Variable	OR	95% CI	*P* (Trend)
Cooked green vegetables[a]			
<5/wk	1.00	Reference	.03†
5–6/wk	0.78	0.59–1.04	
1+/day	0.76	0.59–0.97	
Legumes[b]			
<1/mo	1.00	Reference	.02†
1/mo–3/wk	0.90	0.62–1.30	
3+/wk	0.67	0.44–1.01	
Dried fruit[c]			
<1/wk	1.00	Reference	.03†
1–2/wk	0.77	0.59–1.01	
3+/wk	0.76	0.58–0.99	
Brown rice[d]			
Never	1.00	Reference	.007†
<1/mo	0.94	0.69–1.29	
1–2/m	0.84	0.63–1.14	
1+/wk	0.60	0.42–0.87	

[a] Multivariate model adjusted by age, gender, body mass index (BMI), and education.

[b] Multivariate model adjusted by age, gender, BMI, education, and meat intake.

[c] Multivariate model adjusted by age, gender, BMI, and education.

[d] Multivariate model adjusted by age, gender, BMI, education, and salad.

† *P* value < 0.05.