Association Between Dietary Fiber and Incident Cases of Colon Polyps: The Adventist Health Study

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ABSTRACT

Background: Colorectal cancer (CRC) is a leading cause of cancer death in the United States. Most cases of CRC arise in adenomatous polyps. It has been estimated that 25%–35% of colon adenoma risk could be avoidable by modification of dietary and life-style habits.

Methods: We estimated the association between total dietary fiber and fiber intake from fruits, vegetables, and grains, and the risk of physician-diagnosed colon polyps among 2818 men and women who had undergone colonoscopy. Data were drawn from 2 cohort studies—the Adventist Health Study-1 (AHS-1) of 1976 and the Adventist Health Study-2 (AHS-2) conducted from 2002 to 2005. Dietary information was obtained from the self-administered questionnaire from AHS-1, while outcome was assessed from AHS-2 data. Multivariate logistic regression analysis was used to estimate the period risk of incident cases of polyps.

Results: A total of 441 incident cases of colon polyps were identified. After adjusting for age, sex, body mass index, physical activity, education, and alcohol and meat consumption, total fiber intake was inversely associated with the risk of colon polyps (odds ratio [OR] for highest vs lowest quartile = 0.71, 95% confidence interval [CI] 0.51–0.99). This association showed a dose-response effect ($p = .04$). Analyses of various sources of fiber showed the most clear effect of fiber from vegetables including legumes (OR for highest vs lowest quartile = 0.65; 95% CI 0.47–0.90; $p = .02$).

Conclusions: In this population comprising a high proportion of vegetarians, persons who consumed low amounts of fiber, especially fiber contained in vegetables, had a higher risk of developing colon polyps.

Gastrointest Cancer Res 4:161–167.

Submitted: May 6, 2011
Accepted: June 24, 2011

Colorectal cancer (CRC) is the fourth most common cancer in men and the third most common in women worldwide.[1] It is the second leading cause of cancer-related death in the United States, third after prostate cancer among men and third after breast cancer among woman.[2] The number of new cases of CRC has been increasing in certain countries where the incidence was historically low (Japan, Puerto Rico).[1] In high-risk countries, trends are gradually increasing (England), stabilizing (New Zealand), or declining (United States) with time. In the United States, rates have been decreasing for most of the last 2 decades, perhaps partially due to screening for detection and removal of colorectal polyps (adenomas) before progression to cancer, and interventions reducing the effects of lifestyle and dietary changes.[1]

It is estimated that about 30% of middle-aged or elderly people have colon polyps. Since they are found in populations with a high incidence of CRC, and colorectal adenomas are considered to be potential precancerous lesions, it is believed they share a common pathogenesis.[3] Adenomatous polyps are thought to arise from a failure in a step of the normal process of cell proliferation and apoptosis. It is generally accepted that most CRC originates within previously benign adenomas through a multistep process. Adenomas develop as a consequence of factors involved in tumorigenesis and progress to carcinoma because of factors acting as tumor promoters.[4]

Numerous environmental factors can increase the risk of CRC, presumably by modulating these pathways. Evidence suggests that both hereditary factors and environment contribute to colonic adenoma susceptibility. For adenomas to form and progress to cancer, several lifestyle and dietary factors would act in concert. One

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factor would be responsible for the initial development of adenomas, another would enhance the growth of adenomas, and one or more carcinogens or tumor promoters would finally give rise to cancer.[4,5]

Results from international correlation and migrant studies suggest that environmental factors, especially diet, likely account for most colon cancers, as compared to genes.[6–8] Different case-control[9–13] and prospective studies[14–20] suggest that low intake of vegetables, fruits, and dietary fiber is associated with the risk of CRC and/or colon polyps. This shows the importance of environment, rather than genetics, in the epidemiology of CRC. Some factors correlating with a predisposition to CRC are also associated with a risk of colonic adenomas.

Despite the hypothesis postulated by Burkitt endeavoring to explain dietary fiber being protective against large bowel cancer,[21] epidemiologic studies of this possible link are inconclusive.[20,22–25] We prospectively examined the relation between dietary fiber intake and the risk of colon polyps among California Adventists who had undergone colonoscopy.

MATERIALS AND METHODS

Study Population

The study population is a survivor cohort that responded to 2 lifestyle questionnaires, the Adventist Health Study-1 (AHS-1) administered in 1976–1977 and the Adventist Health Study-2 (AHS-2) in 2002–2004. AHS-1 was designed to examine the risk of cancer, coronary heart disease, and all-cause mortality among non-Hispanic California Seventh-Day Adventists.[26] AHS-2 is an ongoing investigation among Adventist church members throughout the United States and Canada. The purpose of AHS-2 is to provide more precise and comprehensive results investigating the relationship between diet and the risk of selected cancers.[27] Details of how respondents to these 2 cohort studies were identified and their information linked have been described elsewhere.[28]

In total, 5095 non-Hispanic white subjects participated in both cohort studies. For the purpose of this study, we excluded data from (1) persons with prevalent cases of colon polyps (82 cases), (2) those who reported in their baseline questionnaire that they had a previous history of colorectal cancer prior to the diagnosis of colon polyps (7 cases), (3) persons with a history of inflammatory intestinal conditions such as ulcerative colitis or Crohn's disease (9 cases), and people diagnosed with diverticulitis (104 cases). To minimize detection and selection bias, we excluded persons who had not undergone colonoscopy within the period 1976–2002 as well as those who had a diagnosis of polyps before colonoscopy (n = 2075). The total number of cases excluded was 2277. Hence, the analytic population consists of data from 2818 persons.

Dietary and Lifestyle Assessment

Dietary and lifestyle information was assessed with the use of a self-administered questionnaire from AHS-1 in 1976. This questionnaire also included questions concerning demographics, past medical history, and psychosocial factors. The dietary section consisted of 55 nonquantitative food-frequency questions, where 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." For bread products only, there were questions about the type of bread (white, 100% whole wheat or whole grain, sprouted wheat or wheat berry, and "other"). For white bread, there was also a frequency category for its consumption that ranged from "never" to "over 5 times per day."

For each food item, frequencies were converted into frequency per month, and it was assumed that each frequency corresponded to one standard serving size. The standard serving size corresponding to the food items under study was obtained from the report of the Nationwide Food Consumption Survey 1977–78 conducted by the US Department of Agriculture (USDA) from April 1977 through March 1978.[29] In terms of weight, the amount of fiber contained in each serving size of food items was calculated using the USDA National Nutrient Database for Standard Reference.[30] The final intake of dietary fiber consumed for each of the participants was computed by multiplying the frequency of consumption of each food item by the fiber content of the specific standard portion sizes.

Food sources for the "vegetable index" included legumes (canned beans, lentils, split peas, etc), green salads (tossed salad, coleslaw salad, etc), tomatoes, and cooked green vegetables (green beans, green peas, chard, broccoli, spinach, cabbage, etc). The "fruit index" represents the summation of the variables: dry fruit (raisins, dates, etc), fresh citrus fruit (not juice), fresh fruit commonly available in winter (apples, bananas, pears), and other fresh fruit. For the "grain index," we used the variables bread (white, 100% whole wheat or whole grain, sprouted wheat or wheat berry and "other" [rye, cracked wheat, pumpernickel, soy, etc]), and rice (brown and white). The "meat index" was determined from responses to 6 questions on the current frequency of consumption of specific meats (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 previously been used in this population for assessment of associated CRC.[18]

For physical activity, the questionnaire included 10 items on work, recreational, and leisure-related physical activity. A 4-level index activity was developed as follows: (1) "little or none" for rarely or never participation in vigorous activity, (2) "low" for some vigorous activity ($<$ 15 min per session, $<$ 3 times per week), (3) "moderate" for regular moderate-level leisure exercise ($<$ 15 min per session, $\geq$ 3 times per week), and (4) "high" for regular vigorous activity ($\geq$ 15 min per session, $\geq$ 3 times per week). This physical activity index has been used in previous studies using the same population.[28,31]

Family history of CRC was evaluated from response to whether a parent ever had bowel cancer. The answer to this question was categorized as either "Yes," one or both parents, or "No," neither parent. The variable "education" was obtained according to the highest education level reported by the participant at the time of the 1976 study. The possible answers were collapsed into 3 levels: (1) high school graduate or less education, (2) some college, and (3) college graduate or higher education.

Case Ascertainment

Assessment of colon polyps was performed using the baseline AHS-2 lifestyle questionnaire. This included questions about specific disorders including colon polyps. In the same question they were 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," "5–9 years ago," "10–14 years ago," "15–19 years ago," and "20+ years ago. Those who had been diagnosed more than 20 years ago were considered prevalent cases in 1976 and were therefore excluded from our study population. A total of 590 new physician-diagnosed cases of colon polyps were identified during the 26 year follow-up, since enrollment in the AHS-1. After exclusion criteria were applied to the cohort, 441 incident cases of colon polyps were included in the analytic population of 2818 subjects.

Statistical Methods

Chi-square tests were used to evaluate the association between potential categorical predictor factors and incident colon polyps. Differences in means of dietary fiber intake between persons with colon polyps those were polyp-free were assessed using independent *t* test.

Food fiber indexes (vegetables, fruits, and grains) were categorized into quartiles, as was total dietary fiber. The risk of colon polyps associated with these indices was assessed using logistic regression analyses. Candidate covariates were selected based on review of the literature and included age, gender, body mass index (BMI), family history of CRC, education, physical activity, history of constipation, alcohol use, smoking, meat consumption, vitamin E supplements, vitamin C supplements, multivitamins, dairy index, intake of sweets, and vegetarian protein products (gluten, soy meat alternatives, or nutmeats). Consumption of water and nuts was also assessed due to their demonstrated effect on other diseases in this population.[32–34] Food variables were assessed using meaningful categories appropriate for this population. Since a large proportion of this population are vegetarians, the meat index variable was divided into 4 "frequency-of-consumption" levels: (1) vegetarian (never eat meat), (2) $<$ 1 time/week, (3) 1–4 times/week, and (4) $>$ 4 times/week.

A basic model with fiber, age, sex, and BMI was first constructed. The other candidate variables were introduced into this model one at a time. Only those variables that changed the main effect of fiber more than 10% were included in the final model.[35] Of the candidate covariates, only alcohol and meat consumption met this criterion and were included in the final model. In addition, physical activity was included, based on its strength of association as an independent risk factor for colon adenomas. Education was also included to control for socioeconomic status.

Additional multivariable analyses were developed for specific food group sources of fiber such as vegetables, fruits, and grains. For grains, a new categorical variable was created based on its refined or nonrefined status: (1) whole wheat bread and brown rice, (2) no rice, other bread different than whole wheat or white bread, and (3) white bread and white rice.

RESULTS

During the approximate 26 year follow-up, a total of 441 incident cases of colon polyps were identified from the analytic population of 2818 subjects.

Baseline characteristics of persons who developed colon-polyps and polyp-free participants are presented in Table 1. In general those who developed colon polyp were older and had higher BMI. A higher proportion of men than women reported incident colon polyps. Those who developed polyps also tended to be less physically active, use alcohol more frequently, and consume more meat than did those who were polyp-free.

The mean daily intake of total dietary fiber was slightly higher among polyp-free participants compared to those found to have polyps (Table 2), with the same pattern observed for each of the 3 sources of fiber (vegetables, fruits, and grains). However, only total fiber intake showed a statistically significant difference between cases and controls.

Table 3 shows ORs and 95% CI calculated for colon-polyp population by quartiles of total dietary fiber and various sources of fiber intake (vegetables, fruits, and grains) with adjustment for age, gender, BMI, physical activity, education, and meat intake. An inverse dose-response association was found for quartiles of total dietary fiber intake with the highest quartile associated with a 29% reduction in risk of polyps.

When analyzing the effect of each source of fiber (vegetables, fruits, and grains) separately there emerged again an inverse dose-response association, with participants in the highest quartile of vegetable fiber consumption showing a significant 35% decrease in risk of colon polyps compared with those in the lowest quartile of consumption ($p = .01$). Likewise, the risk of colon polyps seemed to decrease with increasing amounts of grains consumed. There was no clear association with fiber from fruits. Simultaneous adjustment for all 3 sources of fiber in a multivariate model did not materially change the results for vegetables for the highest vs lowest quartile of intake. The linear association also remained significant ($p = .04$). Also for grains, the point estimates remained virtually unchanged.

We further explored the role of specific components of the vegetable fiber by evaluating the effect of vegetable consumption after excluding one specific component (total vegetable fiber without legumes, total vegetable fiber without green salad, total vegetable fiber without cooked green vegetables, and total vegetable fiber without tomatoes) and compared the highest vs lowest quartile of intake. Total vegetable fiber remained in the protective direction with a statistically significant correlation even after green salad was removed from the model. When tomatoes, legumes, and cooked green vegetables were excluded from the total vegetable fiber index, the OR was diminished by 20.1%, 25.8% , and 35.2%, respectively, and the amended fiber-adenoma association lost statistical significance. Thus these foods may be of importance.

We evaluated the effect of each source of fruit fiber in the same manner. Fruit fiber showed a statistically significant protective correlation in the multivariate model when winter fruit fiber was excluded (OR = 0.70, $p = .01$). No significant change in the OR was evident when the other fruit components were excluded (Table 4). Thus, winter fruits may not contribute to protection.

Table 1. Baseline subject characteristics associated with the risk of colon polyps, Adventist Health Study, California, 1976–2002

Characteristic	Incidence of colon polyps (n = 441)	Polyp-free participants (n = 2377)	*p* value
Age (mean ± SD)	73.4 ± 9.2	71.2 ± 9.7	<.01
Body mass index (mean ± SD)	24.5 ± 6.5	23.9 ± 3.7	<.01
Sex			
Female	52.2%	61.2%	<.01
Male	47.8%	38.8%	
Family history CRC			<.01
Yes	9.72%	5.05%	
No	90.28%	94.95%	
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%	
Meat (Servings)			
Never	38.0%	39.4%	.04
< 1/wk	25.1%	24.8%	
1–4/wk	15.0%	18.8%	
> 4/wk	21.8%	17.0%	

Abbreviations: SD = standard deviation; CRC = colorectal cancer.

Table 2. Daily mean intake of dietary fiber at baseline among subjects with incident colon polyps and polyp-free participants, Adventist Health Study, California, 1976–2002

	Incidence of colon polyps (n = 441)	Polyp-free participants (n = 2377)	
Fiber intake	Mean	Mean	*p* value*
Total fiber intake g/d	11.2 ± 4.3	11.7 ± 4.8	.04
Fruit fiber g/d	4.4 ± 2.7	4.7 ± 3.1	.07
Vegetable fiber g/d	5.0 ± 2.5	5.2 ± 2.6	.14
Grain fiber g/d	1.8 ± 0.6	1.9 ± 0.5	.42

*$p < .05$ by *t* test.
Abbreviation: g/d = grams per day.

The multivariate analysis for categories of grain fiber did not show a statistically significant association with colon polyp risk.

DISCUSSION

In this cohort, total dietary fiber intake, specifically from vegetables, was inversely associated with colon polyps, with a clear dose-response effect. Fiber intake from fruits and grains did not show a statistically significant effect on colon polyps, though the risk estimates trended in the protective direction. Our results were not altered by mutually adjusting the fiber sources (including vegetables, fruit, and grain fiber in a single model).

Our findings suggest that fiber from legumes, cooked green vegetables, and tomatoes, but not green salad, are needed for the protective effect of "vegetable fiber." Green salad seems to have no effect on colon polyps risk, perhaps due to its low fiber content, or, since the typical American diet includes green salad in most meals, it is not a discriminating factor. The other vegetable sources may contribute importantly to the protective effect against colon polyp risk.

The protective effects observed might be related not only to fiber content but also because of the presence of chemopreventive phytochemicals.[36] The effects of tomatoes and legumes on CRC, specifically, have been investigated in a small number of epidemiologic studies. In AHS-1, Singh and Fraser (1998) identified a complex association between the intake of red meat and legumes for CRC risk. Their findings raised the possibility that a specific factor in legumes neutralizes one or more of the hypothesized carcinogenic mechanisms associated with higher red meat intake.[18] These findings support our data that legumes are an important factor for the relationship found between vegetables and colon adenomas.

Other epidemiologic studies, with colon adenomas as the outcome of interest, have shown that frequent consumption of legumes was associated with a reduced incidence[14,37] as well as reduced recurrence of colon adenomas.[38] Tomatoes have also been reported as a protective against colon adenomas.[39–41] Their protection has been associated with fiber and lycopene content that may inhibit cancer proliferation by interfering with the insulin-like-growth factor (IGFs) system, possibly through an effect of IGF-binding proteins (IGFBPs).[42]

When evaluating the components of the fruit fiber index, excluding winter fruit modified the index toward a statistically significant protective effect, and a major de-

Table 3. Odds ratio of colon polyps according to total dietary fiber and sources of fiber at baseline, Adventist Health Study, California, 1976–2002

	Quartile of consumption				
Fiber	**Q1**	**Q2**	**Q3**	**Q4**	***p* value***
Total fiber index					
Median (g/d)	6.7	9.8	12.6	16.9	
No. of cases (n = 441)	114	119	115	93	
OR[1]	1.00	0.99 (0.73–1.34)	0.89 (0.65–1.21)	0.71 (0.51–0.99)	.04†
Vegetable fiber					
Median (g/d)	2.5	4.1	5.6	8.0	
No. of cases (n = 441)	122	106	120	93	
OR[1]	1.00	0.82 (0.61–1.12)	0.86 (0.64–1.17)	0.63 (0.45–0.87)	.01†
OR[2]	1.00	0.86 (0.63–1.18)	0.91 (0.66–1.24)	0.68 (0.48–0.96)	.04†
Fruit fiber					
Median (g/d)	1.5	3.4	5.0	7.9	
No. of cases (n = 441)	110	123	105	103	
OR[1]	1.00	1.12 (0.81–1.51)	0.86 (0.61–1.19)	0.95 (0.68–1.31)	.40
OR[2]	1.00	1.16 (0.85–1.58)	0.94 (0.67–1.31)	1.07 (0.75–1.50)	.91
Grain fiber					
Median (g/d)	1.1	1.9	2.0	2.4	
No. of cases (n = 441)	118	120	110	93	
OR[1]	1.00	1.11 (0.82–1.51)	0.95 (0.69–1.29)	0.81 (0.58–1.12)	.13
OR[2]	1.00	1.05 (0.77–1.44)	0.93 (0.68–1.27)	0.83 (0.60–1.16)	.23

[1]Multivariate models included age, sex, body mass index, education, physical activity level, and alcohol and meat intake plus one fiber source of interest.
[2]Multivariate models included same adjustments as model 1 plus all the 3 sources of fiber.
**p* value is from 2-sided tests of trend.
Abbreviations: g/d = grams per day; OR = odds ratio.

crease in OR compared to when winter fruit was included in the index. Thus, "winter fruit" may not be a discriminating variable since these popular fruits are usually available year-round. Therefore, adding this variable to the total fruit fiber index may have masked its effect. For grain sources (brown rice, white rice, wheat bread, white bread, or other types of bread), no statistically significant association was found with colon polyp risk. However, due to the limited ability of the food-frequency questions to assess total grain intake we cannot negate an important relation with the outcome.

Our findings support the hypothesis that high intake of dietary fiber protects against first occurrence of colon adenomas. This is supported by only one other prospective study, which found a higher magnitude of protection.[43] Similar findings related to the effect of vegetables have been reported in some national[11,12,44] and international[37] case-control studies. For fruits and grains, 2 studies performed in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial found an inverse association between these foods and adenoma risk.[45,46] Results from the Nurses' Health Study (NHS) showed an inverse association between frequent consumption of fruits and colorectal adenoma occurrence.[14] Results from 2 trials (Polyp Prevention Trial and Wheat Bran Fiber) indicate a protective effect of fiber on recurrent colorectal adenomas, especially among men.[47] Using cluster analysis to investigate dietary patterns and the risk for colorectal adenoma, a case-control study also found a protective effect for high fruit intake.[13]

Nevertheless, other epidemiologic data on incidence,[20,23] as well as on recurrence of colon polyps,[38,48,49] have not detected an association between dietary fiber and colon adenomas. The possible reasons for these null findings may be the limited dietary fiber information derived from the food-frequency questions, misclassification of true fiber intake due to misreporting, and a limited ability to evaluate long-term dietary exposure.

The major strength of our study is its prospective design with 26 years of follow-up. This eliminates the possibility of recall bias when assessing exposure, including food intake. About 80% of this population (unpublished data) made no major changes in their dietary intake during these years of follow-up, which also reduces the risk of measurement error in the exposure status. However, based on the health recommendations of the Adventist church, it is possible that participants may have overestimated their fruit and vegetable consumption as a result of increased awareness of the potentially beneficial effects on cancer or due to social desirability. But this type of misclassification is most likely nondifferential, biasing the results toward the null.

The unique lifestyle of the Adventist population, with a low percentage of alcohol consumption and tobacco smoking, reduces the possibility of confounding by these nondietary factors. We did not have hospital records of colonoscopy, but only self-reported physician-diagnosed colon polyps. This increases the possibility of measurement error in the outcome assessment. But again, the misclassification is most likely nondifferential. The survivor cohort who volunteered to participate in AHS-2 may have been healthier than the original cohort. This could bias the estimates of colon polyp risk in the target population. Finally, the food-frequency questions were limited in that no data were

Table 4. Multivariate* risk of colon polyps according to sources of vegetable and fruit fiber at baseline, Adventist Health Study, California, 1976–2002

Highest vs lowest quartile	OR	95% CI	*p* value
Vegetable fiber			
Excuding "green salad"[1]	0.78	0.58–1.06	.04†
Excluding "tomatoes"[2]	0.79	0.57–1.09	NS
Excluding "legumes"[3]	0.85	0.62–1.17	NS
Excluding "cooked green vegetables"[4]	0.97	0.70–1.34	NS
Fruit fiber			
Excluding "winter fruit"[5]	0.70	0.50–0.97	.01†
Excluding "citrus fruit"[6]	0.90	0.65–1.27	NS
Excluding "other (seasonal) fruit"[7]	0.94	0.68–1.30	NS
Excluding "dried fruit"[8]	0.98	0.71–1.36	NS

*Multivariate models included age, sex, body mass index, education, physical activity, alcohol, and meat consumption, and comparing highest vs lowest quartile of intake.
†*p* value is from 2-sided tests of trend.
[1]Total vegetable fiber intake without the effect of fiber from "green salad."
[2]Total vegetable fiber intake without the effect of fiber from "tomatoes."
[3]Total vegetable fiber intake without the effect of fiber from "legumes."
[4]Total vegetable fiber intake without the effect of fiber from "cooked green vegetables."
[5]Total fruit fiber intake without the effect of fiber from "winter fruit."
[6]Total fruit fiber intake without the effect of fiber from "citrus fruit."
[7]Total vegetable fiber intake without the effect of fiber from "other seasonal fruits."
[8]Total vegetable fiber intake without the effect of fiber from "dried fruit."
Abbreviations: CI = confidence interval; NS = not significant; OR = odds ratio.

available on portion sizes and specific food items. Therefore, we used standard portion sizes to estimate consumption. Moreover, we could not adjust for energy intake, an important known factor to consider when evaluating colon adenomas risk.

In conclusion, our findings identify dietary fiber, specifically from vegetables (including legumes), as an important protective factor against colon polyps with a dose-response effect. Fruits (but not winter fruits) may also contribute. Further studies with more complete dietary information throughout the follow-up are needed to verify our findings.

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Acknowledgment

The study was supported in part by NHI grants 2RO1-CA 14703-15 and 5RO1 CA 094594.

Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.