Gastroenterology 2014;146:689–699

Dietary Fiber Intake Reduces Risk for Colorectal Adenoma: A Meta-analysis

Qiwen Ben,[1] Yunwei Sun,[1] Rui Chai,[2] Aihua Qian,[1] Bin Xu,[1] and Yaozong Yuan[1]

[1]Department of Gastroenterology, Ruijin Hospital, Shanghai Jiaotong University, Shanghai, PR China; [2]Department of Colorectal Surgery, Zhejiang Provincial People's Hospital, Hangzhou, Zhejiang, PR China

BACKGROUND & AIMS: Reports on the association between dietary fiber intake and risk of colorectal adenoma (CRA), the precursor of colorectal cancer, have been inconsistent. We conducted a meta-analysis of case-control and cohort studies to analyze this association. **METHODS:** We searched the MEDLINE and EMBASE databases to identify relevant studies published through July 2013. A random-effects model was used to estimate summary relative risks (SRRs) and 95% confidence intervals (CIs) for associations between fiber intake and CRA risk. Heterogeneity among studies was assessed using the Cochran Q and I^2 statistics. **RESULTS:** Our meta-analysis included 20 studies involving 10,948 subjects with CRA. The SRRs of CRA for total dietary fiber were 0.72 (95% CI, 0.63–0.83) in a high- vs low-intake analysis and 0.91 (95% CI, 0.87–0.95) per 10-g/day increase in fiber intake in a dose-response model. Subgroup analyses indicated a significant inverse association between total fiber intake and CRA risk in case-control studies (SRR, 0.66; 95% CI, 0.56–0.77), but not in cohort studies (SRR, 0.92; 95% CI, 0.76–1.10). The SRRs of CRA were 0.84 for fruit fiber (95% CI, 0.76–0.94; n = 6 studies), 0.93 for vegetable fiber (95% CI, 0.84–1.04; n = 6 studies), and 0.76 for cereal fiber (95% CI, 0.62–0.92; n = 9 studies) in high- vs low-intake analyses. **CONCLUSIONS:** Our findings support the hypothesis that high dietary fiber intake is associated inversely with CRA risk. Further studies with prospective designs that use validated questionnaires and control for important confounders are warranted.

Keywords: Colon Cancer; Risk Factor; Food; Reduction.

About 1.2 million new cases of colorectal cancer (CRC) are diagnosed and nearly 530,000 deaths from this disease occur annually worldwide.[1] Epidemiologic studies have suggested that dietary factors contribute to the etiology of CRC, but only intake of alcohol in men, and red and processed meat, have been identified convincingly as dietary risk factors for this disease.[2]

The association between dietary fiber and colorectal neoplasia has been investigated intensively since 1970. Results of the World Cancer Research Fund/American Institute for Cancer Research reported in 2011 were deemed to provide "probable," but not "convincing," evidence of this association.[2] A pooled analysis conducted in 2005 showed that dietary fiber intake was associated inversely with the risk of CRC in age-adjusted analyses, but that this association did not remain significant after adjusting for other risk factors.[3] More recently, a meta-analysis of 25 prospective studies showed that the risk of CRC decreased by 10% (95% confidence interval [CI], 6%–14%) per 10-g/day increase in dietary fiber intake.[4] Proposed underlying mechanisms include increased stool bulk and dilution of carcinogens in the colonic lumen, reduced transit time, and bacterial fermentation of fiber to short-chain fatty acids.

As precursor lesions of CRC, colorectal adenomas (CRAs) are informative end points for colon carcinogenesis. However, little is known about risk factors for CRAs other than age, smoking,[5] family history,[6] obesity,[7] and physical inactivity.[8] Most,[9–14] but not all,[15–18] epidemiologic studies have suggested that dietary fiber is associated inversely with the risk of CRA. Interestingly, clinical trials, including 2 large randomized clinical trials (the Polyp Prevention[19] and Wheat Bran Fiber[20] trials), have failed to find evidence that high-fiber consumption protects against recurrent adenoma.

We thus performed the present meta-analysis to assess this association, following the meta-analysis of observational studies in epidemiology guidelines.[21]

Materials and Methods

Data Sources and Searches

Two investigators (Q.W.B. and Y.W.S.) independently performed computerized literature searches of the MEDLINE and EMBASE databases to identify relevant studies published through July 2013. The following text and/or medical subject heading terms were used: (1) "food" OR "diet" OR "consumption" OR "dietary" OR "intake" OR "fiber" OR "fibre," (2) "adenoma" OR "polyp" OR "neoplasm" OR "neoplasia," (3) "colorectal" OR "colon" OR "rectal" OR "large bowel," and (4) "risk" OR "incidence" OR "prevalence." The reference lists of reviews and retrieved articles were searched manually. We did not consider abstracts or unpublished reports for inclusion in the meta-analysis.

Abbreviations used in this paper: **AA, advanced adenoma; CI, confidence interval; CRA, colorectal adenoma; CRC, colorectal cancer; FFQ, food frequency questionnaire; NAA, nonadvanced adenoma; NOS, Newcastle–Ottawa Scale; RR, relative risk; SRR, summary relative risk.**

0016-5085/$36.00
http://dx.doi.org/10.1053/j.gastro.2013.11.003

Study Selection

Two authors (Q.W.B. and Y.W.S.) independently assessed the titles and abstracts of potentially eligible studies using the following inclusion criteria: (1) original article, (2) case-control or cohort design, and (3) reporting of relative risk (RR) estimates with 95% CIs for the association between dietary fiber intake and the risk of CRA adjusted at least for age. Animal and mechanistic studies, non–peer-reviewed articles, ecologic assessments, and correlation studies were excluded. Studies lacking CRA-specific data or data about adenoma recurrence or growth also were excluded. When several publications reported on the same study, we selected the publication with the most complete data for inclusion in the meta-analysis.

Data Extraction

From each study, 2 researchers (Q.W.B. and Y.W.S.) independently extracted the following information: first author's last name, publication year, geographic location(s), patients' sexes and ages, number of cases, definition and number of controls, method of dietary variable ascertainment (types of food item and whether the assessment method had been validated), quantity of intake, duration of follow-up evaluation in cohort studies, RR estimates with corresponding 95% CIs for the highest vs lowest level, and adjustments for confounders. From each study, we extracted the risk estimates that reflected the greatest degree of control for potential confounders.

Quality Assessment for Individual Studies

Two researchers (Q.W.B. and Y.W.S.) used the Newcastle–Ottawa Scale (NOS)[22] to assess study quality. The NOS uses 3 quality parameters for case-control or cohort studies, as follows: selection (maximum score = 4), comparability (maximum score = 2), and exposure/outcome assessment (maximum score = 3). The maximum total score is 9, with a score of 7 or higher indicating a high study quality. Studies with insufficient information for full evaluation with the NOS were considered to be of low quality.

Statistical Methods

All statistical analyses were performed using Stata (version 11.0; StataCorp, College Station, TX) and R package (version 2.11.0 beta, R Development Core Team, NJ) statistical software. A 2-tailed P value less than .05 was considered significant. We used a random-effects model to calculate summary relative risks (SRRs) of CRA with 95% CIs, considering within- and between-study variation.[23] We used a fixed-effects model to obtain overall combined estimates for CRA risk for studies that reported results separately for males and females,[17,24,25] nonadvanced adenomas (NAAs) and advanced adenomas (AAs),[26] adenomas with overexpression and no expression of p53 protein,[27] or colon adenomas and rectal adenomas.[15]

For the dose-response meta-analysis, we used the generalized least-squares trend estimation method developed by Greenland and Longnecker[28] and Orsini and Greenland.[29] This method requires that the distribution of cases and person-years or noncases and RRs with variance estimates is known for at least 3 quantitative categories of use. When this information was not available, we estimated dose-response slopes using variance-weighted least squares regression.[28,29] The generalized least-squares trend and variance-weighted least squares methods require median values for categories of intake levels. If such values were not reported, we took the estimated midpoint between the upper and lower boundaries in each category as the average intake level. If the highest category was open ended, we assumed the size of the open-ended interval to be the same as that of the closest interval. For one study[30] with an extreme upper boundary of the highest category that may have led to exaggerated ranges of intake, we used the width of the adjacent interval to calculate the upper boundary and midpoint. When the lowest category was open ended, the lowest boundary was considered to be zero. For one study that reported intakes in g/1000 kcal/day,[14] the intake in g/day was estimated using the average energy intake reported in the article. Dose-response results are presented for every 10-g/day increase in dietary fiber and for fiber sources.

A potential nonlinear dose-response relationship between total fiber intake and CRA risk was examined using the best-fitting fractional polynomial models,[31] defined as those with the least deviance. A likelihood ratio test was used to determine the difference between nonlinear and linear models to assess nonlinearity.[31]

In assessing heterogeneity among studies, we used the Cochran Q and I^2 statistics. I^2 values represent the amount of total variation explained by variation among studies, with a value of greater than 50% considered to indicate severe heterogeneity and a value of less than 25% indicating the absence of significant heterogeneity.[32] Prespecified subgroup analyses were performed to assess the potential modifying effects of the following variables on outcomes: study design, patient sex, geographic location, type of food frequency questionnaire (FFQ), number of cases, study quality score, and confounders that were adjusted for the following: smoking, body mass index (BMI), physical activity, folate intake, and dietary energy intake. Heterogeneity between subgroups was evaluated by meta-regression. We also conducted a sensitivity analysis to investigate the influences of single studies on the overall risk estimate by omitting one study in each turn. Publication bias was assessed using funnel plots, the Begg adjusted rank correlation,[33,34] with P values less than .10 considered to indicate potential publication bias. To reduce the potential influence of publication bias, we used the trim-and-fill method.[35]

Results

Search Results, Study Characteristics, and Quality Assessment

The search strategy generated 10,578 citations, of which 50 were considered of potential value; the full texts of these publications were retrieved for detailed evaluation (Figure 1). Thirty-three of these 50 articles subsequently were excluded for various reasons, and our review of reference lists led to the inclusion of 3 additional articles. Thus, reports of 20 studies involving 10,948 subjects with CRA were included in the meta-analysis (Supplementary Tables 1 and 2). These studies were conducted in the United States (n = 12), Europe (n = 6), and Asia (n = 2). FFQs were used to assess exposure to certain food items in all but one study,[36] which used a 5-day dietary record. The diagnosis of adenoma was based on histologic findings in all studies.