

【PL-3】

DIETARY FIBER AND COLON CANCER: WHERE DO WE STAND

Joanne R. Lupton, Ph.D.

Regents Professor, University Faculty Fellow and William W. Allen Endowed Chair in Nutrition Texas A&M University, College Station, TX

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Definition of fiber

In order to understand if fiber is protective against colon cancer we first need to know what fiber is. Surprisingly, there is no definition of fiber in the United States today. Rather, there are accepted Association of Official Analytical Chemists International (AOAC) methods to determine fiber and what is analyzed as fiber by these methods is automatically dietary fiber. In 2002 the Food and Nutrition Board of the Institute of Medicine, National Academy of Sciences put together a panel of fiber experts to define dietary fiber. The new definition, which is now part of the recently released DRI Macronutrient Report, is:

Dietary Fiber consists of nondigestible carbohydrates and lignin that are intrinsic and intact in plants.

Functional Fiber consists of isolated, nondigestible carbohydrates that have beneficial physiological effects in humans.

Total Fiber is the sum of Dietary Fiber and Functional Fiber.

The reason that it is important to keep a definition of fiber in mind is that when we evaluate the strength of the evidence as to whether or not fiber is protective against colon cancer we need to determine what definition of fiber the investigators were using. For example, most epidemiological studies use the USDA database for fiber, sometimes supplemented with data added by the investigators to make it more complete (Hallfrisch et al., 1988; Heilbrun et al., 1989; Miller et al., 1983; Platz et al., 1997). Others base their findings on certain groups of high-fiber foods (consumption of fruits and vegetables, whole grains, breakfast cereals, etc.) (Hill, 1997; Thun et al., 1992). Intervention studies may use fiber supplements. Again, it is important to note the database for food intake in a study that tests the relationship of fiber to colon cancer.

Dietary Fiber and the Prevention of Colon Cancer *Epidemiological studies*

The initial interest in the association of fiber and colon cancer comes from epidemiological studies, which show differences in rates of colorectal cancer associated with differences in fiber intake in different countries (Boyle et al., 1985). In addition, when individuals migrate from a country with a low incidence of colon cancer to one

with a high incidence (e.g. from Japan to the US) and take on the eating patterns of the country with the high incidence, their risk of colon cancer increases (Haenszel and Kurihara, 1968). A review of the earlier epidemiological studies shows that the majority of them showed a protective effect of fiber against colon cancer (Trock et al., 1990) (Lanza, 1990). However, some of the more recent large-scale epidemiological studies have not shown this positive benefit of fiber against colon cancer. For example, in the Nurses' Study, involving a large cohort of women, no relationship was detected between fiber intake and colon cancer incidence (Fuchs et al., 1999). Similarly, six other large prospective studies showed only a weak inverse association or no association between fiber intake and colon cancer (Giovannucci et al., 1994; Heilbrun et al., 1989; Kato et al., 1997; Key et al., 1996; Pietinen et al., 1999; Steinmetz et al., 1994). Of note, however is the recent EPIC study, which prospectively examined the association between dietary fiber intake and incidence of colorectal cancer in 519,978 individuals from ten European countries. They found that dietary fiber in foods was inversely related to incidence of large bowel cancer with an adjusted relative risk for the highest versus lowest quintile of fiber intake of 0.58 (Bingham et al., 2003).

Intervention Studies

There have been a number of small clinical interventions addressing various markers for colon cancer, most of which have shown either a small protective effect or no effect at all (Alberts et al., 1990). Importantly, three major intervention trials have also shown no effect on polyp recurrence (considered a marker for colon cancer development) (Alberts et al., 2000; Bonithon-Kopp et al., 2000; Schatzkin et al., 2000). All were well-designed, well-executed trials in individuals who had had polyps removed. The Polyp Prevention Trial, which incorporated eight clinical centers, included an intervention that consisted of a diet that was low-fat, high-fiber, and high in fruits and vegetables (Schatzkin et al., 2000). There was no difference in polyp recurrence between the intervention and control groups. The Arizona Wheat Bran Fiber trial provided 13.5 g/day versus 2 g/day of wheat bran fiber (Alberts et al., 2000). Again, there was no difference between the control group and the intervention group in terms of polyp recurrence. The third trial used 3.5 g/day psyllium (ispaghula husk) as the intervention (Bonithon-Kopp et al., 2000). The adjusted odds ratio for the psyllium fiber intervention on polyp recurrence was 1.67(p=0.042).

Possible Reasons for the Lack of a Protective Effect of Dietary Fiber in Some Trials

There is considerable debate and speculation as to why clinical intervention trials with respect to fiber intake and colon cancer have not produced the expected beneficial effect of fiber.

Timing of the Intervention. Some of the recent prospective studies, such as the Nurses' Health Study (Fuchs et al., 1999) and the Health Professionals Follow-up Study (Giovannucci et al., 1994) have failed to show a protective effect of fiber intake against

colon cancer when early indications from these same cohorts suggested that they would (Giovannucci et al., 1992). A similar situation was found in the Nurses' Health Study cohort, which initially found that the combination of high fiber and low saturated or animal fat intake was associated with a reduced risk of adenomas (Willett et al., 1990), but these data did not hold up at follow-up in the same cohort (Fuchs et al., 1999). It is possible that intake of fiber may affect the early stages of carcinogenesis but have no effect at later stages of intervention.

The Confounding Role of Other Dietary Factors. Another possible explanation for the lack of a positive effect of fiber on colon cancer may be that there is an interaction between fiber and other components of the diet (e.g. fat) which when unaccounted for may mask the protective effect of fiber.

Subjects May Not Consume Sufficient Amounts of Fiber or the Right Type of Fiber. Neither the prospective studies nor the three large intervention trials reported aspects of colonic function (Alberts et al., 2000; Bonithon-Kopp et al., 2000; Schatzkin et al., 2000). It is possible that bulkier stools and/or faster transit through the colon reduce the risk of bowel cancer (Cummings et al., 1992), but that the amounts and/or types of fibers consumed did not result in these physiological effects. Finally, positive benefits of fiber with respect to colon cancer may not occur until fiber intake is sufficiently high; for example, greater than the median 32 g/day for the highest quintile in The Health Professionals Follow-up Study of men (Giovannucci et al., 1994; Platz et al., 1997) and 25 g/day in the Nurses' Health Study (Fuchs et al., 1999).

Given the conflicting data on fiber and colon cancer intake, does this mean that we should stop recommending that individuals increase their consumption of high fiber foods?

The recent report from the National Academy of Sciences strongly suggests otherwise. When the macronutrient panel looked at all the data on fiber and disease they came to the conclusion that a specific type of DRI, called an AI (adequate intake) was justified for total fiber. The basis for this decision was the inverse relationship for fiber intake and coronary heart disease incidence. The new AI for total fiber is set at 38 and 25 g/day for young men and women, respectively, based on the intake level observed to protect against coronary heart disease. Therefore, the recommendations to increase fiber intake still stand.

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