A Review of the Associations between Dietary Fiber Intake and Cancer Prevention or Prognosis

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Abstract: The increase in tumor incidence is closely related to dietary factors. In recent years, many researchers have carried out in-depth research to investigate whether increasing the intake of dietary fiber can prevent tumors and improve the prognosis, but the results have been unclear. We herein searched the literature in common academic databases and incorporated and summarized the relevant articles. The literature clearly indicates that dietary fiber can protect against the following cancers: colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, and head and neck cancer. There is also evidence that dietary fiber intake can exert protective effects against cancers of the liver, lung, stomach, small bowel, kidney, and esophagus, as well as lymphoma, but the data have so far been relatively limited. The effects on endometrial cancer and prostate cancer still remain uncertain. In terms of the effects on the cancer prognosis, dietary fiber does not appear to have an impact on colorectal cancer or breast cancer. Although more research is needed for some kinds of cancer, it is clear that increasing the intake of dietary fiber is beneficial for preventing the occurrence and development of several major types of cancer, with no major adverse effects. We therefore recommend that most of individuals increase their intake of dietary fiber.

Key words: Dietary fiber; Cancer; Soluble dietary fiber; Insoluble dietary fiber

Introduction

With the development of better screening and diagnostic approaches and more effective treatments, cancer has become a chronic disease [1]. Due to the changes in lifestyle, the environment and dietary structure, the cancer burden (the number of new cancer cases or deaths) has shown an upward trend in recent years. Fifteen million new cancer cases and 12 million deaths were predicted in 2020 [2]. Colorectal cancer is the third most common cancer type and the fourth leading cause of cancer death in the world, with an estimated 1.4 million new cases and nearly 700,000 deaths in 2012. It increased to 1.8 million new cases and nearly 900,000 deaths in 2018 [3]. The global burden of colorectal cancer is expected to increase by 60% in 2030, meaning that there will be approximately 2.2 million new cases and 1.1 million deaths that year unless significant changes are made to prevention or treatment [4]. According to previous epidemiological studies, alcohol and red meat consumption increase the risk of colorectal cancer [5].

In addition, there are about 330,000 pancreatic cancer deaths worldwide each year, accounting for about 4% of all cancer cases [6]. Epidemiological studies suggest that dietary imbalances are a major cause of pancreatic cancer, while dietary risk factors mainly include high intake of red and processed meat and a lack of vegetables, fruits and dietary fiber [7-9]. Breast cancer is the most common

malignant tumor in women. About 1.7 million people worldwide were diagnosed in 2012 [10]. The occurrence of breast cancer is also considered to be related to an unhealthy lifestyle, and effective prevention is essential to reduce the incidence of invasive breast cancer. Ovarian cancer is the second most common malignant tumor in the female reproductive system. Identifying modifiable risk factors is expected to reduce the occurrence of ovarian cancer. According to reports from developed countries, the incidence of endometrial cancer is on the rise and surpasses cervical cancer, making it the most common cancer in the female reproductive system. Of note, dietary factors are associated with endometrial cancer, and can interact with other factors (i.e., endocrine disruptors), and have an important influence on the incidence and outcome of the disease [11-13].

The World Health Organization analyzed numerous factors affecting human health, and showed that dietary factors appear to be among the most important factors, followed by genetic factors (15%)[14]. The role of dietary fiber in the prevention and treatment of cancer has been the most studied topic, with studies mainly focused on colorectal cancer, breast cancer, ovarian cancer, liver cancer, endometrial cancer, prostate cancer, and esophageal cancer.

Dietary fiber is found in a wide range of human foods, mainly in cereals, potatoes, beans, vegetables, fruits and plant-based foods. More mature plants have a higher fiber content, and the fiber content is an important determinant of the tenderness of grains, with more tender grains have a lower fiber content. Dietary fiber can be divided into soluble dietary fiber (SDF) and insoluble dietary fiber (IDF) based on whether it is soluble in water. The former category includes inulin, pectin, fructooligosaccharide, and

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konjac. Major members of the IDF group include cellulose, lignin and methyl cellulose. Dietary fiber can improve the gut microbial state by selectively stimulating the growth or activity of one or more bacteria in the intestine, and are called probiotics. Due to its unique biological characteristics, dietary fiber can help to prevent tumors, as described below.

Prevention of Cancer by Dietary Fiber

Colorectal cancer

Studies about the preventive role of dietary fiber against colorectal cancer have suggested that it affects the composition and metabolism of intestinal microbes, particularly the amount of butyric acid and deoxycholic acid in the colon, reducing the risk of colorectal cancer [15]. However, there was no statistically significant relationship between dietary fiber intake and colon cancer

risk in different tumor subsites [16]. An analysis of dietary fiber types showed that increasing the fiber intake by 10 g/d reduced the risk of colorectal cancer by 9% for cereals; 16% for vegetable fiber and 22% for every 10 g increase in consumption of fruit fiber per day [17]. A large body of studies indicate that dietary fiber “safeguards” the colon and rectum against cancers. As shown in Table 1, numerous studies have demonstrated that grain, fruit and vegetable-based fiber consumption can all have protective effects against colorectal cancer [18-23]. However, other studies indicated that dietary fiber is not associated with a reduction in the colorectal cancer risk, with a few even finding a positive correlation between fiber consumption and cancer. Because all of these foods also contain other bioavailable ingredients, such as β -carotene and lycopene, the different levels in different foods may affect the results. In addition, the combination of these nutrients may have synergistic

Table 1 Meta-analyses of the correlation between dietary fiber and colorectal cancer.

Item referenced	Ma Y et al. [16]	Oh H et al. [17]	Masrul M et al. [18]	Gianfredi V et al. [19]
Study design	Meta-analysis (11 cohorts)	Meta-analysis (10 perspective studies)	Meta-analysis (8 case-control, 2 cohort)	Meta-analysis (7 case-control, 18 cohort)
Investigation method	Food-Frequency questionnaire	Food-frequency questionnaire	Food-frequency questionnaire, Prosky-AOCA	Food-frequency questionnaire, dietary questionnaire, 7-day recipe
Disease	Colorectal cancer	Colorectal cancer, colorectal adenomas	Colorectal cancer	Colon cancer
The source of dietary fiber	Dietary fiber, cereal fiber, whole grain products	Fruits, grains, vegetables, cereals, legumes	Fruits, vegetables, grains	Dietary fiber
Number of subjects	9,618	12,771 (8,248 colorectal cancer, 4,523 colorectal adenomas)	49,964	20,961
Population/age	American, European; $\geq 35y$	European, American; $\geq 25y$	Asian; 18~85y	Japanese, Chinese, American, European, Canadian; 20~93y
Results	The summary RR of proximal colon cancer and distal colon cancer for individuals with the highest dietary fiber intake relative to those with the lowest intake was 0.86 (95% CI: 0.78~0.95) and 0.79 (95% CI: 0.71~0.87), respectively.	The summary RRs of colorectal cancer associated with each 10 g/d increase in fiber intake were as follow: Cereal fiber: 0.91 (95% CI: 0.82~1.00; $I^2 = 0\%$); Vegetable fiber: 0.95 (95% CI: 0.87~1.03, $I^2 = 0\%$); Fruit fiber: 0.91 (95% CI: 0.78~1.06, $I^2 = 0\%$); Legume fiber: 0.84 (95% CI: 0.63~1.13, $I^2 = 45\%$); All fiber sources were inversely associated with incident adenoma (Per 10 g/d increase: RR [95% CI]): Cereals: 0.81 [0.54~1.21]; Vegetables: 0.84 [0.71~0.98]; Fruits: 0.78 [0.65~0.93].	High dietary fiber intake prevents colorectal cancer. OR = 0.66 (95% CI: 0.56~0.77, $P = 0.008$)	Dietary fiber intake protects against colon cancer risk. ES = 0.74 (95% CI: 0.67~0.82, $P = 0.000$)

RR: Relative risk; OR: Odds ratio; CI: Confidence Interval

effects [24-25].

Pancreatic cancer

The risk of pancreatic cancer is inversely associated with dietary fiber intake, and it was observed that increasing the daily intake by 10 g reduced the risk by 0.88. Even though some studies have shown that dietary fiber does not reduce the risk of pancreatic cancer, it is thought to be beneficial for decreasing the damage caused by heavy intake of red and processed meat [26-28]. Some relevant studies are detailed as follows.

We included two meta-analyses and two case-control studies. The summary OR of pancreatic cancer associated with whole grain fiber intake was 0.76 (95% CI: 0.64~0.91; $P = 0.002$) in Lei QC et al. study [27]. And in Mao QQ et al. study showed there was a significant inverse relationship between high fiber intake and pancreatic cancer risk (OR = 0.52, 95% CI: 0.44~0.61) [28]. In other studies, some selected types of fiber and total fiber are inversely related to pancreatic cancer. Total fiber intake was inversely related to the risk of pancreatic cancer (OR = 0.4, 95% CI: 0.2~0.7). An inverse association emerged between pancreatic cancer and both soluble (OR = 0.4; 95% CI: 0.2~0.7) and total insoluble fiber (OR = 0.5; 95% CI: 0.3~0.8). Fruit fiber intake was inversely associated with pancreatic cancer (OR = 0.5; 95% CI: 0.3~0.8), whereas grain fiber was not. People who consumed 2 servings of whole grains daily had a lower risk of pancreatic cancer than people who consumed < 1 serving/d (OR = 0.6, 95% CI: 0.31~1.2). Consuming more whole-grain or high-fiber foods may reduce the risk of pancreatic cancer [29-30]. Therefore, dietary fiber has a protective effect on pancreatic cancer.

Cancers in women

Breast cancer

Most studies have shown that dietary fiber can reduce the risk of breast cancer, and that fiber intake is inversely associated with the risk of breast cancer [31-33]. This is especially true for soluble dietary fiber from cereals, fruits and vegetables when compared to dietary fibers from alternative sources [10]. For every 10 g/d increase in dietary fiber intake per day, the risk was significantly reduced by 7%, which provides evidence that regular consumption of dietary fiber, plant fat, plant protein, and nuts during adolescence can help to reduce the cancer risk [10,34-42]. However, in a prospective study of Chinese women published by Wen W, et al., dietary fiber intake was not associated with the risk of breast cancer [43].

Endometrial carcinoma

The results of epidemiological studies about the relationship between dietary fiber intake and endometrial cancer risk remain inconclusive. Three related meta-analyses have been performed. On the basis of 7 case-control studies, the random-effects summary risk estimate

was 0.82 (95% CI: 0.75, 0.90) per 5 g/1000 kcal dietary fiber. The random-effects summary estimate was 0.71 (95% CI: 0.59, 0.85) for the comparison of the highest with the lowest dietary fiber intake in 8 case-control studies [44]. A significant negative association was observed between total dietary fiber intake and endometrial cancer risk in 11 case-control studies (OR = 0.76, 95% CI: 0.64~0.89) [45]. But no association was found in the cohort study, even positive correlations of higher total fiber and cereal fiber intake with endometrial cancer risk [44-45]. Li HJ et al. [46] found a significant association between dietary fiber intake and endometrial carcinoma (RR = 0.86, 95% CI: 0.78, 0.93). The findings revealed that the consumption of dietary fiber was associated with a 14% reduction in endometrial carcinoma risk. They showed a clear protective role of dietary fiber.

Ovarian cancer

Epidemiological studies have shown that dietary factors play an important role in the etiology of ovarian cancer, including dietary glucose loading [47], fat [48], phytoestrogens [49], vegetables and fruits [50]. Vegetables, fruits and grains are the main sources of dietary fiber, and the previous studies of the correlation between dietary fiber and ovarian cancer are shown. We included three meta-analyses. In Zheng B et al. study including 10 case-control and 3 cohorts, showed that the pooled multivariable RRs of ovarian cancer for the highest vs. the lowest category of dietary fiber intake was 0.78 (95% CI: 0.70, 0.88). A dose-response analysis showed a significant inverse association between dietary fiber intake and ovarian cancer risk (for an increase of 10 g/d; combined RR: 0.88; 95% CI: 0.82, 0.93). The risk of ovarian cancer was reduced by 22% in the group with the highest dietary fiber intake compared with the lowest. Furthermore, a 12% reduction in risk of ovarian cancer was found for per 10 g increase per day [51]. Xu H et al. meta include 14 case-control and 5 cohorts showed that the summary RR of the association between dietary fiber intake and ovarian cancer risk was 0.70 (95% CI: 0.57~0.87; $I^2 = 83.5\%$, $P < 0.001$). A dose-response analysis suggested that ovarian cancer risk decreased by 3% (RR = 0.97, 95% CI: 0.95~0.99) for each 5 g/d increase in dietary fiber intake [52]. Huang X et al. analysis of the primary pooled statistics revealed that the highest category of dietary fiber intake was associated with a significantly reduced risk of ovarian cancer compared with the lowest category (RR = 0.76; 95% CI: 0.702~0.823; $P < 0.001$). The association between dietary fiber intake and ovarian cancer risk was significant in both case-control studies and cohort studies [RR (95% CI): 0.753 (0.682~0.832), 0.763 (0.633~0.920)] [53]. There is a protective role in preventing cancer.

According to the above contents, dietary fiber plays a positive role in the prevention of malignant cancers (such as breast cancer, endometrial cancer and ovarian cancer) in women.

Other malignancies

In addition to the above, there have been studies of the potential preventive effects of dietary fiber on several other cancers, including head and neck cancer, prostate cancer, liver cancer, upper gastrointestinal cancer, gastric cancer, esophageal cancer, renal cancer, and lymphoma.

The studies of head and neck cancers included cancers of the oral cavity cancer, rhinocarcinoma, pharyngeal carcinoma, and salivary adenocarcinoma. The majority of cohort studies have shown that dietary fiber intake is inversely associated with the risk of head and neck cancer, with higher cereal fiber intake reducing the by about 48% [54-59]. A similar relationship was shown for the prostate cancer risk in cohort studies and meta-analyses, with especially potent effects for insoluble dietary fiber and legume fiber [60-62]. However, Suzukin R [63] and Wang RJ et al.[64] showed that dietary fiber was not associated with prostate cancer.

Dietary fiber does appear to play a protective role for liver and kidney cancer, especially grain fiber intake. However, the results for bran fiber intake were unclear [65-67]. In a pooled analysis of lung cancer, dietary fiber and yogurt consumption synergistically reduced the risk of lung cancer [68]. In studies of upper gastrointestinal cancer, gastric cancer, esophageal cancer, and small bowel cancer, dietary fiber was considered to be inversely associated with tumor risk, and an increase in fiber intake by 10 g/d reduced the risk of gastric cancer by 44%, and reduced the risk of esophageal cancer by 31%. Individuals with the highest intake of whole grains and yellow/orange vegetables had risk factors of 0.53 and 0.58, respectively, compared to those with the lowest intake with regard to the development of upper gastrointestinal cancer [69-73]. The intake of vegetable and fruit fibers, especially green leafy vegetables and cruciferous vegetable fibers, was found to be linked to a

reduced risk of non-Hodgkin's lymphoma [74-75].

Prognostic Impact of Dietary Fiber

The literature about the prognostic impact of dietary fiber on various cancers is limited. A few studies reported an inverse relationship between dietary fiber intake and the recurrence and death from colorectal adenoma. However, most studies have shown that dietary fiber is not linked to the prognosis of colorectal cancer. In a four-year supplementary dietary fiber intervention study, participants receiving dietary fiber had a higher risk of experiencing intestinal cancer than the control group, with an absolute increase in risk of 1% [9,76-83]. Similarly, dietary fiber did not reduce the recurrence rate or mortality of breast cancer, even though there appeared to be a trend for fiber to decrease the incidence of the disease. However, these data were not statistically significant [84-85]. Henson CC et al. analyzed the gastrointestinal toxicity in adults receiving pelvic radiotherapy after nutritional intervention, and showed that adjusting the dietary fiber intake had no appreciable effect on diarrhea caused by radiotherapy [86].

Mechanisms Underlying the Anticancer Effects of Dietary Fiber

The main mechanisms underlying the anticancer effects of dietary fiber include [87], as shown in Figure 1: ① The strong hydrophilicity of dietary fiber can promote higher fecal volume and weight, which enhances intestinal peristalsis and facilitates fecal excretion. In this way, it can dilute the concentration of carcinogens and shorten their retention time in the intestine [8]; ② SDF can be degraded by bacteria to form short-chain fatty acids (SCFA) in the colon. SCFA promote the growth of beneficial bacteria, and inhibit the growth and reproduction of spoilage bacteria. Promoting this change in bacterial colonization is beneficial

Figure 1 Mechanism of dietary fiber on tumors. SCFA: Short-chain fatty acids; SDF: Soluble dietary fiber.

to the normal intestinal barrier, thereby inhibiting carcinogen production and promoting the decomposition of carcinogens [88]; ③ Dietary fiber is the main substrate of intestinal bacterial fermentation, which produces a series of beneficial metabolites, especially butyrate [89], which can inhibit the growth of bacteria, nourish colon wall cells, inhibit tumor cell proliferation, inhibit cell transformation, inhibit oncogene expression, and improve lipid metabolism [87,90]; ④ Dietary fiber can increase satiety and limit energy intake, it also promotes lipid oxidative metabolism and inhibits fat storage, thereby helping control body weight. It can also increase the production of deoxycholic acid and hepatic intestinal circulation, which can help reduce the occurrence of liver cancer [91]; ⑤ The absorption of cholesterol, fatty acids and endogenous toxins can be reduced by the increased adsorption to bile acids [92,93]; ⑥ SDF can delay and inhibit the digestion of sugar and improve the insulin sensitivity of peripheral tissues, so the postprandial blood glucose level can be reduced [90]; ⑦ By strengthening mastication to promote saliva secretion, which may also lead to anti-cancer effects [87].

Conclusion

Dietary factors can alter the risk of various cancers. High dietary fiber intake plays a role in preventing multiple cancers. In addition to preventive effects, adjusting a patient's diet is also important for improving the response to cancer treatment. Our findings are consistent with previous reports. A systematic review published by Makarem N et al. [59] showed that whole grain fiber plays a protective role in head and neck cancer, renal cancer, and gastrointestinal cancer. The view that dietary fiber reduces the risk of gastrointestinal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer is relatively explicit, but there is a lack of research support with regard to the impact on other cancers.

The previously-published studies show that different sources of dietary fiber play different roles in the risk of cancer, even for the same tumor type. For example, whole grain and bran have potential preventive effects against liver cancer, but no such role has been found for fiber from other sources. Similarly, the source of dietary fiber found to have the most beneficial effects is not consistent in the studies of endometrial cancer, breast cancer and so on. Consequently, determining the specific type, dose, and timing of dietary fiber intake is key to explore the effects on tumor growth and development. In terms of the prognosis, most studies have not found any significant positive effect, but further studies are needed due to the relative lack of data.

Patients who have inadequate dietary fiber intake are at an increased risk for several types cancer. However, while extensive dietary fiber intake promotes the excretion of toxic and harmful substances, it also can remove some essential nutrients and lead to symptoms such as malnutrition, intestinal flatulence, indigestion, and diarrhea.

Thus, while the intake of an adequate amount of fiber is beneficial, the increase in fiber intake should be moderate to avoid potential adverse effects.

Much effort has been invested in deciding on the recommended dietary fiber intake. The Food and Agriculture Organization of the United Nations recommends that healthy individuals should consume 27 g/d. The German Society for Nutrition recommends at least 30 g/d, with a recommended ratio of IDF to SDF of 2 : 1. British dietitians recommend that individuals should consume 25~30 g/d. The U.S. Food and Drug Administration similarly recommends 25~30 g/d. The Chinese Nutrition Society recommends that healthy individuals should consume 30 g/d, with an additional 10~15 g/d [94] recommended for some groups (those with diabetes, cardiovascular and cerebrovascular diseases).

Dietary fiber can significantly protect against the following cancers: colorectal cancer, breast cancer, pancreatic cancer, ovarian cancer, head and neck cancer. Increasing dietary fiber intake by 10 g/d can reduce the risk of colorectal cancer, pancreatic cancer, breast cancer, ovarian cancer, gastric cancer, and esophageal cancer. The effects of fiber intake on cancers of the liver, lung, stomach, small bowel, kidney, and lymphoma appear to be beneficial, but further studies are needed. The protective effect of dietary fiber on endometrial cancer and prostate cancer are also still being debated. In terms of cancer prognosis, dietary fiber does not seem to be associated with recurrent colorectal cancer or breast cancer. Thus, we consider that increasing the amount of dietary fiber intake is beneficial for preventing the occurrence and development of several major types of tumors, such as colorectal cancer, pancreatic cancer, breast cancer, ovarian cancer, gastric cancer, esophageal cancer, but this needs to be a lifelong dietary habit in order to achieve benefits. A short-term increase in consumption does not appear to have a significant impact, nor does consumption after a specific cancer type has already been diagnosed.

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Conflict of Interest

The authors declare no conflict of interest.

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