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Diet and colon: what matters?

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Abstract

Purpose of review—Colorectal cancer (CRC) is one of the most common cancers and the fourth leading cause of cancer-related deaths worldwide. Diet has a significant impact on the risk of developing CRC, but though processed meat is a known positive contributor, the effects of other dietary components are largely mixed. This review focuses on dietary patterns to describe the complexity of dietary diversity and overall food consumption and to examine the relationship between dietary patterns and risk of CRC.

Recent findings—After searching human studies published in 2017–2018, we selected and evaluated 30 articles, including meta-analyses, cohort studies, and prospective studies. These studies suggest that the prudent or Mediterranean dietary pattern significantly decreases the risk of CRC compared to the Western dietary pattern; a lower dietary inflammatory index or a higher dietary quality index associates with a lower risk of CRC; closely following all aspects of the World Cancer Research Fund/American Institute for Cancer Research cancer prevention guidelines and recommendations correlates with a reduced risk of CRC.

Summary

The risk of developing CRC can be reduced by adopting a healthier lifestyle. More studies of the impact of diet on clinical outcomes of CRC are needed.

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Conflicts of interest

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Keywords

colorectal cancer; dietary inflammatory index; dietary patterns; epidemiologic studies; World Cancer Research Fund/American Institute for Cancer Research guidelines

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer in men, the second in women [1[■]], and the fourth leading cause of cancer-related deaths world-wide [2[■]]. The incidence of CRC varies greatly among countries and correlates with indices of economic development. More developed countries in Oceania and Europe have a higher incidence of CRC, whereas Africa and Asia have a lower incidence [1[■],2[■]]. With advances in early screening and treatment, the incidence of CRC is stabilizing or even decreasing in more developed countries, though it still ranks among the highest among cancer types. However, the silver lining is that CRC is largely preventable and that diet has a great impact on the risk of developing the disease.

The World Cancer Research Fund (WCRF) and American Institute for Cancer Research (AICR) publish and continuously update global reports of cancer data [2[■]]. In addition, our previous review summarized major epidemiologic studies and examined the relationship between CRC incidence and various dietary components such as red/processed meat, fish, fiber, and fruits and vegetables [1[■]]. Other than red/processed meat – whose positive contributions to CRC have been confirmed by several recent studies [3–6] – findings for other dietary components are mixed and controversial [1[■],2[■]]. However, it is likely that a dietary *pattern* – rather than a single food – may significantly influence the incidence and outcomes of CRC. Thus, the current review updates the findings on dietary patterns and risk of CRC. We conducted a PubMed search for human studies published from January 2017 to September 2018, using key words including CRC, diet, nutrition, and epidemiology. Articles that described and compared the impact of diets on CRC were screened and selected for eligibility. Collectively, 30 publications were examined. These studies suggest that a healthy dietary pattern, a lower dietary inflammatory index (DII), or greater adherence to the WCRF/AICR guidelines contribute to a lower risk of developing CRC.

THE RELATIONSHIP BETWEEN DIETARY PATTERNS AND COLORECTAL CANCER

Compared with data on individual food items, dietary pattern data can better describe the complexity of dietary intake and measure overall food consumption. Thus, examining potential associations between dietary patterns and the risk of developing CRC may lead to more practical guidelines for preventing and treating the disease (Table 1).

A meta-analysis identified 93 studies, including 21 studies of CRC, that examined the association between healthy/unhealthy dietary patterns with risk of cancer [7[■]]. The healthy patterns consisted mainly of fruit and vegetable-based diets, whereas the unhealthy patterns were described as ‘Western,’ ‘animal,’ ‘fatty and salty,’ or ‘refined.’ Both the case–

control studies and prospective studies in this meta-analysis showed that healthy dietary patterns negatively associated with the risk of CRC [case– control studies: pooled relative risk (RR) = 0.48, 95% confidence interval (CI): 0.27–0.84; prospective studies: RR = 0.89, 95% CI: 0.83–0.95]. In contrast, the unhealthy dietary patterns showed the reverse (case– control studies: RR = 1.54, 95% CI: 1.31–0.82; prospective studies: RR = 1.13, 95% CI: 1.03–1.23) [7[■]]. In addition, this analysis revealed that unhealthy dietary patterns associated with higher BMI, whereas healthy dietary patterns correlated with healthier lifestyle factors, including more physical activities and absence of smoking [7[■]].

Five regional studies, including two in Europe (the multicase–control study MCC-Spain and the UK Women’s Cohort Study) [8[■],9[■]] and three prospective studies in the United States (the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, PLCO; the Health Professionals Follow-up Study, HPFS; and the Nurses’ Health Study, NHS) [10–11,12[■]], observed similar results: that the Western dietary pattern associates with increased CRC risk. Interestingly, prudent diets – those rich in whole grains and dietary fiber – associated with decreased risk of CRC [multivariable hazard ratio (HR) = 0.43, 95% CI: 0.25–0.72] [11,12[■]] only in *Fusobacterium nucleatum*-positive cancers (HR = 0.95, 95% CI: 0.77–1.17) [12[■]]. These results suggest that the intestinal microbiota is a critical regulator of the diet–CRC relationship. In addition, the MCC-Spain study revealed that the Mediterranean dietary pattern elicited stronger protection against CRC than prudent diets [Mediterranean: odds ratio (OR) = 0.65, 95% CI: 0.53–0.80; prudent: OR = 0.94, 95% CI: 0.76–1.15] [8[■]]. Similarly, the UK Women’s Cohort Study indicated that greater adherence to the Mediterranean dietary pattern associated with a lower risk of developing CRC (HR = 0.82, 95% CI: 0.57–1.17), especially rectal cancer (HR = 0.38, 95% CI: 0.20–0.74) [9[■]]. The potential protective effects of Mediterranean diets could be attributed to their high content of oily fish, nuts, olives, and olive oil. Indeed, higher consumption of nuts and fish has been shown to associate with better disease-free survival, recurrence-free survival, and overall survival of CRC patients [13,14].

Collectively, these studies support the hypothesis that healthy dietary patterns decrease the risk of developing CRC. Not surprisingly, individuals who consume healthy diets also have a lower BMI and adopt healthier behaviors, indicating that an overall healthy lifestyle, not just diet, needs to be maintained to prevent CRC.

THE RELATIONSHIP BETWEEN DIETARY INDEX AND COLORECTAL CANCER

Acute inflammation typically occurs as a normal response for tissue repair, whereas chronic inflammation is a persistent condition that can lead to tissue destruction. Chronic inflammation has been reported to contribute to the development and progression of many types of cancer, including CRC. Thus, measuring the inflammatory potential of diets is advantageous for comparing individuals who consume different dietary patterns.

Pro-inflammatory dietary components usually include carbohydrates, proteins, total fat, trans fat, cholesterol, and saturated fatty acids. Anti-inflammatory diets contain mainly fiber, polyunsaturated fatty acids, minerals, vitamins, anthocyanidins, isoflavones, and β -carotene.

Several dietary indices for measuring the inflammatory potential and quality of diets have been used by different groups (Table 2). They include the empiric dietary inflammatory pattern (EDIP) score [15[■],16[■]], an energy-adjusted DII score [17], an empirical dietary index for hyperinsulinemia [19], a dietary nonenzymatic antioxidant activity index (NEAC) [20], the Healthy Eating Index (HEI), the Alternate Healthy Eating Index (AHEI), the Dietary Approaches to Stop Hypertension Score, and the Mediterranean Diet Score [18[■]].

Two meta-analyses observed a positive association between higher DII scores and increased risk of CRC [21[■],22[■]]. Individuals with the highest DII scores had an overall 40% increased risk compared to those with the lowest DII scores (RR = 1.40, 95% CI: 1.26–1.55) [21[■],22[■]]. Similar results were observed by other large regional epidemiologic studies, such as NHS, HPFS, the Women's Health Initiative (WHI), MCC-Spain, and the Multiethnic Cohort (MEC) [15[■],16[■],17,18[■],19,20,23]. Interestingly, when using HEI, AHEI, Dietary Approaches to Stop Hypertension Score, and Mediterranean Diet Score to measure the quality of diets, one group found weaker inverse associations between dietary quality and CRC for African Americans than for Native Hawaiians, Japanese Americans, Latinos, and whites [18[■]], suggesting that nondietary factors play a more important role in African Americans than in the other four racial/ethnic groups. In addition, analyses of NHS and HPFS indicated that the degree of peritumoral lymphocytic reaction significantly influenced the relationship between the scores and the risk of CRC [16[■]]. With an absent or low reaction, higher EDIP scores associated with increased risk of CRC (HR = 2.60, 95% CI: 1.60–2.43). However, this association was not observed in individuals with an intermediate (HR = 0.99, 95% CI: 0.80–1.22) or high (HR = 0.91, 95% CI: 0.57–1.45) peritumoral lymphocytic reaction, suggesting that a strong immune response is potentially protective against pro-inflammatory diets [16[■]]. Consistent with the protective effects of prudent diets on *F. nucleatum*-positive cancers [12[■]], higher EDIP scores (indicating pro-inflammatory dietary patterns) associated with increased risk of CRC only in *F. nucleatum*-positive cancers (HR = 1.63, 95% CI: 1.03–2.58) [15[■]]. These results indicate dynamic interactions among the immune system, gut microbiota, and diet during the development of CRC.

Collectively, the results of these studies are consistent with those that examined dietary patterns. In the same way that calorie counts are provided on almost all food labels, DII scores might better indicate the inflammatory potential and quality of food items. Using this approach, precision design of diets for preventing and/or treating CRC would be both possible and warranted.

THE RELATIONSHIP BETWEEN ADHERENCE TO CANCER PREVENTION GUIDELINES AND COLORECTAL CANCER

First published in 2007 and updated in 2011 and 2018, WCRF/AICR guidelines offered eight recommendations (relating to body weight, physical activity, and diet) for cancer prevention [2[■]]. In addition, the American Cancer Society's Guidelines on nutrition and physical activity for cancer prevention (ACS guidelines) emphasizes the following key points: keep body weight within the healthy range, become physically active, maintain a diverse and healthy dietary pattern, and avoid smoking and drinking. By combining all these

behavioral factors together, it is possible to estimate an individual's overall risk of developing CRC.

Studies that investigated the relationship between adherence to cancer prevention guidelines and risk of CRC are shown in Table 3. One analysis of two Italian case-control studies directly examined the relationship between degree of adherence to the WCRF/AICR recommendations and the risk of developing CRC [24]. Higher adherence associated with a significantly decreased CRC risk (OR = 0.67, 95% CI: 0.56–0.80). For diet-specific recommendations, inverse associations were also observed for higher adherence scores (OR = 0.71, 95% CI: 0.61–0.84) [24]. Similarly, the UK Women's Cohort Study also found that individuals with higher adherence scores had lower risk of CRC (HR = 0.73, 95% CI: 0.48–1.10) [25]. The Cancer and Leukemia Group B 89803/Alliance Trial, on the other hand, investigated the impact of following the ACS guidelines on the survival of patients diagnosed with stage III colon cancer [26]. On a scale of six (one point each for BMI, physical activity, intake of vegetables, fruits, whole grains, and red/processed meats), patients with scores 5–6 had a 42% decreased risk of death and improved disease-free survival compared with patients with scores 0–1 (HR = 0.58, 95% CI: 0.34–0.99). When considering alcohol consumption in an adjusted scale of eight (2 points for alcohol intake), patients with scores 6–8 had markedly better overall survival (HR = 0.49, 95% CI: 0.32–0.76), disease-free survival (HR = 0.58, 95% CI: 0.40–0.84), and recurrence-free survival (HR = 0.64, 95% CI: 0.44–0.94) than patients with scores 0–2 [26]. Furthermore, two regional prospective studies – the UK Biobank study [27] and the Shanghai Men's Health Study in China [28] – produced similar results: that adopting all healthy behaviors (low alcohol intake, no smoking, healthy BMI, physical activity, and a healthy diet) most significantly reduced the risk of developing CRC.

Collectively, these studies highlight the importance of closely following the guidelines, not only for preventing CRC among the general population but also for improving the clinical outcomes of CRC patients.

CONCLUSION

The current review summarizes the findings of epidemiologic studies that were published between January 2017 and September 2018. These studies focused on the relationship of dietary pattern, DII, and adherence to guidelines and the risk of developing CRC. Overall, they recommend healthy dietary patterns, anti-inflammatory diets, and behaviors outlined in the WCRF/AICR guidelines for preventing and treating CRC.

It is not surprising that prudent and Mediterranean dietary patterns decrease the risk of CRC, whereas the Western dietary pattern does the reverse. Dietary indices are relatively new concepts, but they have drawn much attention as they provide a practical way to evaluate the quality of individuals' diets. More importantly, they can function as a basic platform on which to personalize dietary suggestions for preventing and/or treating CRC, because predefined dietary patterns may not be acceptable to everyone. The indices have limitations, however. For example, the inflammatory potential of most food items remains unclear and needs to be thoroughly examined. In addition, the 'bad luck' theory of cancer development

[29,30] is still controversial, and the findings of epidemiologic studies could be described as observations and analytic correlations. However, the relationships between diet and clinical outcomes of cancer patients can be evaluated directly, and more such studies are urgently needed. Furthermore, it is likely that combining all healthy behaviors is more critical than just following one aspect of the guidelines for preventing and/or treating CRC.

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KEY POINTS

- CRC is very prevalent and has a high death rate, but it is also preventable.
- Compared to the Western dietary pattern, the prudent or Mediterranean dietary pattern associates with a significantly decreased risk of developing CRC.
- Dietary indices are practical tools for measuring the inflammatory potential and quality of individuals' diets, and they can be used to make personalized recommendations.
- CRC prevention involves adopting all the components of a healthy lifestyle, including healthy dietary patterns and behaviors such as maintaining physical activity, not smoking, limiting alcohol intake, so on.
- Most epidemiologic studies focus on the impact of diets on the incidence of CRC, but more studies need to investigate the effects of diet on clinical outcomes of CRC patients.

Table 1.

Characteristics of studies of dietary patterns and colorectal cancer

Study	Analytical category	Analytical comparison	Relative risk	Reference
Meta-analysis of case-control studies	Healthy vs. unhealthy	Healthy	0.48, (0.27–0.84)	[7■]
Meta-analysis of prospective studies	Healthy vs. unhealthy	Unhealthy	1.54, (1.31–1.82)	[8■]
		Healthy	0.89, (0.83–0.95)	
		Unhealthy	1.13, (1.03–1.23)	
MCC-Spain	Prudent vs. Mediterranean vs. Western	Western	1.50, (1.20–1.87)	[9■]
		Prudent	0.94, (0.76–1.15)	
		Mediterranean	0.65, (0.53–0.80)	
UK Women's Cohort Study	Adherence to the Mediterranean diet, 0–2 vs. 3 vs. 4 vs. 5–6 vs. 7–10	7–10 vs. 0–2	0.82, (0.57–1.17)	[10]
		Per two unit increment	Rectum: 0.38, (0.20–0.74)	
			0.88, (0.78–0.99)	
PLCO	Fruits and vegetables vs. Western vs. sweet and salty	Fruits and vegetables	Rectum: 0.69, (0.56–0.86)	[11]
			Multiple adenomas in women: 0.53, (0.28–1.00)	
			Multiple adenomas in men: 1.51, (1.17–1.94)	
NHS, HPFS	Prudent vs. Western	Prudent	0.86, (0.77–0.95)	[12■]
		Western	1.31, (1.15–1.48)	
		Prudent	<i>F. nucleatum</i> positive: 0.43, (0.25–0.72)	
	Prudent vs. Western, <i>Fusobacterium nucleatum</i>		<i>F. nucleatum</i> negative: 0.95, (0.77–1.17)	
			<i>F. nucleatum</i> positive: 1.69, (0.98–2.90)	
			<i>F. nucleatum</i> negative: 1.25, (0.99–1.58)	

HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

Table 2.

Characteristics of studies of dietary indices and colorectal cancer

Study	Analytical category	Analytical comparison	Relative risk	Reference
NHS, HPFS	EDIP, <i>Fusobacterium nucleatum</i>	Highest vs. lowest	<i>F. nucleatum</i> positive: 1.63, (1.03–2.58)	[15]
			<i>F. nucleatum</i> negative: 1.07, (0.89–1.28)	
	EDIP, peritumoral lymphocytic reaction	Highest vs. lowest	Peritumoral lymphocytic reaction absent/low: 2.60, (1.60–4.23)	[16]
			Peritumoral lymphocytic reaction intermediate: 0.99, (0.80–1.22)	
MEC	An energy-adjusted DII score	Highest vs. lowest	Peritumoral lymphocytic reaction high: 0.91, (0.57–1.45)	[17]
	HEI	Highest vs. lowest	1.21, (1.11–1.32)	[18]
			African American: 0.81, (0.65–1.01)	
			Native Hawaiian: 0.71, (0.46–1.09)	
			Japanese American: 0.76, (0.62–0.92)	
			Latino: 0.69, (0.54–0.89)	
			White: 0.75, (0.60–0.94)	
NHS, HPFS	an empirical dietary index for hyperinsulinemia	Highest vs. lowest	1.26, (1.12–1.42)	[19]
MCC-Spain	NEAC	Highest vs. lowest	Men: 0.67, (0.47–0.96)	[20]
			Women: 0.53, (0.32–0.85)	
Meta-analysis	DII	Highest vs. lowest	1.40, (1.26–1.55)	[21]
Meta-analysis	DII	Highest vs. lowest	1.43, (1.26–1.62)	[22]

DII, dietary inflammatory index; EDIP, empiric dietary inflammatory pattern; HEI, Healthy Eating Index; HPFS, Health Professionals Follow-up Study; MEC, Multiethnic Cohort; NEAC, nonenzymatic antioxidant activity index; NHS, Nurses' Health Study.

Table 3.
Characteristics of studies of adherence to cancer prevention guidelines prevention of colorectal cancer

Study	Analytical category	Analytical comparison	Relative risk	Reference
Italian case-control	Adherence to the WCRF/AICR recommendations (0–7)	5 vs. <3.5	0.67, (0.56–0.80)	[24]
	Adherence to the diet-specific WCRF/AICR recommendations (0–5)	3.5 vs. 2	0.71, (0.61–0.84)	
UK Women’s Cohort Study	Adherence to the WCRF/AICR recommendations (category 1–3)	3 (highest) vs. 1 (lowest)	0.73, (0.48–1.10)	[25]
CALGB 89803/ Alliance	Adherence to the ACS guidelines (0–6)	5–6 vs. 0–1	Overall mortality: 0.58, (0.34–0.99)	[26]
			Disease-free survival: 0.69, (0.45–1.06)	
			Recurrence-free survival: 0.78, (0.51–1.20)	
			Overall mortality: 0.49, (0.32–0.76)	
UK Biobank	Adherence to the ACS guidelines (0–8)	6–8 vs. 0–2	Disease-free survival: 0.58, (0.40–0.84)	[27]
			Recurrence-free survival: 0.64, (0.44–0.94)	
Shanghai Men’s Health Study	Adherence to healthy behaviors (0–5)	5 vs. 1	0.75, (0.58–0.97)	[28]
		4–5 vs. 0–1	0.83, (0.78–0.89)	

ACS, American Cancer Society; HEI, Healthy Eating Index; NEAC, nonenzymatic antioxidant activity index; WCRF/AICR, World Cancer Research Fund/ American Institute for Cancer Research.