Dietary Patterns and Their Effect on the Colorectal Cancer Risk

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Abstract: Colorectal cancer (CRC) the third most commonly diagnosed cancer, excluding skin cancers, worldwide. In 2018 alone, there were close to 2 million new cases all over the globe (World Cancer Research Foundation International 2019). In 2020, CRC accounted for about 10% of all cancer cases and deaths, recording about 1.9 million new diagnoses and 935,000 fatalities (Sung 2020). In this year, it is projected that there will be an estimated 104,000 new diagnoses of colon cancer, and about 45,000 new diagnoses of rectal cancer (De Stefani 2011). There is a 4.3% risk of developing CRC for men, and a 4.0% risk for women (World Cancer Research Foundation International 2019). Therefore, colorectal cancer has caused a huge burden on social and economic development worldwide. More and more studies have shown that eating more foods rich in dietary fiber and dairy products can reduce the incidence of colorectal cancer, while eating more red meat and processed meat products can increase its incidence (World Cancer Research Fund and American Institute for Cancer Research 2017).

1 INTRODUCTION

There is evidence that dietary and lifestyle factors contribute to the risk of developing CRC, and a number of foods have been studied and reported on in relation to their associated CRC risk. For instance, research shows that consuming whole grains, dairy products, foods high in dietary fibre and taking calcium supplements lowers CRC risk, while consuming processed meats, red meat and alcoholic drinks increases relative CRC risk (World Cancer Research Fund and American Institute for Cancer Research 2017). However, the above-named foods are rarely consumed individually, and instead are components of a larger dietary pattern. Studying food and nutrient combinations better elucidates the dietary patterns of a population and their associated CRC risk, since chronic diseases usually result from many interacting variables.

This review looks at studies ranging from 1998 to 2021. We review the literature on the relationship between different dietary patterns and the relative risk (RR) for CRC to provide a reference for the public healthy diet model, and for the primary prevention strategy of colorectal cancers.

2 METHOD

PubMed-NCBI was searched for articles up to June 2021 that researched potential correlations between dietary patterns or foods and the relative risk for CRC. The search included the following keywords or phrases: diet, dietary pattern, colorectal cancer, and epidemiology. Studies that reported risk estimates (odds ratios [ORs], and RR) of cancer and measures of variability (SEs or 95% CIs from which these could be derived) were selected preferably. Primary papers were selected preferably where possible, but meta-analyses were not excluded.

3 RESULTS

The papers studied had a number of different classifications of dietary patterns. While some of the studies included less popular dietary patterns, including the traditional and the substitute patterns, three patterns were consistently found in at least most of the papers: Western, drinker and prudent. For this reason, we have focused on the literature on the three main dietary patterns. Other patterns mentioned in the

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chosen papers have been mentioned briefly in the final section of the results.

3.1 The Western Dietary Pattern

The Western dietary pattern is described as a "modern" diet, including a lot of processed foods. Though the specific elements may vary from study to study depending on the cultures of origin and the authors' research interests, most will be characterized by red meat and processed meats, eggs, refined grains. The Western dietary pattern may also include plenty of processed sugars, fried foods and potatoes, and low intakes of whole grains, fresh vegetables and fruits (Tseng 2000). The Western dietary pattern has shown an association with an increased risk for CRC.

A long study of CRC in Montevideo, Uruguay, spanning from 1996 to 2004, studied 610 cases, with 1220 controls from the same hospitals (Fawehinmi 2012). With the samples and controls divided into three dietary patterns for women (Western, prudent and drinker) and four for men (Western, prudent, drinker and traditional), the study found that the Western dietary pattern showed an Odds Ratio of 2.62 (95 % CI 1.36-5.08) for colon cancer in men, and 1.95 (95 % CI 1.00-3.78) in women. Rectal cancer was not found to be associated with the Western diet, which was defined as consisting of high quantities of total eggs, red meat and processed meats.

Table 1: Western dietary pattern.	T-1-1-	1.	MIT	1: - 4	
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Gender	Odds Ratio	95%CI*
Men	2.62	1.36-5.08
Women	1.95	1.00-3.78
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*CI confidence interval

A similar study running for 32 years did a followup of 3260 cases of CRC among health professionals across the US, comparing CRC risk associated with Western and prudent diets (Mehta 2017). Participants who had more of the Western dietary pattern showed an increased risk of CRC, while those who scored higher in prudent dietary patterns had a lower risk of CRC. The relative risk for CRC correlated with the Western diet was also found to have differences in anatomic subsites. Distal colon and rectal tumors had a relative risk of 1.55 (95% CI, 1.22-1.96) and 1.35 (95% CI, 1.03-1.77) respectively. Proximal colon cancers, in contrast, had an RR of 1.11 (95% CI, 0.91-1.35). Notably, this paper also studied the correlation between dietary patterns and different molecular subtypes of CRC. Though the findings still required further refining, the study found that the Western dietary pattern was also more strongly correlated with

BRAF- and KRAS-wildtype, and CIMPnegative/low tumors.

Table 2: The relative risk.

	95%CI*
1.55	1.22-1.96
1.35	1.03-1.77
1.11	0.91-1.35

*CI confidence interval

Fung et al. found that a Western diet consisting of large intakes of sweets and desserts, processed and red meats, refined grains and French fries reported a high relative risk for colon cancer, at 1.46 (95% CI, 0.97-2.19) (Giovannucci 2002). This paper studied 121,700 women between the ages of 30 and 55 across 11 states, over 12 years of follow-up. Similar to the aforementioned study by De Stefani et al. in Uruguay, this study found little to no significant correlation between the Western dietary pattern and rectal cancer. This paper reinforces the earlier study by providing evidence that the impact of the Western diet on relative CRC risk is generally the same, irrespective of sex.

Some studies have gone a step further in their characterizations of dietary patterns. For instance, Slattery et al. described the Western diet as containing a higher intake of dietary cholesterol and total energy, and a greater body mass (Slattery 1998). This diet was found to be correlated with a higher RR for colon cancer in both men and women. A meta-analysis of 40 studies investigating the effects of the Western diet also showed that this dietary pattern may increase the RR of CRC (Fung 2003). One study included an analysis of dietary patterns by the duration during which the participants partook in them. The results showed that the duration definitely matters (Song 2015). This study found that partaking in a Western dietary pattern over an extended period of time was associated with a higher RR for CRC, highlighting that the prevalent diet during adolescence has a longlasting effect, regardless of adult diet. After a CRC diagnosis, a higher indulgence in the Western diet further increases the risk of recurrence after treatment, and mortality.

3.2 The Drinker Dietary Pattern

The drinker dietary pattern, though not as extensively studied as the Western and prudent patterns, has also been studied and implicated in an increased relative risk for CRC. This pattern is characterized by high quantities of alcoholic beverages, and this is what most studies focus on. Some studies have suggested that the drinker dietary pattern may include poor nutritional intake, like Fawehinmi et al. that heavy and moderate drinkers consumed less favorable loadings of nutritious and healthy foods than nondrinkers (Feng 2017).

The drinker dietary pattern was consisted mainly of younger men who consumed wine, beer and hard liquors, and also smoked heavily in a study by De Stefani (Salaspuro 2009). This group showed a positive association with a higher RR for CRC. Though the sample of women under the drinker dietary pattern classification featured less intensive smokers, they also showed poor nutritional intake and cholesterol consumption, and mirrored the male sample in CRC risk. The Slattery et al. definition of the drinker pattern also included smokers, though this category featured less red meat and more poultry and fish in this study (Slattery 1998). The drinker pattern recorded a very weak positive association with colon cancer in men. The 'alcohol-consumption' pattern, as it was termed in a meta-analysis ty Feng et al. was reported to potentially increase the relative risk for CRC, regardless of gender (Fung 2003).

3.3 The Prudent Dietary Pattern

Although the description of the prudent dietary pattern is determined specifically by the authors of a paper for their study, there are general features that apply across the board in many studies. This diet features an abundance of fresh fruits and green vegetables, salads and carrots (Salaspuro 2007). Each of the studies discussed above has slightly different qualifiers of a "prudent" dietary pattern, but they are all built on the same basics as listed. These studies have one other thing in common: they all provide evidence that the prudent dietary pattern protects against colon and rectal cancers.

For the study in Montevideo, Uruguay, the prudent diet was described as having high intakes of dairy foods, white meat, total fruits and raw vegetables. This pattern was found to be strongly effective in preventing rectal cancer (Pietinen 1999). Mehta et al demonstrated that prudent dietary patterns, consisting of high quantities of whole grains, fruits, vegetables and fish, generally have a lower association with colon and rectal tumors, irrespective of molecular subtypes and anatomical subsites (Pöschl 2004). In Fung et al. prudent dietary patterns including the regular whole grains, fruits and vegetables plus poultry, legumes and fish, showed an inverse correlation with colon cancer, but showed little to no significant correlation with RR for rectal cancer in women (Cancer.org. 2021).

Slattery et al described the prudent dietary pattern as being associated with smaller body size, rigorous leisure physical activity and higher quantities of dietary folates and fibers (Pietinen 1999). This study included age variations in the subjects, and found that the prudent diet was correlated with a decreased RR for colon cancer, particularly in younger individuals. These results were further confirmed by a metaanalysis by Feng et al (Fung 2003), which showed that the 'healthy' dietary pattern, with the same features as the prudent dietary pattern, may reduce the RR for CRC. Song, Garrett and Chan showed that the prudent pattern is protective against CRC, especially when the diet is adhered to from adolescence (Song 2015). This study also showed that following a diagnosis of CRC, the prudent dietary pattern is recommended to prevent recurrence and to improve disease prognosis.

3.4 Other Dietary Patterns

Although the three dietary patterns discussed above are the most commonly studied in the literature, some studies include less common patterns. De Stefani et al studied the traditional dietary pattern but only in men (Salaspuro 2009). It was described as having high quantities of cooked vegetables, desserts, legumes and tubers. This diet shared many similarities with the Western diet, but was classed separately considering the geographical location and cultural background of the area under study. Most of the men who reported under the traditional pattern were poorly educated and lived in the rural areas of Uruguay. The traditional dietary pattern was found to have an inverse association with both colon and rectal cancers.

Slattery et al had five dietary patterns: prudent, drinker, Western, substituters and high fat/sugar dairy. The first three have been discussed above (Pietinen 1999). Substituters switched out butter, red meat, high fat dairy products and refined grains in favor of margarine, poultry, low fat dairy products and whole grains, respectively. This pattern is perceived as healthier than the Western pattern. However, this study showed that this substitution did not significantly reduce the RR for colon cancer. The high fat/sugar dairy pattern contained high quantities of yogurt and dairy products rich in fat and sugar. This dietary pattern was not studied for relative risk of colorectal cancer.

4 DISCUSSIONS

Most of the papers studied for this review found that

dietary patterns have an association with the relative risk for CRC in both men and women. The exception was Pietinen et al which studied the relative risk for CRC of different diet components rather than dietary patterns, and found that high intake of calcium, milk products and milk protein had an inverse correlation with the RR for CRC, while high intake of fat, dietary fiber, fried meats, vegetable and fruits had no significant association with risk for CRC (Pöschl 2004). The food components found to have no association with CRC risk cut across both the prudent and Western dietary patterns, by the general characterizations of both patterns. Extrapolating the results of this study to our model of dietary patterns, Pietinen et al. found that dietary patterns in general have no correlation to the relative risk of CRC, and rather it is specific foods, especially dairy products and other calcium-rich foods that have an impact on CRC relative risk.

The main tentative conclusion of this review is that the Western and drinker dietary patterns show a positive correlation with an increased relative risk for colon cancers, but this association is much less definite in rectal cancers.

This review highlights the differences in the constitutions of different dietary patterns, as well as the differences in classifications, to different researchers. Though these differences may seem subtle (the difference is usually only in a few food groups), when considered as forming a daily diet that spans decades of an individual's life, individual foods make a significant difference in the overall effect of a diet. This consideration thus has us wondering whether it is in fact effective to study the effect of broad dietary patterns rather than isolated foods.

Even so, the majority of the papers studied for this review showed that the prudent dietary pattern is the healthiest and the most protective, with the highest negative association with colorectal cancers, regardless of gender, age, molecular subtypes and anatomical subsites. The prudent dietary pattern notably contains fresh green vegetables (some papers specify that the green vegetables have to be eaten raw to qualify under the prudent pattern). Fresh green vegetables are high in dietary fiber. Fruits and cereals, which may also be indicated as part of this diet are also sources of fiber. It was demonstrated in a screening trial that participants who regularly consumed higher quantities of dietary fiber had a lower risk of colorectal adenomas (Mehta 2017). Further, the components of the prudent dietary pattern are also high in antioxidants, which would confer protection, not just from colorectal cancers, but from other cancers as well.

The Western dietary pattern, in all its versions in the papers studied for this review, included high loadings of processed meats and red meat, and it has been shown definitively to have an increased relative risk for CRC. These results are consistent with the findings of the International Agency for Research on Cancer (IARC) (Cancer.org. 2021), which reported that consumption of red meat and processed meats is mutagenic and carcinogenic to humans. Though red meat contains high quantities of important proteins and micronutrients like iron and vitamin B, it also contains haem iron which when broken down, forms N-nitroso-compounds (NOC) are released, which are carcinogenic. Meat processing and cooking can also result in the formation of NOC and polycyclic aromatic hydrocarbons (PAH), particularly with hightemperature preparations such as barbecuing or grilling. It is therefore no wonder that diets featuring high loadings of these meats would show a higher RR for CRC and other cancers (Aykan 2015).

The drinker dietary pattern has been consistently shown to increase the risk of CRC by the papers in this study, even though it is more consistently associated with colon cancers than with rectal cancers. These results are backed up by research that shows that alcohol consumption has a causal relationship with an increased risk of digestive system cancers, including those of the colon and rectum, and also of the breast in women (Bouvard 2015). The exact mechanism of the association of alcohol consumption and colorectal cancer is still under study. One epidemiological study suggested that this action is because alcohol affects the metabolism of dietary folates, where folates are thought to reduce the relative risk of CRC and other cancers (Kunzmann 2015). A more substantial explanation for the correlation between CRC and alcohol consumption is that ethanol metabolism releases acetaldehyde and reactive oxygen species (ROS). Acetaldehyde has been shown to be mutagenic and carcinogenic, and has been implicated as a common denominator in the development of many alimentary tract cancers (Salaspuro 2009). It binds to proteins and DNA and disrupts folate. Research has also shown that acetaldehyde can be produced by oral bacteria. The fact that the drinker dietary pattern is commonly characterized by moderate to heavy smoking may also be a factor in the results seen. Smoking is known to alter the flora of oral bacteria, which may impact the production of acetaldehyde (Pöschl 2004). Cigarettes also contain acetaldehyde (Salaspuro 2007).

5 CONCLUSIONS

The study of dietary patterns and their disease association has become popular as a way to better understand the impact of combining well studied and documented individual foods. The literature shows multiple classifications of dietary patterns, but the three most common are the "Western" diet, the "drinker" diet and the "prudent" diet. Of the three, the Western diet has consistently shown the highest positive association with an increased relative risk for CRC, though the association is stronger with colon cancers than with rectal cancers. This is presumably because of the high intake of carcinogenic meats, and the low intake of beneficial vitamins and antioxidants. The drinker dietary pattern has shown a less consistent association with an increased risk for CRC, but it has not shown a negative correlation in any of the studies reviewed in this paper. The prudent dietary pattern has consistently shown to be the healthiest, even when other patterns such as the substitute pattern are considered. This pattern provides high quantities of beneficial nutrients and antioxidant, and contains low quantities of carcinogenic foods. Even so, the vast differences in how each of these dietary patterns is characterized in the literature could be a potential avenue for confusion. The research shows that perhaps recommending an increase in some foods and a reduction of others may be more beneficial in creating guidelines for healthy living and the prevention of CRC, than recommending a larger dietary pattern whose details are left to interpretation.

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